Response to recent media reports about IMMPACT and ACTTION

Robert H. Dworkin, PhD, and Dennis C. Turk, PhD

Recent media reports have misinterpreted the purpose and significance of two important scientific initiatives with which we have worked closely. These projects were undertaken to facilitate scientific research and encourage collaboration among all interested parties for the purpose of improving pain treatment. The focus of these efforts has been the research methods used in clinical trials and their sensitivity and validity. These projects were not intended to influence federal policy in inappropriate ways, and they did not result in recommendations about approval, administration, or scheduling of drugs. These projects were conducted openly and transparently among a large group of stakeholders. They were broadly publicized, and their principal work has been published and made widely available.

The first initiative, known as the Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials (IMMPACT), was a multidisciplinary consortium formed to develop consensus reviews and recommendations for improving the design, execution, analysis, and interpretation of clinical trials of treatments for pain. Participants typically included 30-50 physicians, nurses, biostatisticians, research psychologists, clinical pharmacologists, epidemiologists, and patients; these individuals represented academia as well as the Food and Drug Administration (FDA), the National Institutes of Health (NIH), the Veterans Administration (VA), patient advocacy groups, and industry. They came from institutions and organizations across the United States and from many other countries.

One or two meetings of IMMPACT were held every year from 2002 to 2011. There was extensive preparation for each meeting, including development of agendas, background research, and identifying and enlisting participants who had particular expertise regarding the specific topics to be considered. These meetings resulted in multiple consensus recommendations, systematic reviews, and research studies that have informed the design of pain clinical trials (see www.immpact.org). These peer-reviewed articles have been cited more than 1,400 times in over 400 different biomedical journals across a diverse range of medical specialties.

In 2011, IMMPACT was folded into the Analgesic, Anesthetic, and Addiction Clinical Trial Translations, Innovations, Opportunities, and Networks (ACTTION) public-private partnership with the FDA. The ACTTION Executive Committee includes representatives from academia, national and international professional societies, government regulatory and research agencies, patient advocacy groups, and industry. ACTTION has sponsored a diverse range of research studies, consensus meetings, and other activities (see www.acttion.org). Its primary objective is to make information available to improve the design and performance of clinical trials so as to accelerate the development of safer and more effective treatments for pain.

IMMPACT and ACTTION activities have not been directed at specific medications or pain treatments. Instead, the focus is on clinical trial methods and related issues. It must be emphasized that these activities have never involved setting policy, making policy recommendations, providing regulatory guidance, or developing treatment guidelines. Moreover, they have never included conducting clinical trials of treatment efficacy or safety. Indeed, IMMPACT and ACTTION recommendations are nothing but suggestions, which are as evidence-based as possible, and that investigators -- whether from academia, government, or industry – can choose to consider, follow, or ignore.

The impetus for the recent media attention to IMMPACT apparently relates to concerns over the safety and potential abuse and overuse of opioid analgesics. Questions also have been raised about whether IMMPACT and ACTTION represent improper ways to influence FDA policy regarding the regulation and approval of opioid analgesics. The FDA's efforts devoted to the safety and efficacy of opioid analgesics have been separate from the principal objectives of IMMPACT and ACTTION, which have focused on improving clinical trial research methods for pain treatments, not on the efficacy or safety of specific pain medications. As with most scientific endeavors, there have been topics for which there have been differences of opinion. The nature of IMMPACT and ACTTION encourages open discussion of areas of disagreement for a fuller understanding of all issues and perspectives. To reiterate, the major thrust of IMMPACT and ACTTION has been to facilitate the development of improved medications and other pain therapies that have greater effectiveness and better safety than existing treatments.

Concerns also have been raised about seeking industry support for the activities of IMMPACT and ACTTION, and that industry representatives had the opportunity to meet with FDA personnel and perhaps influence them in private. These concerns are misplaced for several reasons.

First, typically 2-5 scientists from different FDA divisions would attend IMMPACT and ACTTION meetings. This made it possible for FDA scientific personnel to observe presentations, participate in discussions, and contribute to publications. The percentage of individuals from industry at each meeting was never more than one-third, and these individuals had MD, PhD, or other advanced degrees and represented the research and clinical development divisions of their companies. Discussion of company-specific products or issues was not permitted, and the participation of multiple sponsoring companies prevented any one company from dominating the discussion.

The purpose of having most IMMPACT and ACTTION meetings limited to specific invitees largely was practical. This made it possible to assemble an international group of scientists with the greatest expertise, to keep the number of participants (50 or fewer) compatible with in-depth discussions, and to efficiently and effectively develop consensus recommendations regarding best practices for research. The meetings consisted of highly informative presentations and interactive discussions about state-of-the-art research issues, and all participants were free to discuss the meeting content with whomever they wished. As soon as possible following IMMPACT meetings, background materials, meeting presentations, industry sponsors, and names of all participants were placed on the IMMPACT website. Each meeting resulted in at least one published article describing the meeting literature reviews, discussions, and recommendations.

Financial support for IMMPACT was sought from pharmaceutical and device manufacturers with interest in any type of pain treatment. These funds were used to defray all the costs of the IMMPACT meetings and related expenses, including systematic reviews and research studies, as well as to provide relatively modest honoraria to academic participants and cover their travel expenses. In addition, this financial support resulted in contributions to research accounts that compensated post-doctoral fellows and also provided other research-related expenses and reasonable compensation to Drs. Dworkin and Turk for the time and effort they devoted to IMMPACT. Industry sponsors that supported IMMPACT had no authority over the meeting topics, agenda, or speakers, or how the funds were distributed, and such funds had no influence on public officials. Funding decisions were implemented consistent with grant administration practices specifically applicable to each of these initiatives. No honoraria were provided to any

FDA or other government employees. ACTTION has been financially supported by a 1-year contract and 5-year research grant from FDA as well as by industry sponsorship. These funds have been used to cover a portion of the academic effort of Drs. Dworkin and Turk but not any extra compensation for them or any support for non-ACTTION activities.

We are proud of the work that has been done to date by IMMPACT and ACTTION and all of their participants. These initiatives have been successful because of the hard work, dedication, and commitment of an extraordinarily talented group of scientists. We believe there is great benefit in having fostered improved collaboration and communication among government, academic groups, industry, and patient advocates interested in improving serious public health problems. This work has received broad acclaim, with the Institute of Medicine's influential report on "Relieving Pain in America" emphasizing that "One particularly effective collaboration over the past decade has been IMMPACT…, which has yielded multiple consensus reports designed to foster improvements in clinical trial design and execution and in interpretation of pain treatment studies… Although the goals and objectives of IMMPACT and ACTTION relate directly to promoting the development of analgesics, their indirect effect has been to promote knowledge and consensus on a broad array of methodological, measurement, and trial design issues relevant to research more broadly" (2011, p. 246). We have every confidence that these collective efforts will result in improved ways to treat pain and thus stand to benefit millions of people.

Institute of Medicine (IOM). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington, DC: The National Academies Press, 2011.