**Food and Drug Administration**
**Center for Drug Evaluation and Research**
ACS Building, 5630 Fishers Lane, Rockville, MD

# Summary Minutes of the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee October 17, 2002

***Members Present***

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| Jody Pelusi, R.N., Ph.D. | Donna Przepiorka, M.D., Ph.D. | Gregory Reaman, M.D. |

***Consultants***

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| Victor Santana, M.D. | Alice Ettinger, R.N. | Jerry Finklestein, M.D. |
| Patrick C Reynolds, M.D. | Robert Nelson, M.D., Ph.D. | Ruth Hoffman (patient rep.) |
| Peter Adamson, M.D. | Susan Weiner, Ph.D. (patient rep.) | |

***Guests***

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| Dave Poplack, M.D. | Malcolm Smith, M.D. | Edward Sausville, M.D. |
| Barry Anderson, M.D. | Bruce Morland, M.D. | Joachim Boos, M.D. |
| Peter Houghton, M.D. | Susan Blaney, M.D. | Eric Kodish, M.D. |

***Industry Guest Attendees***

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| Judith Ochs, M.D., Astra Zeneca | Anne Hagey, M.D., Abbott | David Emanuel, M.D., Pharmacia |
| Steven Weitman, M.D., Ilex Corp | Wayne Rackoff, M.D., Janssen *(On Phone)* | |

***FDA Participants***

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| Richard Pazdur, M.D. | Joseph Gootenberg, M.D. | Steven Hirschfeld, M.D. |

These summary minutes for the October 17, 2002 meeting of the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee were approved on October 31, 2002.

I certify that I attended the October 17, 2002 meeting of the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee, and that these minutes accurately reflect what transpired.

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Thomas H. Perez, M.P.H., R.Ph.
Executive Secretary

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Victor Santana, M.D., Chair
Chair

The Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee, of the Food and Drug Administration, Center for Drug Evaluation and Research met October 17, 2002 at the FDA's Advisors and Consultant Staff conference facility at 5630 Fishers Lane, Rockville, MD

The Committee discussed the timing of the initiation of pediatric oncology clinical studies in a drug development program. The input from this meeting will be used in developing FDA policy to the application of the Pediatric Rule and the issuance of Written Requests under the Best Pharmaceuticals for Children Act.

The Committee had received a briefing document from the FDA.

There were approximately 40 persons in the audience. The meeting was called to order at 8:25 a.m. by the Chair, Victor Santana, M.D. The Committee members and discussants introduced themselves. Thomas H. Perez, Executive Secretary of the Pediatric Oncology Subcommittee of the Oncologic Drugs Advisory Committee read the Meeting Statement. A welcome, and opening comments were provided by Richard Pazdur, M.D., Director, Division of Oncology Drug Products and Steven Hirschfeld, M.D., Ph.D., who provided the background and the charge to the committee.

The scheduled presentations began at 8:50 a.m. and proceeded as follows.

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| Preclinical Models: What can they tell us | Peter Houghton, Ph.D. |
| Applying Preclinical Data to Clinical Studies | Edward Sausville, M.D. |
| Applying Preclinical Data to Clinical Studies | C. Patrick Reynolds, M.D. |
| Committee Discussion | |

*Current Practice*

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| Children's Oncology Group Perspective | Peter Adamson, M.D. |
| Industry Perspective | Steve Weitman, M.D. |
| European Perspective | Bruce Morland, M.D. |
| European Perspective | Joachim Boos, M.D. |
| Committee Discussion | |

The Committee paused for a brief Break at 11:30 a.m. and reconvened at 11:40 with the following topics.

*Identifying & Overcoming Barriers:*

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| Children's Oncology Group Perspective | Gregory Reaman, M.D. |
| National Cancer Institute Perspective | Barry Anderson, M.D. Ph.D. |
| Children's Hospital & Specialty Group Perspective | Susan Blaney, M.D. |
| Committee Discussion | |

At 12:35 p.m. the Committee paused for Lunch, and reconvened at 1:15 with the Open Public Hearing. There was one presenter who represented Immuno Medics, and spoke for three minutes. The committee then heard from the remaining scheduled presenters, who continued on the topic of Identifying & Overcoming Barriers.

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| Industry Perspective | David Emanuel, M.D. |

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| Industry Perspective | Wayne Rackoff, M.D. |
| Patient & Family Perspective | Ruth Hoffman |
| Committee Discussion | |

The Committee began its deliberations of the questions to the Panel at 2:15 p.m., and the meeting was adjourned at 4 p.m.

The Committee discussed the following questions. Transcripts of the meeting will be placed on the web when they become available, in approximately 2 to 3 weeks.

**Questions for the Committee**

1. Should adult safety studies precede the initiation of pediatric oncology clinical studies?

   *The Committee noted that there is no single answer to the question. As a general practice, an adult Phase I study should precede pediatric oncology clinical studies in order to determine preliminary safety and dosing information. There may be an exception for some drugs that may be exclusively developed in pediatrics. The committee acknowledged that current preclinical testing may not be able to identify about 1/3 of clinical toxicity; however, the development of newer preclinical models may have better correlation with both activity and toxicity. It may be possible with predictive preclinical data of sufficient scope and plausibility to begin clinical studies directly with pediatric patients, particularly if the planned indication is a pediatric tumor type, and there is a reasonable expectation of clinical benefit in relation to a potential risk.*

2. Should demonstration of activity in any adult tumor precede pediatric oncology clinical studies?

   *No. Demonstration of activity is generally expected at the end of Phase II, but demonstration of activity earlier in the process is a factor to consider if positive results are obtained that may help to prioritize new agents for pediatric clinical studies.*

3. Should activity in similar or related tumors in adults precede pediatric oncology clinical studies?

   *No, but results of adult studies demonstrating some activity may help to prioritize new agents for pediatric clinical studies.*

4. On what basis can pediatric oncology clinical studies proceed if no activity is shown in adult studies?

   *If there is biological plausibility, some expectation of benefit, a reasonable expectation of safety, and an available drug supply studies may proceed. Biological plausibility would be determined by preclinical support.*

5. What would the ideal situation be?

   *See the answer to question 7.*

6. Potential development plans for new cancer therapies could include combined adult and pediatric studies, separate but simultaneous adult and pediatric studies with continuos information sharing, sequential adult and pediatric studies with information sharing, or completely independent programs.

What the potential advantages and drawback of coordinating adult and pediatric early clinical development?

*The committee noted that there is no justification for completely independent programs and that once a pediatric program is initiated there should be at a minimum mutual information sharing between both development programs. The advantages are numerous and include more rapid development of therapies for children with cancer, greater understanding of the potential uses of a product, and a more efficient overall development program.*

7. What should the FDA adopt as a general recommendation regarding the timing of the initiation of pediatric oncology clinical studies in a drug development program?

*As a general position, pediatric oncology clinical studies should immediately follow the completion of adult phase I studies, because adult Phase I study usually precede pediatric oncology clinical studies in order to determine preliminary safety and dosing information. The information that would justify initiating pediatric oncology clinical studies are biologic plausibility, sufficient information to choose an appropriate starting dose, an expectation of benefit and a reasonable expectation of safety. Case by case determinations can be made on the basis of the type of agent, the mechanism of action, what is known about the safety profile, and the potential indication.*