Personal Preparedness Discussion

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SUMMARY REPORT
of the
NATIONAL BIODEFENSE SCIENCE BOARD
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BIOMEDICAL ADVANCED RESEARCH AND DEVELOPMENT AUTHORITY (BARDA)

Robin Robinson, Ph.D., Deputy Assistant Secretary and Director, BARDA, Office of the Assistant Secretary for Preparedness and Response

The presentation delivered by Dr. Robinson focused on the U.S. Department of Health and Human Services (HHS) Public Health Emergency Medical Countermeasures Enterprise (PHEMCE) for medical countermeasures for chemical, biological, radiological, and nuclear (CBRN), pandemic influenza, and emerging infectious disease threats. BARDA's role in the Enterprise was presented.

Dr. Robinson noted that BARDA is considering how individuals, businesses, and health care organizations could use stockpiling of medical countermeasures to address potential inequities in availability and timing of delivery should the Strategic National Stockpile be inadequate in a public health emergency. Home-stockpiling is one concept that takes advantage of individuals' interest in personal preparedness and desire for self-reliance.

The HHS Centers for Disease Control and Prevention (CDC) germinated the idea of home-stockpiling when it sponsored the concept of personal supplies of antibiotics for anthrax in 2004. In 2006, the CDC conducted a pilot-test sending medical toolkits (also known as MedKits) to consumers in St. Louis. CDC found that 97% of those who received the MedKits followed the instructions for storage and potential use correctly.

Since 2007, BARDA has been considering a MedKit containing antibiotics against anthrax as well as influenza antivirals that would be an adjunct to community mitigation measures. HHS has drafted home-stockpiling guidance for antimicrobials and is drafting guidance on home use of antivirals for pandemic flu.

Dr. Robinson said several manufacturers are planning label comprehension, compliance, and simulation studies of existing influenza antivirals, as well as conducting market research, with an eye toward licensing an antiviral MedKit for use by the general adult public in mid-2010, with kits specifically for elderly and pediatric populations to follow. Computer modeling suggests that the MedKits may have a limited impact on their own

but may ameliorate the effects of national antiviral stockpile depletion. BARDA will begin its own studies later this year and, if appropriate will conduct testing during the annual influenza season.

Similarly, BARDA is looking at an antimicrobial MedKit for anthrax. It has compliance data from the CDC-sponsored, St. Louis pilot project and is planning a palatability study this year (i.e., evaluating the feasibility of crushed pills taken with food for people who cannot swallow pills). BARDA has issued a request for proposals to study label comprehension for doxycycline. At least seven manufacturers of generic antibiotics have expressed interest in conducting market research and manufacturing of these products. The CDC has drafted advisory guidance for physicians and consumers on the use of doxycycline for home-stockpiling. HHS is considering antibiotics against anthrax as a preventive measure for target populations. For example, U.S. Postal Service workers may receive antibiotics under emergency use authorization as early as December 2008. HHS and the U.S. Department of Homeland Security (DHS) are also considering emergency use authorization for first responders and emergency care providers. Home antibiotic MedKits for the general public could be licensed by the end of 2009.

Dr. Robinson posed the following questions for consideration by the Board:

- Should pre-pandemic influenza vaccination be expanded?
- Should the pandemic influenza medical countermeasures portfolio include pneumococcal and streptococcal vaccines? Should staphylococcal vaccines be developed?
- What is the right mix of shared responsibility for influenza antivirals for pandemic prophylaxis?
- Should prime-boost vaccination strategies for BARDA medical countermeasures be offered before an event? Should they be commercially marketed?
- Are there better ways to prepare other than stockpiling?
- What are the emerging infectious diseases on the horizon?
- Is home-stockpiling of medical countermeasures a safe and effective preparedness measure?

DISCUSSION

Dr. Jutro asked whether BARDA's federal focus was exclusively on HHS and DHS first responders and emergency care providers, or whether Dr. Robinson was only using those agencies as illustrative exemplars. Dr. Robinson then asked for suggestions from the Board about whom else, including personnel from other federal agencies, should be included in an emergency use authorization (EUA) order for prophylactic antibiotics.

PERSONAL PREPAREDNESS

Robin Robinson, Ph.D., Deputy Assistant Secretary and Director, BARDA, Office of the Assistant Secretary for Preparedness and Response

Dr. Robinson explained that some public health emergencies (e.g., wide-area release of aerosolized *Bacillus anthracis*) would require timely mass chemoprophylaxis to prevent

catastrophic loss of life, but few, if any, municipalities are prepared for such events. HHS recognizes that some citizens may wish to reduce their dependency on public agencies by stockpiling prescription drugs at home. Board members were provided two draft letters—one intended for health care providers and the other for consumers—that provide guidance on home storage of antimicrobial drugs (specifically doxycycline). Dr. Robinson noted that doxycycline (among other antibiotics) is approved for post-exposure prophylaxis against anthrax but prescription in anticipation of a bioterrorism incident could be considered an off-label use of the drug.

Dr. Robinson raised several questions regarding home-stockpiling of antimicrobials:

- Is this approach a needed threat preparedness measure?
- Is home-stockpiling a viable component of personal preparedness?
- Does this approach increase the possibility of antibiotic resistance emergence?
- How fast can the Strategic National Stockpile deliver antimicrobials?
- Would the general public use antimicrobials they had stockpiled? What would be the overall impact of such use?

As described earlier, HHS is in the early phases of developing an antibiotic MedKit that could be available for the general population, and the CDC has drafted advisory letters to health care providers and consumers on home-stockpiling.

In closing, Dr. Robinson described a potential scenario in which an anthrax attack affected a city of 3 million people. Under existing capabilities, it was estimated that all available drug would be dispensed within 4-6 days of the attack and 660,000 people would have died within 6 days of the attack if surge response with antibiotic dispensing does not occur promptly.

DISCUSSION

Richard Besser, M.D., of the CDC noted that the issues surrounding dispensing and distributing antibiotics in the event of a large-scale anthrax attack are formidable. He emphasized that the CDC does not support the concept of home-stockpiling right now outside of a licensed MedKit. However, the CDC drafted guidance to health care providers and consumers to ensure that they have good information on the safe storage and use of antibiotics if they are being prescribed for home stockpiling.

Dr. Besser pointed out that the CDC does support personal preparedness. He noted that in contrast to a typical prescription of pills in a bottle, the CDC antibiotic MedKits contain doxycycline and ciprofloxacin in a special envelope printed with large warnings about their use; the envelopes include patient information on when to use the drugs, and that information is based on CDC data about how people use and store medicines in their homes. The CDC's pilot project found that 97% of those who had a MedKit were able to locate it 4–6 months after they received it in the mail. They also felt more secure having this in their home and were willing to pay for the kits.

However, we know from extensive research that antibiotics, drugs designed to treat specific bacterial infections, are frequently misused by the public and taken for the

treatment of viral infections. This is one of the primary factors promoting the development of antibiotic resistance. Given the paucity of new antibiotics being developed, we must teat antibiotics as a scare, limited, national resource. A home-stockpiling program should maximize the likelihood that the drugs would be stored correctly and would be available during an emergency.

Dr. Besser urged the Board and BARDA to consider several issues before moving forward. It is important to consider home-stockpiling not just through the Biodefense lens, but also through the broader lens of public health. In the broader public health context, would encouraging individuals to request antibiotics from their health care providers affect the utility of these drugs for other conditions? Antibiotic resistance is a real concern. Doxycycline has been found to encourage resistance to other agents. CDC has begun to see a rise in resistance to doxycycline since its introduction as a drug used to teat methicillin-resistant Staphylococcus aureus (MRSA). In 2001, no strains of Group A streptococcus in the Active Bacterial Corps Surveillance system were resistance to tetracycline (a drug related to doxycycline). In 2006, 15% of strains were resistant to tetracycline. To ensure that doxycycline remains effective against MRSA we must ensure that it is not misused. The home-stockpiling proposal must be considered in light of other strategies to combat antibiotic resistance, Dr. Besser said. He was an active participant in the development of the federal Plan to Combat Antimicrobial Resistance. We need to ensure that as we move forward, our actions are consistent with that plan.

Dr. Besser continued that the medical and public health communities are in the middle of a complicated debate, weighing the competing benefits of science and public policy. Without buy-in from both communities, the public may not warm to the idea of home-stockpiling, and the approach would not be effective without broad uptake.

Dr. Besser added that a home-stockpiling policy would have to address safety issues, such as the possibility of overdose, allergic reaction, use by children, side effects, effects of outdated products, and proper disposal of expired drugs. It would have to address accessibility for at-risk and vulnerable populations, for example, those who cannot afford to pay for the drugs. It would have to take into account regulatory requirements of the Food and Drug Administration (FDA), specifically, whether home-stockpiling is equivalent to over-the-counter use of a prescription drug. The policy would also have to address how to recover, replace, and dispose of expired drug supplies in people's homes.

Boris Lushniak, M.D., M.P.H., of the FDA also emphasized the difference between the MedKit and an individual's prescription bottle. The FDA and HHS have identified a path forward for a potential MedKit that, if approved, by the FDA, could be marketed for use in the home setting. This path requires that the MedKit undergo the FDA's drug approval process. Home-stockpiling of individually proscribed medications, however, is a very different issue and clearly raises all the concerns about safety and inappropriate use discussed by Dr. Besser.

Dr. Lushniak noted that there are concerns about the instructions and labeling given to patients in the draft guidance. If the instructions recommend the drug for a new indication, or different indication than which it was approved, there could be concerns regarding mislabeling or off-label usage. While health care providers may prescribe

drugs off-label, significant liability issues may arise if the Federal government is seen as encouraging off-label use. Even providing home preparation instructions for pediatric populations or for people who cannot swallow pills could be considered re-labeling and therefore problematic under FDA regulations.

Finally, Dr. Lushniak said the FDA has concerns about the wording of the draft guidance. It should be precise and state clearly that individuals may wish to consult with their health care providers; however, it should avoid suggesting that individuals do so or raising expectations that their health care providers will write them a prescription if they ask for one.

Kenneth Dretchen, Ph.D., expressed concern about the possible misuse of prescription drugs stored at home. He pointed to incidents during the first Gulf War in the early 1990s in which Israelis who had home medicine kits, including autoinjectors as countermeasures for chemical attacks received false alarms; as a result, several children suffered from atropine poisoning. He also said a recent label comprehension study indicated that two thirds of those surveyed did not correctly interpret the instructions "take two tablets twice a day". If home-stockpiling efforts were to move forward, Dr. Dretchen said, the labeling must be clear and simple.

James James, M.D., Dr.PH., M.H.A., emphasized the importance of relying on science to make recommendations. He noted that there was no evidence that ciprofloxacin is superior to doxycycline in treating anthrax, yet ciprofloxacin was the drug of choice during anthrax scares in the United States. Dr. James said a large-scale anthrax attack occurred in Russia in 1979, and evidence from that incident should be reviewed carefully. He also said the efficacy of vaccination should be evaluated.

Albert DiRienzo wondered how the "signal" to use the drug would be communicated. He also called for evaluation of new technologies that could help identify when drug vials are opened unnecessarily. Consider using other approaches (i.e., providing screening tools (e.g., lab on a chip) instead of a therapy. Not that lab on a chip is required or appropriate for everything (e.g., anthrax), yet it could be useful for other applications (e.g., bacterial or viral concerns). Consider prevention-oriented tools and methodologies, instead of always looking to a reactive solution. Finally, consider other therapy distribution forms or workflows, instead of simply looking to home-based distribution.

John Grabenstein, R.Ph., Ph.D., said that if home-stockpiling is intended to address the barriers to timely distribution, perhaps a wider network of small-scale distribution centers should be considered instead.

Andrew Pavia, M.D., noted that the draft guidance would be construed by the public as a recommendation for home-stockpiling, no matter how neutral the message is intended to be. He pointed out that people who have antibiotics in their homes tend to use them frequently and at their own discretion. Dr. Pavia raised concerns that confusing and premature advice on this issue could have lasting negative effects on the public's trust in the public health system, eroding the ability to communicate successfully in the future.

Ruth Berkelman, M.D., added that prescription drugs are often misused and noted that,

instruction sheets are likely to be separated from a bottle of pills without special packaging. She noted the difference between a permissive strategy (e.g., allowing but not advocating healthcare providers to prescribe prescription drugs for home-stockpiling) and a pro-active strategy, and queried whether government release of instruction sheets would be perceived as a pro-active strategy. She felt the MedKit approach should be taken into consideration along with other strategies.

John Parker, M.D., stated that he considered individual preparedness a major part of national preparedness and reiterated others' concerns about the safety of expired drugs and the costs of the drugs. He added that providing antibiotics could create a false sense of security as well as an opportunity to engineer an anthrax bacterium that is less sensitive to the drug. Dr. Parker said the military has experience with "just-in-time" distribution that should be considered. He suggested considering alternative distribution tactics, such as using pharmacies as distribution points and extending product life expectancy. Dr. Parker also strongly suggested that the documents intended to go to physicians and individuals undergo the intense rigor of risk communication documents to include testing before distribution. It should also be iterated that there is a "Relationship Gap" between the Federal and State jurisdictions concerning prescribing regulations.

Jon Krohmer, M.D., of DHS (sitting in for Diane Berry, Ph.D.) said his agency is looking at ways to address distribution concerns. He supports the concept of personal preparedness, noting that people routinely seek out preventive measures when traveling overseas, for example. Dr. Krohmer said home-stockpiling could be a component of individual readiness.

Patrick Scannon, M.D., Ph.D., observed that the Board should deliberate carefully on this matter, weighing the issues of safety and security.

The public was invited to comment, and Julie Hantman of the Infectious Diseases Society of America agreed that any guidance from HHS would be construed as a recommendation for home-stockpiling. She asked for clarification about the threat of anthrax to support the notion that the benefits of home-stockpiling outweigh the risks. She echoed concerns about eroding the public's trust in government and the public health system, alluding to previous government recommendations regarding smallpox vaccination and the use of duct tape to protect from a chemical attack. She asked for more public discussion and a coherent public health policy that takes into account post-exposure treatment, vaccination, and other approaches.

Gerald Parker, D.V.M., Ph.D., M.S., Principal Deputy Assistant Secretary for Preparedness and Response, pointed out that the draft guidance prepared by the CDC was provided to the Board for their information and should not be construed as recommendations, although he conceded that such misinterpretation is a risk. He said that the draft guidance is an effort to provide guidelines to those already requesting and prescribing antibiotics for home-stockpiling and under those circumstances he asked, "doesn't the CDC have a responsibility to provide guidance for safe and responsible use?" Neither the timeline for clearance of the documents nor the plan for disseminating them have been determined. Dr. Robinson added that the agency would appreciate input from the Board on the draft guidance but plans to move forward with the documents and

its other studies unless the Board has strenuous objections.

Stephen Cantrill, M.D., said the draft guidance is written at too high a reading level for the general public, that it contains inaccuracies, and that it should be translated into other languages. Eric Rose, M.D., added that the draft guidance is poorly written and raises concerns about conflicts with FDA regulations. Dr. John Parker suggested that the CDC follow its own Red Book guidance on risk communication and appropriate development and testing of guidance.

Dr. Grabenstein categorized the Board's comments into several areas that should be addressed before any program promoting personal preparedness is undertaken: The draft guidance is not ready as presented, and needs revision to address misuse, concerns about antibiotic resistance, product expiration dates, and readability. Graphics should be added to help those of low literacy. The consumer document might be reformatted to provide a 1-page summary, followed by additional detail. Any public communication should emphasize the responsibility of health care providers to minimize misuse through effective patient counseling and that the antibiotics should only be used when explicit instructions from their own local public-health officials are provided. Further, the home stockpiling concept should be subject to research on label comprehension, compliance to instructions, and palatability, just as the MedKits are.

Patricia Quinlisk, M.D., M.P.H., added that health care providers need to be informed about the potential medicolegal issues that could arise with the off-label use of individually prescribed antibiotics for home-stockpiling.

RECOMMENDATION

The Board recommends that a working group be formed to address personal preparedness measures.

ACTION ITEM

Because all the voting members of the Board indicated a desire to take part in a personal preparedness working group, the staff will convene a conference call of the Board on personal preparedness, with further logistics of working group membership to be determined.

RECOMMENDATION

The Board recommends that the Secretary take the comments made at this meeting by Board members and others into consideration before proceeding with the personal preparedness measures described or the CDC draft guidance.

ACTION ITEM

The NBSB staff will send the Secretary the relevant discussion points on personal preparedness from this meeting, excerpted from the meeting summary.