FOOD AND DRUG ADMINISTRATION (FDA)
CENTER FOR DRUG EVALUATION AND RESEARCH (CDER)
Joint Meeting of the
Antiviral Drugs Advisory Committee and the Nonprescription Drugs Advisory Committee
Hilton Washington, DC/Rockville
October 29, 2008

The Antiviral Drugs Advisory Committee and Nonprescription Drugs Advisory Committee of the Food and Drug Administration, Center for Drug Evaluation and Research met on October 29, 2008 at the Hilton Hotel, Washington DC/Rockville, the Ballrooms, 1750 Rockville Pike, Rockville, 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 300 persons in attendance. There was 1 speaker for the Open Public Hearing sessions.

Attendance:

Antiviral Drugs Advisory Committee Members Present (Voting):
Ian McGowan, M.D., Ph.D, FRCP, Barbara Alexander, M.D, Tracy Swan, Janet Andersen, Sc.D, Peter Havens, M.D., Marshall Glesby, M.D., Ph.D, Craig Hendrix, M.D., Amneris Luque, M.D.

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

Nonprescription Drugs Advisory Committee Member (Voting)
Marie Griffin, M.D., Jan Hewett, J.D., BSN, William Shrank, M.D.

Nonprescription Drugs Advisory Committee Member (Non-voting)
Edward Nelson, M.D. (Industry Representative)

Drug Safety and Risk Management Advisory Committee Member (Voting)
Terry Davis, Ph.D.

Special Government Employee Consultants Present (Voting):
Yoshihiko Murata, M.D., Ph.D, Marc Lipsitch, M.D, John Bradley, M.D., Robert Mauskapf, M.P.A., Ruth Parker, M.D., Richard Neill, M.D., Marilyn Eichner, Ruth Day, Ph.D, Leslie Walker-Harding, M.D., Neal Benowitz, M.D., Eric Brass, M.D., Ph.D, Neil Farber, M.D.

Regular Government Employee Present (Voting):
Alexander Klimov, Ph.D, Sc.D, Tim Uyeki, M.D, M.P.H, Chester (Bernie) Good, M.D.

FDA Participants: (Non-voting)
Edward Cox, M.D., Debra Birnkrant, M.D., Andrea Leonard-Segal, M.D., Capt. Laura Shay, RN, Linda Lewis, M.D., Scott Proestel, M.D.

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Guest Speakers: (Non-voting)
John Tegeris, Ph.D, Health and Human Services, BARDA
Frederick Hayden, M.D., University of Virginia School of Medicine
Brit Oiulfstad, DVM, M.P.H., National Associations of County and City Health Officials (NACCHO) (by Phone)
Doug Campos-Outcalt, M.D., M.P.A., American Academy of Family Physicians (AAFP) (By Phone)
Litjen (L.J.) Tan, M.S., Ph.D, American Medical Association (AMA) (by Phone)
Luciana Borio, M.D, Infectious Diseases Society of America (IDSA)
Henry (Hank) Bernstein, D.O. American Academy of Pediatrics (AAP)
Cynthia Reilly, B.S., Pharm., American Society of Health-System Pharmacists (ASHP)
Marcie Bough, Pharm.D, American Pharmacists Association (APhA)
James Blumenstock, Association of State and Territorial Health Officials (ASTHO)

Guest from EMEA joined by Telephone:
Anne-Sophie Henry-Eude, EMEA

Sponsor Participants: (Non-Voting)
Judith Ng-Cashin, M.D, Global Clinical Vice President, GlaxoSmithKline
Michael McGuire, M.D, Vice President, Anti-Infectives, Hoffmann-La Roche

Open Public Hearing Speakers:
Ben Schwartz, M.D., HHS/NVPO

Designated Federal Official:
Paul Tran, R.Ph.

Issue:

The committee will provided advice on types of studies and trial designs needed for an influenza antiviral MedKit for the treatment or prophylaxis of influenza during a pandemic and discuss publicly the proposed development program that would support an application for such a MedKit.

8:00 a.m. – 8:10 a.m.	Call to Order	**Ian McGowan, M.D., Ph.D, FRCP.** Chair
8:10 a.m. – 8:15 a.m.	Introduction of Committee	Antiviral Drugs Advisory Committee (AVDAC)
	Conflict of Interest Statement	**Paul Tran, RPh.** Executive Secretary, AVDAC

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8:20 a.m. – 8:35 a.m.	Opening Remarks	**Debra Birnkrant, M.D**. Director Division of Antiviral Products CDER, FDA
8:35 a.m. – 8:48 a.m.	Influenza Antiviral Drug Medkits: HHS Perspectives	**John Tegeris, Ph.D**. Senior Program Manager, Antiviral Drug Program Department of Health and Human Services (HHS)/BARDA
8:48 a.m. – 9:06 a.m.	Epidemiology of Seasonal and Pandemic Influenza	**Tim Uyeki, M.D., M.P.H**. Deputy Chief, Epidemiology and Prevention Branch Influenza Division Centers for Disease Control and Prevention
9:07 a.m. – 9:32 a.m.	A Perspective on Influenza Treatment and Prophylaxis	**Frederick Hayden, M.D.** Professor of Clinical Virology University of Virginia School of Medicine
9:33 a.m. – 10:00 a.m.	Influenza Resistance	**Alexander Klimov, Ph.D** Chief, Virus Surveillance and Diagnosis Branch Centers for Disease Control and Prevention
10:00 a.m. – 10:15 a.m.	Break	
10:15 a.m. – 10:30 a.m.	Overview of Consumer Studies	**CAPT Laura Shay R.N., M.S., C-ANP** Social Science Analyst Division of Nonprescription Clinical Evaluation CDER, FDA
10:30 a.m. – 11:00 a.m.	Relenza MedKit: Potential Use for Pandemic Influenza and Proposed Development Plan".	**Judith Ng-Cashin, M.D.** Global Clinical Vice President Infectious Diseases Medicines Development Center GlaxoSmithKline

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11:00 a.m. – 11:30 a.m.	TAMIFLU® MedKit for Pandemic Influenza	**Michael McGuire, M.B.A.** Vice President Anti-Infectives Hoffmann-La Roche
11:30 a.m. – 12:00 a.m.	Clarifying Questions for the Sponsors	
12:00 a.m. – 12:55 p.m.	**Presentations from Associations**	**NACCHO, AAFP, IDSA, AMA, AAP, ASHP, APhA, ASTHO**
12:00 a.m. – 12:05 p.m.	Home stockpiling; Who benefits?	**Brit Oiulfstad, DVM, M.P.H.** National Association of County and City Health Officials (NAACHO)
12:05 a.m. – 12:11 p.m.	AAFP Viewpoint	**Doug Campos-Outcalt, M.D., M.P.A.** American Academy of Family Physicians (AAFP)
12:12 a.m. – 12:17 p.m.	American Medical Association Perspective on Use of Influenza Antiviral "MedKit" during a Pandemic Influenza Outbreak.	**Litjen (L.J.) Tan, M.S., Ph.D.** American Medical Association (AMA)
12:18 p.m. – 12:21 p.m.	IDSA comments regarding the Antiviral Medkits Proposal	**Luciana Borio, M.D.** Infectious Diseases Society of America (IDSA)
12:22 p.m. – 12:30 p.m.	American Academy of Pediatrics' Perspective of Home Antiviral Drug Stockpiling	**Henry (Hank) Bernstein, D.O.** American Academy of Pediatrics (AAP)
12:30 p.m. – 12:39 p.m.	Distribution of Antivirals for Pandemic Influenza: Public Health Impact and Research Recommendations	**Cynthia Reilly, B.S. Pharm.** American Society of Health-System Pharmacists (ASHP)
12:40 p.m. – 12:48 p.m.	The American Pharmacists Association's Comments on Stockpiling Pandemic Influenza Medkits	**Marcie Bough, Pharm.D.** American Pharmacists Association (APhA)

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12:48 p.m. – 12: 55 p.m.	State Public Health Agency Perspective on Pan Flu Antivirals MedKits	**James Blumenstock** Chief Program Officer, Public Health Practice The Association of State and Territorial Health Officials (ASTHO)
12:55 p.m. – 1:50 p.m.	Lunch	
1:50 p.m. – 2:00 p.m.		Open Public Hearing (OPH) Session **Ben Schwartz, M.D., HHS/NVPO**
2:00 p.m. – 2:05 p.m.	Charge to the Committee	**Debra Birnkrant M.D.** Director, Division of Antiviral Products CDER, FDA
2:05 p.m. – 5:00 p.m.		Advisory Committee Discussion
5:00 p.m.		Adjourn

Questions to the Committee:

1. Please comment on the concept of a prescription influenza antiviral MedKit intended for use during a pandemic. Specifically address potential risks and benefits, for individual consumers and the U.S. population, if prescription MedKits were approved with the intention of home stockpiling.

There was general consensus from the committee that safety is less of a concern particularly as the public health benefit could be enormous in a pandemic setting. The committee wanted more granularity of the Federal's and States' plans of rolling out responses during pandemic because these will impact the efficacy and effectiveness of the drugs when they are not in the right place at the right time. The committee indicated safety is important but less of a concern than efficacy. Issues such as resistance, circulatory viruses, distinguishable between seasonal versus pandemic flu were brought up by the committee. The committee also brought up concerns regarding equity of access as the plans are formulated and moving forward. The committee has additional concerns such as will individuals able to understand what they have at home, able to use the Medkits correctly, dose titration and different formulations available in the Medkits.

(Please see the transcripts for detailed discussion)

2. Will the phase 3 clinical trials that supported approvals and favorable results from the proposed "consumer use" studies (e.g., label comprehension, simulated use, etc.) allow for safe and effective use of the MedKits by individuals who may not be under direct medical supervision at the time of antiviral drug use?

[Voting question].

Yes: 6 **No: 20** **Abstain: 1**

If no, what additional studies are needed?
The committee discussed both questions # 2 and # 6 together. Please see question # 6 below for further discussion.

(Please see transcripts for detailed discussion)

3. Please comment on the use of a MedKit for treatment versus prophylaxis of influenza during a pandemic. Specifically, taking into account the characteristics of the drugs included in the proposed MedKits:

> Are both treatment and prophylaxis indications appropriate for MedKits for both of the proposed products?
>
> If both indications are appropriate, is it acceptable for the same MedKit to be used for both indications?

There was general consensus of broad acceptance of the fact that the indications were appropriate for both treatment and prophylaxis. The committee is concerned whether individuals receiving the intervention are aware of the differences in the indications.

(Please see transcripts for detailed discussion)

4. The Tamiflu MedKit proposal includes instructions for dosing children using the contents of the 75 mg adult capsules although Tamiflu is also available commercially as 30 mg and 45 mg capsules as well as an oral suspension. What is the most appropriate formulation to be used for pediatric dosing in this setting?

The committee felt it was important to have choices when treating pediatric patients, both in the Medkits and choices in the U.S. stockpiling program. The committee has concerns regarding parents could reasonably and appropriately reproduce the drugs in the many options for mixing vehicles for use in children.

(Please see transcripts for detailed discussion)

5. Comment on specific elements of labeling, packaging, or instructions that are critical for safe and effective use of a MedKit.

The committee suggested the Medkit should include a thermometer. The labeling should be clear regarding the use in prophylaxis versus treatment situation. Some committee members suggested having different color on the packaging label to indicate the standard seasonal flu versus for use in a pandemic(Tamiflu-PD). There were also suggestions of having the capsules color coded to clearly identify the different strengths. The committee also has concern regarding the instructions and reading level of the instructions.

(Please see transcripts for detailed discussion)

6. Please comment on additions or modifications to the proposed studies (e.g., label comprehension, simulated use, or additional studies) that would help to assess risks and benefits. For example:

> What is a reasonable percentage of study subjects who should understand various components of the labeling and/or be able to refrain from using the product for seasonal influenza?
>
> What types of additional studies would be helpful to assess how users would behave in a real-life situation?

The committee focused primarily on the expansion of the already proposed comprehension study. The committee wanted to see a more real-world study design characteristics. There were suggestions for conducting more operational studies in term of rollout distribution, perhaps including prescribing behavior from physicians. The committee also suggested looking at the subgroups of at risk patients such as pregnant women and very young children. The committee also wanted to look at consequences of under and overdosing. There was a suggestion of a ~80% comprehension rate as a reasonable percentage.

(Please see transcripts for detailed discussion)

7. Please comment on the type of availability that would best be suited to provide MedKits to the American public and state your reasons for your comments. If availability without a prescription is considered an option, please describe any additional studies that would be needed to support a switch from prescription to nonprescription availability.

The committee brought up some concerns for both by prescription versus over-the-counter availability of the Medkits. The committee also suggested to both Sponsors and FDA of exploring alternative mechanisms for distributions of the Medkits.

(Please see transcripts for detailed discussion)