DEPARTMENT OF HEALTH AND HUMAN SERVICES

NATIONAL INSTITUTES OF HEALTH

NATIONAL CANCER INSTITUTE

SUMMARY OF THE 59th DIRECTOR'S CONSUMER LIAISON GROUP MEETING

NIH Campus, Stone House (Building 16)

Bethesda, Maryland

February 29 & March 1, 2012

Members Present

Ms. Gwen Darien, Chair
Dr. Jeff Allen
Ms. Susan G. Brown
Dr. Adam Clark
Ms. Andrea Ferris
Ms. Joya Delgado Harris
Ms. Linda House
Ms. Cheryl Jernigan
Mr. Jeff Kaufman
Dr. Deborah Morosini
Mr. Jon Retzlaff
Ms. Phyllis Pettit Nassi
Mr. Josh Sommer
Mr. Max Wallace

Speakers

Dr. Harold Varmus, Director, National Cancer Institute (NCI)
Dr. James H. Doroshow, Deputy Director, NCI
Dr. Bruce A. Chabner, MGH Cancer Center, Massachusetts General Hospital
Dr. Sherry Glied, Assistant Secretary for Planning and Evaluation, U.S. Department of Health and Human Services
Dr. Sandra L. Kweder, Center for Drug Evaluation and Research, U.S. Food and Drug Administration
Dr. Mace Rothenberg, Pfizer Oncology
Ms. Anne M. Vickery, Hogan Lovells U.S. LLP
Ms. Anne Lubenow, Acting Deputy Executive Officer, NCI
Ms. Amy Bulman, Acting Director, Office of Advocacy Relations (OAR), NCI

Facilitator

Mr. Robert Mittman

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Opening Remarks

Dr. Harold Varmus

- Drug shortages are occurring in many areas of medicine—almost all injectable generic drugs.
- Dr. Varmus noted the complexity of the issue, and the need to move beyond legislative solutions.
- While the problem is too complex for any individual or group to solve, Dr. Varmus believes that patient advocacy groups can play a role in identifying solutions. Dr. Varmus concluded with a charge to the DCLG: the DCLG can lead the way in reducing oncology drug shortages and open doors for further action in areas outside of oncology.

Dr. James Doroshow

- Dr. Doroshow explained how drug shortages affect the cancer community, with an emphasis on research. On an individual level, people are affected because their treatment drugs are unavailable. Clinical trials in which the comparison group receives standard treatment are also affected. Dr. Doroshow estimated that a third of cancer clinical trials have been adversely affected. Similarly, the NCI's entire clinical research program is affected.

Drug Shortage: A Critical Challenge for the Cancer Community

Dr. Bruce Chabner

- Dr. Chabner has several theories about the origins of the cancer drug shortage:
    - Economic factors—possible that financial incentives have been compromised
    - The "gray market," minor distributors with supplies, but inflated prices
    - A combination of drug pricing, profit margins, poorly managed facilities, lack of manufacturing redundancy, and group purchasing organizations (GPOs)
- Dr. Chabner believes that a solution will involve both private industry and federal intervention. He has identified several potential solutions, including:
    - Legislation could provide penalties for poor performance and reward good citizenship
    - Expedited review of new applications for generic manufacturers that meet demand
    - Examination of the international drug market

Panel: Understanding Cancer Drug Shortages

Dr. Sherry Glied

Dr. Sandra Kweder
Dr. Mace Rothenberg

Meeting Industry's Challenge: Supplying Essential Cancer Drugs

Dr. Mace Rothenberg

- An estimated 94% of cancer treatment facilities have experienced shortages since 2009, and 84% have had to modify treatments.
- In Dr. Rothenberg's opinion, four factors in particular have resulted in the perfect storm for drug shortage:
    - Quality assurance and control—plants are having to shut down due to raw material and quality issues.
    - Patent protections—one in five shortages is due to the manufacturer ceasing to make the drug, often because it has opted to produce a new drug that just lost patent protection.
    - Expiration of premium pricing—after the 12 month price premium of new generic drugs expires, it is likely that they become less attractive to make.
    - Lack of redundancy—a facility's schedule may be set two years out so if a quality problem is identified and the drug cannot be made or sold, there is no way to re-manufacture the drug quickly.
- Dr. Rothenberg reported that Pfizer's response has been to ramp up production of generic oncology drugs. They are building a robust oncology portfolio composed of legacy drugs as part of its commitment to help solve this problem. Pfizer is committed to patient access, patient safety, high quality, and to preventing drug shortages by meeting demand on a consistent basis.
- Dr. Rothenberg outlined several avenues that he believes will help solve this problem, including
    - Better communication channels between the FDA and manufacturers,
    - Shortened review times,
    - Imposing civil penalties, and adding incentives such as expedited review for branded new products for companies that help with the generic problem,
    - And a grass roots rating system for generic manufacturers.

Understanding Cancer Drug Shortages

Dr. Sherry Glied

- Dr. Glied provided a detailed description of the market for generic injectables and explained how—unlike other markets—price is not influenced by demand or supply. Instead, supply is constrained by manufacturer capacity, so there is no difference in price when the supply is limited.

- Manufacturers have introduced a 24 hour, 7 days a week production schedule. Production schedules are set months in advance. When a plant goes down to fix things, the supply schedule is off for the next six months. This helps to explain cascading shortages throughout the class of drugs.

- More drugs are going off patent, and about 45 drug combinations are approved each year.

- Dr. Glied explained the role of Medicare Part B, which affects how doctors are paid, but she believes that Medicare is a lagging indicator and is not constraining the market.

- She believes that in order to fix the shortage manufacturers need to be able to increase capacity faster and better manage supply.

- Dr. Glied suggested addressing three fronts. First, make sure the FDA has the tools to address the problems. Second, ensure that private purchasers can get what they want out of the market. The third part is talking with patients and families without causing anxiety. She suggested providing examples of actions that the patient community can take to address the issue.

U.S. Drug Shortages

Dr. Sandra Kweder

- Reporting requirements only apply when a manufacturer is the sole source provider. In the event of a pending shortage, the FDA has no ability or authority to require anyone to make anything. It is all voluntary.

- Data from 2010 and 2011 show the proximate causes of these shortages: more than 75% are related to quality concerns and delays in manufacture. Discontinuations account for only 11% of the shortages. Raw materials explain only 5%; new demand accounts for about 4%.

- Quality problems include lack of sterility, foreign matter getting into the production line, crystallization of the active ingredient, precipitate formation, new impurities or degradants, equipment breakdowns, and natural disasters. Dr. Kweder believes that most of these cannot be anticipated.

- Dr. Kweder warned that such problems need repair, but the factories are running 24 hours a day, 7 days a week, with no redundancy; they cannot stop and fix the problem.

- Much of the FDA's shortage information comes from pharmacists, hospitals, patients, and industry. The FDA prevented 38 shortages in 2010, all due to firms notifying the agency in advance of pending shortages. The FDA works with companies to avoid drug shortages. In rare cases, the FDA will also import drugs from overseas.

- Dr. Kweder believes that the 2011 Executive Order resulted in a 6-fold increase in the number of notifications. Since the beginning of November last year, 195 shortages have been prevented, 18 this year alone, as of February 9.

- She predicts that this problem will continue for several years. The FDA has multidisciplinary teams working on it continually; they are committed to maintaining a reliable supply of medicines, at the quality demanded by the U.S. public.

- Dr. Kweder suggested making sure that the FDA has the tools to hold companies accountable. Patients need help working through these difficult problems. It is also important to ask these companies what they are doing to demonstrate and live a culture of quality. She does not believe that stockpiling is a solution. Drugs expire and the costs would be prohibitive.

Highlights from dialogue between panelists and the DCLG

- Differences between branded and generic drug markets may influence drug shortage. While branded drugs only have one manufacturer, generic drugs have several and the number of manufacturers changes often. Also, competition between GPOs and between manufacturers exist in the generic market. Since branded drugs are sole-source products, a mentality and a culture accompany the drug—companies build relationships with patients and providers.

- Generic drug companies produce enough drugs so that inventory does not exceed demand, otherwise drugs will expire without being sold.

- There is a huge backlog of generic applications. The proposed legislation to include a generic user fee could help fix this backlog. Expedited review can be useful for isolated cases.

- It does not seem that GPOs have much power because individual hospitals are not committed to the volume contracts. A GPO could recognize manufacturers that are stable over time, thus promoting a culture of quality, but hospitals can undercut the premium price.

- Advocates must recognize the problem's complexity and interact with legislators. Advocates need to recognize situations that are within the control of a company and those that are not. It's also important to understand that the added costs to ensure quality measures may increase the cost of generics. If the DCLG is to effectively advocate on the subject of generic drug

shortages, they must understand the different facets of the generic market and have discussions with generic companies.

DCLG Discussion:

- The solution to this problem is not necessarily controlled by patient advocates. However, patient advocates can have an impact on patient education. Advocates can educate themselves and understand the issues, then explain the problem to others, and share how this can affect cancer communities.

Potential actions for the DCLG, included:

- Use the generic drug user fee act to open discussions with the FDA. Such a program might alleviate the backlog by bringing resources to enhance FDAs capacity.
- Answer the question about excess capacity and whether it is the government's role to provide it, either by funding it or requiring it so shortages are less likely.
- Advocate for a track and trade system so that in times of drug shortages hospitals with extra drug can give to hospitals that are experiencing affected by the shortage.
- Focus on the culture of quality and hold manufacturers accountable.
- Investigate the use of clearing houses to supply the drug during shortages.
- Take a closer look at international barriers to trade and how they relate to capacity building and capacity assessments.
- Draft a paper stating that these drug shortages are causing patients to not be treated and endangering clinical research, then promulgate it in Op Eds, testimony to Congress, etc.
- Find out if there a way to integrate advocacy groups like the DCLG into the cross-agency task force.
- Communicate what is going on to members' constituencies and share the message of quality control. There has to be concern about creating anxiety, but that has to be balanced with being open to patients' needs. Decipher how difficult this problem is to understand and what information is available.
- Answer the question of what it means to those on Capitol Hill.
- Provide guidance for a contingency plan.
- The cancer centers are likely aware of what can be substituted. The DCLG should figure out how far that has permeated into the community, and what educational transparency exists.

- Use the DCLG's voice and convening power.

The session adjourned at 3:50 p.m.

Certification

I hereby certify that the foregoing minutes are accurate and complete.