

ADVANCES IN DRUG DEVELOPMENT

Current Developments in Oncology Drug Research

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The FDA's New Oncology Office

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H&O Is this the first oncology office at the US Food and Drug Administration?

RP Yes. Previously, oncology drug review was dispersed in several divisions and offices within the Center for Drug Evaluation and Research. The new Office of Oncology Drug Products will have 3 divisions: the Oncology Drug Division, which I headed prior to my new role, reviews oncology drugs and chemoprevention agents; a separate division reviews biologic agents; and a third division will review diagnostic imaging products and hematology products. The Radioactive Drug Research Committee Program will be administratively located in the new oncology office. In addition, an “oncology program” will be located in this new office. This program is aimed at coordinating the oncology activities both within the US Food and Drug Administration (FDA) and with our external stakeholders—commercial sponsors, patients and advocacy groups, professional organizations, academic investigators, and other governmental agencies, such as the National Cancer Institute and Center for Medicare and Medicaid Services. We are also devoting additional resources to our pediatric oncology program. Pediatric oncologist Dr. Karen Weiss, the deputy director of our Office, will be heading this effort.

H&O What are the goals of the new office?

RP One goal is to provide consistency in the review of oncology products, including those being reviewed under INDs (Investigational New Drugs), NDAs (New Drug Applications) and BLAs (Biologic Licensing Applications). Meetings attended by the review staffs of all oncology divisions will discuss applications and advice given to sponsors to ensure consistency. Guidelines that clearly outline practices will be formulated. The new office will

have oversight in coordinating reviews and training of medical officers and nonclinical reviewers. The combined resources of the 2 oncology divisions (drugs and biologics) will provide greater staffing flexibility—important in allocating necessary resources to priority reviews.

Another goal is to foster and enhance the career development of the medical oncologists and other scientific reviewers employed in the office. We have emphasized greater collaboration with the American Society of Clinical Oncology (ASCO) and the American Association for Cancer Research (AACR) in developing programs in oncology drug and biologic development to promote the career development of our review staff.

Additional resources will be allocated to the Office of Oncology Drug Products to enhance our efforts at improving transparency of our review process. These efforts will be coordinated by the oncology program within the new office. We want the American public to have a clear understanding of our regulatory principles and actions. To accomplish this goal we have included patients on our advisory committees, developed a patient advisory program, and attempted to improve communication through publication of our reviews in oncology journals. We have also increased our participation in national and international oncology meetings.

Another goal is to enhance our communication within the international regulatory community—specifically our regulatory colleagues in the European Medicines Agency (EMA), Japan, Canada, and Australia. We have been having annual meetings of oncology drug regulators and plan to expand these activities to monthly teleconferences with the EMA to discuss regulatory principles and specific products.

H&O In what way will the office expedite reviews of new drugs?

RP We are anticipating increasing our staff to review oncology products. In addition, the inclusion of both oncology divisions in one office structure will provide staffing flexibility in assigning IND and NDA reviews. These efforts will result in expediting the completion of our regulatory work without comprising quality

H&O What aspects of the drug review process have been inconsistent?

RP We need to ensure that consistent advice is given to investigators and sponsors. This includes advice on clinical trial designs, endpoints used in clinical trials, number of trials needed to support an indication, and the selection of applications chosen for discussion at meetings of the Oncology Drug Advisory Committee (ODAC). Since my arrival at the FDA, we have incorporated a greater use of “special protocol assessments”—a protocol review conducted by the oncology divisions prior to initiation of registration trials. Special protocol assessments ensure agreement between sponsors and the FDA. This agreement between the FDA and sponsors prior to the initiation of a trial will reduce inconsistencies and misunderstandings.

H&O Will the office be considering the use of surrogate endpoints in clinical trial design and evaluation?

RP Several initiatives are underway examining surrogate endpoints and their use in oncology registration trials. We will continue initiatives that were started several years ago. The FDA has been working with AACR, ASCO, and the American Society of Hematology on a series of workshops to examine endpoints used in clinical trials. This information is then used to obtain advice from the ODAC on clinical trial design issues and endpoints.

We have been working on a guidance document dealing with oncology clinical trial designs and endpoints. This guidance will be finalized in the upcoming months.

H&O Accelerated approval has led to challenges regarding the promised completion of phase IV trials. How will the new office handle this issue?

RP Accelerated approval allows the approval of a drug on the basis of a surrogate endpoint “reasonably likely” to predict clinical benefit in life-threatening diseases. The drug should be an advantage over available therapy. There is a requirement that subsequent trials (phase IV trials) be performed that demonstrate clinical benefit—usually considered a overall survival advantage or symptom amelioration associated with the new drug. These trials should be completed with due diligence after the approval of the drug.

In March 2003 we conducted an ODAC meeting to review these phase IV studies. After this meeting, we recommended that sponsors discuss development plans of phase IV studies prior to any accelerated approval. There should be a well-conceived comprehensive drug development plan that includes trials for accelerated approval and

plans for subsequent trials to demonstrate clinical benefit. Approval of a drug and its subsequent commercial availability may have profound effects on the completion of phase IV trials. Hence, sponsors should have early discussions with the FDA on the design, conduct, and analysis of confirmatory studies. We plan on reviewing the accelerated approval program and phase IV commitments in future ODAC meetings.

H&O How will this new office affect the community-based clinician?

RP We want to have a transparent process. Community clinicians need to have a clear understanding of our public health care mission. This includes our rationale for approving drugs, safety concerns for investigational drugs, and postmarketing safety concerns. We plan on providing this transparency by greater participation of our review staff in national and regional medical meetings, published review articles of our drug approval, and articles regarding regulatory science.

H&O In what ways is this new office in line with trends in oncology drug development?

RP In creating this new office, the FDA acknowledged that oncology is a rapidly evolving discipline that needs an expert review staff who will have a continuous dialogue with oncologists, clinical researchers, basic scientists, and patients. We are working on the evolving fields of pharmacogenomics, chemoprevention, and biomarker discovery and validation with both our internal staff and external experts from academia, pharmaceutical and biotechnology sponsors, and government.

Suggested Reading

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