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Submitted Electronically

Federal Coordinating Council on Comparative Effectiveness Research

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Re: Response to the Council's Request for Comments

Dear Secretary Sebelius and Distinguished Council Members:

Pfizer commends the Federal Coordinating Council's (FCC) commitment to transparency and public engagement by calling for stakeholder input on national priorities for comparative effectiveness research (CER), the types of investments that should be made in CER infrastructure, and the criteria that should be used to evaluate these different investment options.

Pfizer is the world's largest research-based biomedical and pharmaceutical company. We want to ensure that people everywhere have access to innovative medicines and quality healthcare by working in partnership with all stakeholders, such as patients, healthcare providers, managed care organizations, government bodies and non-governmental organizations. Pfizer supports scientifically sound research by sponsors, both private and public, to better compare the effectiveness of medical interventions, including pharmaceuticals.

Our objectives here are to: 1) emphasize the importance of developing a national priority-setting framework for CER and the key components to include in such a framework, 2) recommend an emphasis on further development of evidence-based methodological standards to guide the conduct and evaluation of CER, and 3) highlight important considerations in translating and disseminating CER findings effectively.

Developing a Priority-Setting Framework

We understand that Congress mandated the Council to prioritize and coordinate Federal efforts in CER. In order for the Council to fulfill this mandate effectively, we believe it is

critical the Council develop a transparent, fair, and meaningful priority-setting framework that ensures its investments serve the needs of its end users—patients and providers. In addition, the Council should define a set of principles to guide the specific steps it will take to ensure that the Federal government's CER investments have the greatest value to society.

The consideration of a priority-setting process for CER is not a new or unfamiliar concept. The Institute of Medicine (IOM) and leading academics have identified and evaluated the key components of a CER priority-setting process. In addition, domestic and international health technology assessment (HTA) and CER organizations have worked to implement such processes. Moreover, during the March 20, 2009 IOM priority-setting meeting and the Council's first listening session on April 14, 2009, members of the public called for an explicit priority-setting framework to identify and prioritize areas for funding.

Below we outline principles and components we believe are essential to developing a transparent, fair, and meaningful priority-setting process that can be fully accepted by a broad spectrum of healthcare stakeholders.

Build on an Existing Foundation

A 1992 report by the Institute of Medicine (IOM), titled "Setting Priorities for Health Technologies Assessment: A Model Practice," provides a solid foundation on which the Council can build to develop a process and the criteria for setting CER priorities.¹ The IOM report recommends four principles for the priority-setting process:²

1. **The values of the users of the research must be integrated into the priority-setting process.** In this case, the Council's processes and the output of those processes should reflect the needs and values of patients and physicians.
2. **The priority-setting process must consider the information needs of the user by conducting CER on the full spectrum of healthcare interventions used to manage conditions.** The importance of a broad CER scope is emphasized in the American Recovery and Reinvestment Act, which calls for the Department of Health and Human Services (HHS) to support research on "healthcare treatments and strategies." In the context of its overall research agenda, a federal CER program should look to improve the clinical return on overall healthcare expenditure by also examining financing structures (e.g., benefit designs), care management, and delivery systems. Research shows that poor healthcare delivery systems can impede patient access to effective treatments.³

¹ Donaldson MS, Sox HC, eds. *Setting Priorities for Health Technologies Assessment: A Model Process*. Washington, DC: National Academy Press; 1992.

² *Ibid*, p.3

³ McGlynn EA, Asch SM, Adams J, et al. "The quality of health care delivered to adults in the United States." *NEJM* 348 (2003):2635-2645.

The Council should adopt a meaningful approach to working with clinical and methodological experts, as well as patients, to identify how CER funding should be allocated. Without input from a range of clinical experts and patients, there is a risk that the selected investments will be less relevant to the needs of practicing physicians and their patients. In addition, in considering the specific conditions that merit CER funding, the Council should focus on areas where:

- a. There is the greatest burden of disease;
 - b. Overall healthcare spending is concentrated;
 - c. There is variation in the clinical practice of managing the condition; and
 - d. Current research is limited or evidence is not available.
3. **The priority-setting process must be efficient by seeking broad input at the outset, but also having a relatively simple mechanism to identify important research topics.** The Council must establish clear processes and rules, allowing for public input and transparency, for how it will identify topics and information for its priority-setting.
 4. **The priority-setting process must be sensitive to its political context; be objective, open, and fair; invite input from a broad spectrum of stakeholders; and present the logic of the process clearly and carefully to others.** The public and stakeholders need to understand the Council's rationale for how it prioritizes the public research investments.

Additional Recommendations

Additional recommendations the Council should consider as it establishes priorities for research include:

- » **Maintaining a transparent process in which methods are explicitly defined, consistently applied, and publicly available for comment:** In a recent paper describing a conceptual framework for HTA priority setting, Sibbald defines transparency as, "[...] knowing who is making the decision, how the decision will be made, and why the decisions were made."⁴ In keeping with President Obama's commitment to transparency, we suggest that the Council post on a publicly accessible website the following:
 - A schedule of all meetings – both those open and not open to the public – the Council is planning over the next year;
 - A document that outlines its priority-setting process, including principles, methodology and steps the Council will take to identify needed investments, and how it is planning to coordinate across federal agencies;
 - All public comments the Council receives on its activities and its publications, as well as its responses to those comments;

⁴ Sibbald SL, Singer PA, Upshur R, Martin DK. Priority setting: what constitutes success? A conceptual framework for successful priority setting. *BMC Health Services Research* 9:43 (2009).Sibbald

- A draft and final list of recommended areas for investment, including the rationale the Council used to identify them; and
 - Drafts of all government-sponsored CER reports and solicitation of public comment on these reports (e.g., technology assessments conducted by public and private HTA organizations with HHS' CER funds).
- » **Allowing for multiple points of engagement from a diverse group of stakeholders throughout the priority-setting process:** Sibbald asserts that decision makers should adopt multiple techniques to solicit stakeholder feedback, including roundtables, open forums, and administrative meetings.⁵ We commend the efforts that the Council has made thus far in hosting public listening sessions for stakeholders to voice their concerns and recommendations for federal CER. However, we recommend that the Council allow the public to engage with them at the following points: 1) prior to finalizing principles, methodology, and steps the Council will adopt to define investment priorities; 2) prior to finalizing the June 30th report to Congress; and 3) prior to finalizing any processes, investment decisions, or specific research studies.
- » **Ensuring the priority-setting process allows for meaningful input from patients and clinicians:** We support the recommendation provided by the National Working Group on Evidence-Based Healthcare issued in its policy paper of August 2008 that calls for greater patient engagement in defining a CER research agenda through the creation of a patient advisory body.⁶ The Council should establish a similar structure for practicing physicians in order to ensure their views are represented as well.

Pfizer encourages the Council to integrate the IOM's recommendations and the above considerations into its priority-setting process. Below we have provided a case study of acute myocardial infarction to illustrate the importance and interdependency of these components in ensuring an effective priority-setting process to define where needed investments should be made.

Applying a Framework to Establish Priorities in CER – A Case Study of Acute Myocardial Infarction (AMI)

High Prevalence, High Cost

ST-elevation myocardial infarction (STEMI), also known as acute myocardial infarction (AMI) or heart attack, is the leading cause of death in the United States. The estimated annual incidence of heart attacks is 600,000 new attacks and 320,000 recurrent attacks annually. The total direct and indirect cost of coronary heart disease in the United States for 2008 is estimated at \$156.4 billion.⁷ This figure includes health expenditures (e.g., direct costs,

⁵ Sibbald

⁶ National Working Group on Evidence-Based Healthcare:
<http://www.evidencebasedhealthcare.org/download.cfm?DownloadFile=9DE777DF-1372-4D20-C85E4F48846514FD>

⁷ Heart Disease and Stroke Statistics — 2008 Update, American Heart Association

which includes the cost of physicians and other professionals, hospital and nursing home services, medications, home healthcare and other medical durables) and lost productivity resulting from morbidity and mortality (i.e., indirect costs).

A number of treatments have proven effective in reducing mortality among AMI patients, including timely reperfusion, beta-blockers, primary percutaneous coronary intervention (PCI), aspirin, and ACE inhibitors. However, studies show that even among ideal candidates for these treatments, these therapies are underutilized.

Developing the Evidence-Base for AMI

Treatment for a heart attack requires a multi-disciplinary team of professionals: emergency medicine technicians and emergency room doctors; cardiologists, specifically interventional cardiologists; family doctors; and nurses. However, not all of these professions are represented at the table when clinical guidelines are written.

The current or past guidelines for STEMI elucidate several interventional, pharmacological and non-pharmacological therapies to save and improve the lives of patients who experience a heart attack. Depending on the complexity and severity of the patient's condition at presentation, treatment options delivered range from primary PCI and coronary artery bypass graft (CABG) to aspirin, fibrinolytics, and beta-blockers. Given the wide range of options and the diverse backgrounds of the providers, definitive standards are needed to determine when it is appropriate to use these therapies.

In 2004, the American College of Cardiology (ACC) and American Heart Association (AHA) released joint guidelines for treating STEMI. Since then, new clinical trial data on a variety of aspects of STEMI care have emerged, prompting ACC/AHA to update portions of the 2004 joint guidelines in late 2007. The guidelines are written in collaboration with the American Academy of Family Physicians (AAFP) and the Canadian Cardiovascular Society (CCS) and include a rigorous peer-review process to allow experts in the field to comment on the recommendations before they are published.

However, a recent study published in the February 2009 issue of *JAMA* shows that the recommendations issued in the current ACC/AHA clinical practice guidelines are largely developed from lower levels of evidence or expert opinion.⁸ Many clinicians report that their disagreement or skepticism of the strength of the evidence behind clinical guidelines is one of the reasons why they often do not follow certain guidelines.⁹ Therefore, strengthening the evidence behind clinical guidelines may improve guideline adherence in addition to the quality of the guideline itself.

⁸ Tricoci, P, Allen, J, et al. "Scientific Evidence Underlying the ACC/AHA Clinical Practice Guidelines." *JAMA* 301, no.8 (2009): 831-841.

⁹ Kalassian, K, et al. "Translating Research Evidence into Clinical Practice: New Challenges for Critical Care." *Critical Care* 6, no.1 (2002): 11-14.

Filling Research Gaps

Increased use of data from nationally recognized data registries and CER are needed to answer questions around routine clinical practice and to fill existing gaps in the clinical guidelines. The ACC and AHA have now incorporated into their guideline writing process a research priorities agenda based on existing evidence gaps.¹⁰ The ACC has six registries collecting information on cardiovascular patients dealing with pediatric and congenital heart disease, ICD implantations, diagnostic cardiac catheterizations and PCI, acute coronary syndromes, carotid stents and endarterectomy procedures and practice-based cardiology. However, to date, the ACC has not utilized its registries to inform the clinical guidelines it writes.

In the past, the ACC has worked with external stakeholders, such as the Centers for Medicare and Medicaid Services (CMS), industry and other medical specialty societies to sponsor and/or inform the key components when developing its registries. Usually these funds provide the necessary start-up costs for the registry and the fees associated with maintaining the registry are passed on to the participants. Additional funding streams are needed to maintain and enhance current ACC registries that address heart attack patients (e.g., ACTION and CathPCI) as well as a process to mine and the methods to analyze data from the registries to better inform the clinical guidelines and to fill research gaps.

In this context, applying a priority-setting framework as outlined earlier would result in the following activities for the Council:

- Prioritize conditions, such as AMI, to provide new investments in research and infrastructure;
- Examine the broad range of interventions used in the early diagnosis and treatment of AMI, including catheterization, angioplasty, PET scans, defibrillation, use of coronary care unit, and thrombolytics;
- Assess the effectiveness of different frameworks for measuring the quality of AMI care, such as the episode-of-care framework developed by the National Quality Forum for AMI;
- Develop meaningful partnerships with medical specialty societies, patient advocacy groups, and other clinical experts, such as the ACC and AHA to identify areas where there is a paucity of evidence to guide clinical practice;
- Partner with ACC, payers, the pharmaceutical industry and other interested parties to expand ways to incorporate other data streams into evidence;
- Address clinical questions that mirror the real choices patients and physicians are making, such as how to minimize risk of adverse events, re-occurrences of acute events, and co-morbid conditions, (e.g., stroke); and
- Examine treatment and service provisions under differing healthcare systems to assess the impact on effectiveness and quality of

¹⁰ Ibid

alternative health service approaches related to care management, organization, delivery, and financing.

Methodological Standards

Pfizer encourages the Council to recommend the development of evidence-based methodological standards to guide clinical CER. The need to make optimal use of evidence from RCTs, to develop evidence from non-RCT sources, and to combine evidence from all reliable sources, necessitates continued and more intensively focused methodological development in these areas.

Senators Baucus and Conrad's *Comparative Effectiveness Research Act of 2008* (S.3408) and the options paper recently developed by the Senate Finance Committee¹¹ both recognize the need for establishing a methodology committee to develop scientifically based methodological standards for clinical CER. However, within the ARRA, there is no specific mandate for methods and standards to be developed.

Examples of areas where methodological standards are needed include the following:

1. Development of novel methods/designs for bias reduction for non-randomized studies;
2. Improving methods for incorporating research design quality measures in meta-analysis;
3. Guidance for clinical practitioners on Bayesian versus frequentist inference in CER and meta-analysis;
4. Novel methods for incorporating patient preferences into CER;
5. Methods for combining data from varied sources (e.g., claims, registries, EHRs);
6. Methods that improve our ability to reconcile results from RCT-based and non-RCT-based studies;
7. More finely tuned methods for evaluating the benefit-risk tradeoffs between treatments; and
8. Methods for evaluating the optimal set of treatment options that should be made readily available to patient populations to achieve best overall health outcomes.

While there are certainly some relevant methods and standards in existence, both from individual authors and from scientific associations (e.g., International Society for Pharmacoeconomics and Outcomes Research (ISPOR)), generally these areas lack the consensus approach to methods needed to be convincing to decision makers. Thus, in designing and evaluating methods for CER needed to inform real-world decisions, we recommend including researchers/representatives from selected decision-making bodies, such as ISPOR, the Society for Medical Decision Making and the American Statistical Association, particularly its Health Policy Statistics section.

Translation and Dissemination of CER into Practice

A critical element of CER is ensuring that research findings reach the point of care where clinicians, together with patients, can use the information to make informed treatment decisions. According to the 1992 IOM report, "The results of the [priority-

¹¹ Read the options paper, "Transforming the Health Care Delivery System: Proposals to Improve Patient Care and Reduce Health Care Costs," at <http://finance.senate.gov>.

setting] process should be consistent with the needs of the user and should provide information in the form that is most useful.”¹²

As articulated at the IOM Roundtable meeting “Learning What Works” held in July 2008, the central challenge of CER lies not only in establishing the infrastructure to conduct research, but also in the translation of that research into clinical practice. Research on the best decision-making tools to translate research into improvements in healthcare and public policy is imperative. It is important that such decision-making tools effectively communicate which treatments work best, allow for patient heterogeneity and other intervening variables, and give providers the flexibility to tailor the appropriate course of treatment for each patient based on individual patient preferences and clinical circumstances. Using decision-making tools that fail to recognize such variations among patients can interfere with the ability of providers to deliver the most appropriate care for each patient and lead to suboptimal outcomes and increased healthcare costs. It may also lead to inaccuracies in performance assessment in that a clinician may legitimately choose to not use the recommendation produced by the decision-making tool due to patient-specific needs.

As most recently illustrated in a public opinion poll designed by National Public Radio, the Henry J. Kaiser Family Foundation, and the Harvard School of Public Health, the majority of Americans believe they should have access to a variety of treatment options, regardless of whether the treatment is costly and has not been shown to be the most effective response to a health problem.¹³ In brief, while Americans want to have robust information to inform their decisions and their provider’s decisions, they want to have the flexibility to tailor the appropriate course of treatment to their individual preferences and clinical circumstances.

Pfizer encourages the Council to partner with relevant professional societies to make sure research findings are effectively translated into practice. Pfizer, moreover, recommends the Council supports research on what decision-support tools effectively communicate what treatments work best, allow for patient heterogeneity, and give providers the flexibility to tailor treatments to specific patient needs.

Below we have grouped our aforementioned recommendations to respond explicitly to the questions you requested comments on in an April 12 Federal Register notice:¹⁴

1. What types of investments in infrastructure for CER should the Coordinating Council consider?

Pfizer recommends the Council:

- i. Develop a transparent, fair, and meaningful priority-setting framework that ensures its investments serve the needs of its end users—patients and providers
- ii. Fund research on what decision support tools effectively communicate which treatments work best, allow for patient heterogeneity, and give providers the flexibility to tailor treatments to specific patients needs.

¹² Donaldson MS, Sox HC, eds.

¹³ Survey and results available at <http://www.kff.org/kaiserpolls/posr042209pkg.cfm>.

¹⁴ <http://mannen.typepad.com/files/4-09-fed-coordinating-council.pdf>

- iii. Recommend the development of evidence-based methodological standards to guide clinical CER. We recommend including researchers/representatives from selected decision-making bodies, such as ISPOR and ASA.
 - iv. Coordinate CER infrastructure efforts with the federal government efforts to promote the use of health information technology (HIT). With the enactment of ARRA, there are considerable efforts underway to improve the nation's HIT infrastructure. In many regards, infrastructure to improve HIT and CER are complementary. As such, the Council should ensure coordination of efforts and complementary efficiencies in how CER and HIT funds are managed. In particular, we recommend that efforts to drive common data standards through HIT initiatives be developed with CER applications in mind. In addition, we recommend that the FCC support the development of common clinical research data collection standards. Such standards will help enable the aggregated analysis of data from RCTs and integration with other clinical data derived from delivery system data sources.
2. What criteria should the Coordinating Council consider when evaluating different investment options?

Pfizer recommends the Council:

- i. In considering the specific conditions that merit CER funding, focus on areas where there is the greatest burden of disease; overall healthcare spending is concentrated; there is variation in the clinical practice of managing the condition; and current research is limited or evidence is not available. The Council must also consider the full spectrum of healthcare interventions used to manage conditions.
 - ii. Develop a meaningful approach to working with clinical and methodological experts, as well as patients and providers, to identify how CER funding should be allocated.
 - iii. Ensure that the criteria that will be used to evaluate investment options are available for public comment before use and are transparently applied once finalized.
3. What Federal government activities in the area of CER should the Coordinating Council focus its attention on?

Pfizer recommends the Council:

- i. Define a set of principles to guide the specific steps it will take to ensure the federal government's CER investments have the greatest value to society.
 - ii. Engage in the infrastructure activities outlined above in question 1.
4. What steps should the Coordinating Council consider to help ensure that public- and private-sector efforts in the area of CER are mutually supportive?

Pfizer recommends the Council:

- i. Seek public input as it develops its June 30th Report to Congress
 - ii. Partner with relevant professional societies to make sure research findings are effectively translated into practice.

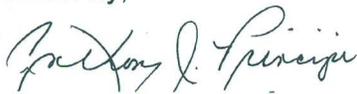
- iii. Build on existing research done by IOM in 1992 on developing a priority-setting framework.
- iv. Develop meaningful partnerships with medical specialty societies, patient advocacy groups, and other clinical experts to identify areas where there is a paucity of evidence to guide clinical practice. These partnerships should be used to highlight where additional funding streams are needed so that these evidence gaps can be filled.

5. What information on the Coordinating Council's activities would be most useful?

- » Pfizer recommends the Council post the following on a publicly Accessible website:
- A schedule of all meetings – both those open and not open to the public – the Council is planning over the next year;
 - A document that outlines its priority-setting process, including principles, methodology and steps the Council will take to identify needed investments, and how it is planning to coordinate across federal agencies;
 - All public comments the Council receives on its activities and its publications, as well as its responses to those comments;
 - A draft and final list of recommended areas for investment, including the rationale the Council used to identify them; and
 - Drafts of all government-sponsored CER reports and solicitation of public comment on these reports (e.g., technology assessments conducted by public and private HTA organizations with HHS' CER funds).

Pfizer appreciates the opportunity to comment on the Council's priority-setting process. We welcome an opportunity to meet with the Council to discuss our comments and recommendations in further detail. Please feel free to contact me or Eleanor M. Perfetto, Ph.D. at 202-783-7070 with any questions you may have.

Sincerely,



Anthony Principi