FOOD AND DRUG ADMINISTRATION (FDA)
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
Antiviral Drugs Advisory Committee
Hilton Washington, DC/Silver Spring
December 2, 2008
OPEN Session

The Antiviral Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on December 2, 2008 at the Hilton Hotel, Washington DC/Silver Spring, the Ballrooms, 8727 Colesville Road, Silver Spring, Maryland. Prior to the meeting, the members and the invited consultants had been provided the background material from the FDA. The meeting was called to order by Ian McGowan, M.D., Ph.D (Chair); the conflict of interest statement was read into the record by Paul Tran, R.Ph. (Designated Federal Official). There were approximately 200 persons in attendance. There were 3 speakers for the Open Public Hearing sessions.

Attendance:

Antiviral Drugs Advisory Committee Members Present (Voting):
Ian McGowan, M.D., Ph.D, FRCP, Peter Havens, M.D., Marshall Glesby, M.D., Ph.D, Patrick Clay, Pharm.D., Amneris Luque, M.D.

Antiviral Drugs Advisory Committee Members Present (Non-voting):
Joseph Camardo, M.D. (Industry Representative)

Arthritis Advisory Committee Member (Voting)
Diane Aronson, B.S.

Special Government Employee Consultants Present (Voting):
Carolyn Kercsmar, M.D., George Ferry, M.D., Colin Parrish, Ph.D., John Burke III (Patient Representative).

Regular Government Employee Present (Voting):
Larry Anderson, M.D., CAPT Louisa Chapman, M.D., M.S.P.H., Milica Chernick, M.D., Eileen Thacker, D.V.M., Ph.D., DACVM, Walid Heneine, Ph.D., Gregory Armstrong, M.D.

FDA Participants: (Non-voting)
Julie Beitz, M.D., Amy Rosenberg, M.D., Anne Pariser, M.D., Barry Cherney, Ph.D., Ethan Hausman, M.D.

Sponsor Participants: (Non-Voting)
Victor Raczkowski, M.D., Virginia Stallings, M.D., Earl Sands, M.D., X.J. Meng, M.D., Ph.D. (Solvay Pharmaceuticals, Inc.)

Open Public Hearing Speakers:
Kenneth Attie, M.D., Vice President, Clinical Development and Medical Affairs, Altus Pharmaceuticals, Inc.
Jane M. Holt, Co-President and Co-Founder**,** National Pancreas Foundation

Tibor Sipos, Ph.D., President, Digestive Care, Inc.

Designated Federal Official:
Paul Tran, R.Ph.

Issue:

The committee discussed the safety and efficacy of new drug application (NDA) 20-725, Creon (Pancrelipase Delayed-Release Capsules), Solvay Pharmaceuticals, Inc., for the treatment of exocrine pancreatic insufficiency.

Agenda:

10:59 a.m. – 11:04 a.m.	Call to Order Introduction of Committee	**Ian McGowan, M.D., Ph.D., FRCP** Chair Antiviral Drugs Advisory Committee (AVDAC)
11:04 a.m. – 11:06 a.m.	Conflict of Interest Statement	**Paul Tran, RPh** Designated Federal Official, AVDAC
11:06 a.m. – 11:08 a.m.	Opening Remarks	**Anne Pariser, M.D.** Medical Team Leader Division of Gastroenterology Products Office of New Drugs, CDER, FDA
11:09 a.m. – 12:09 p.m.	**Presentations from Sponsor**	
	Introduction	**Victor Raczkowski, M.D.** Vice President, US Regulatory Affairs Solvay Pharmaceuticals, Inc.
	Medical Need for Pancreatic Enzyme Replacement Therapy	**Virginia Stallings, M.D.** Director, Nutrition Center Professor of Pediatrics Children's Hospital of Philadelphia
	Clinical Efficacy & Safety	**Earl Sands, M.D.** Vice President, Research & Development Solvay Pharmaceuticals, Inc.

	Assessment of Porcine Viruses	**X.J. Meng, M.D., Ph.D.** Professor of Molecular Virology College of Veterinary Medicine Virginia Polytechnic Institute and State University
	Risk Mitigation Strategies	**Earl Sands, M.D.** Vice President, Research & Development Solvay Pharmaceuticals, Inc.
	Conclusions	**Solvay Pharmaceuticals, Inc.**
12:10 p.m. – 01:00 p.m.	**Presentations from FDA**	
	NDA 20-725 Pancrelipase Delayed-Release Capsules (Creon®)	**Ethan Hausman, M.D.** Medical Officer Division of Gastroenterology Products CDER, FDA
	Viral Safety Issues for Pancreatic Enzyme Products Creon®	**Barry Cherney, Ph.D.** Deputy Director Division of Therapeutic Proteins CDER, FDA
01:00 p.m. – 1:45 p.m.	Lunch Break	
1:45 p.m. – 2: 45 p.m.	Open Public Hearing (OPH) Session	
2:45 p.m. – 2:50 p.m.	Charge to the Committee	**Anne Pariser, M.D.** Medical Team Leader Division of Gastroenterology Products Office of New Drugs, CDER, FDA
2:50 p.m. – 4:30 p.m.	Advisory Committee Discussion	
4:30 p.m.	**Adjournment**	

Questions to the Committee:

1.

a. The risk of cross species infection associated with the presence of PPV or PCV in the pancrelipase product appears to be very low, but could be further reduced by testing for infectivity and ensuring limited patient exposure to these viruses. In that light, should testing for infectious PPV and/or PCV 1 and 2 be conducted for pancrelipase batch release testing?

Vote Yes: 6 No: 10 Abstain: 0

b. If "Yes", which viruses should be tested?
   1) PPV
   2) PCV1
   3) PCV2

The six (6) members voted Yes to question 1A agreed that all three viruses should be tested.

(Please see transcripts for detailed discussions)

c. If testing is warranted, should the acceptance criteria for lot release allow for a limited number of infectious virus?

The six (6) members voted Yes to question 1A were asked to vote again in question 1C.

Vote Yes: 4 No: 2 Abstain: 0

d. If "Yes", is there a viral load below which cross species infectivity is less likely to occur? **Discuss**

There was a general consensus that the batches should be tested for these viruses. Some members felt that there should be a defined level of infectivity which would have consequences of whether or not the batch would be released. Some members did not feel it was a good idea to define a level and not use it as a parameter to withhold a batch into circulation.

(Please see transcripts for detailed discussions)

e. Are there any other viruses of concern that have not thus far shown zoonotic potential, but should be tested on a routine basis?

Vote Yes: 3 No: 11 Abstain: 2

(If Yes, specify which additional viruses**)**

There was a general consensus from the three members voted Yes to question 1E that they would defer to the experts in the field and FDA to figure out which viruses should be tested on a routine basis.

(Please see transcripts for detailed discussions)

2.

a. To control the risk from unidentified emerging viruses, Solvay has proposed a number of options for animal disease surveillance programs and continued risk assessment evaluations for source animals. Should a detailed plan for these programs be required?

Vote Yes: 15 No: 1 Abstain: 0

b. If "Yes", please identify additional measures that should be implemented to mitigate risk. For example, Solvay could use appropriate indicator cell lines and animal testing to evaluate the presence of unknown viruses in the product that might infect humans. **Discuss**

Several members supported the idea of having an S.O.P. in place which should include specifications for when and how the company would pick up the signal and to notify the FDA when a signal is found in the herd. Some members felt that we should build upon existing surveillance systems and not to require the company to create a new surveillance system as this was considered too large a burden for a single company.

(Please see transcripts for detailed discussions)

3.

a. Solvay has not formally submitted a plan for continued viral risk identification and evaluation in patients taking Creon in the post-marketing setting. Should such a plan be provided?

Vote Yes: 16 No: 0 Abstain: 0

b. If "Yes", what components should be included in the plan? For example, what additional studies could be performed post approval in order to better understand the risks? **Discuss**

Most members felt that serologic testing would be most beneficial as well as prospective studies and possible collaboration with organizations such as the NIH, Cystic Fibrosis Foundation and National Pancreas Foundation. Members did not feel resources should be put into looking at retrospective studies.

(Please see transcripts for detailed discussions)

4.

a. Currently, no information regarding the risk from viral contamination is provided to physicians and patients in product labeling. Is there sufficient concern that such information should be provided?

Vote Yes: 16 No: 0 Abstain: 0

b. If "Yes", can you provide guidance on what information should be provided to the patients, their caregivers, and to the public? **Discuss**

Some members felt that no specific viruses should be listed while the label should be written honest, fair, and generic. This is a potential problem for all pancreatic enzyme products. Label should be written in plain language, easy to understand for both physicians and patients. Physicians and patients should know the risk at the same time not to scare the patients into avoiding taking the needed medication.

(Please see transcripts for detailed discussions)