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Roles and contributions of pharmacists in regulatory affairs at the Centers for Disease Control and Prevention for public health emergency preparedness and response

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Abstract

Objective: To provide a general description of the roles and contributions of three pharmacists from the Regulatory Affairs program (RA) at the Centers for Disease Control and Prevention (CDC) who are involved in emergency preparedness and response activities, including the 2009 pandemic influenza A (H1N1) public health emergency.

Setting: Atlanta, GA.

Practice description: RA consists of a staff of nine members, three of whom are pharmacists. The mission of RA is to support CDC's preparedness and emergency response activities and to ensure regulatory compliance for critical medical countermeasures against potential threats from natural, chemical, biological, radiological, or nuclear events.

Conclusion: RA was well involved in the response to the H1N1 outbreak through numerous activities, such as submitting multiple Emergency Use Authorization (EUA) requests to the Food and Drug Administration, including those for medical countermeasures to be deployed from the Strategic National Stockpile, and developing the CDC EUA website (www.cdc.gov/h1n1flu/eua). RA will continue to support current and future preparedness and emergency response activities by ensuring that the appropriate regulatory mechanisms are in place for the deployment of critical medical countermeasures from the Strategic National Stockpile against threats to public health.

Keywords: Centers for Disease Control and Prevention, bioterrorism, emergency preparedness, influenza.

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One of the hallmarks of pharmacy as a profession is the opportunity to contribute to health promotion and disease prevention in various ways. In that tradition, and as a means of describing the diverse effect that pharmacists have on public health, the current work shares experiences of three pharmacists within the Regulatory Affairs program (RA) at the Centers for Disease Control and Prevention (CDC). RA holds unique responsibilities that vary from those held by regulatory affairs programs traditionally within pharmaceutical companies.

The mission of RA is to support the critical task of ensuring availability and use of medical countermeasures that are essential to CDC's preparedness and emergency response programs. RA executes this mission by ensuring regulatory compliance regarding critical medical countermeasures against potential threats from natural, chemical, biological, radiological, or nuclear (CBRN) events. To enable rapid and effective response during emergency events that require appropriate use of medical countermeasures, many of which are only available through CDC, RA is responsible for ensuring that appropriate regulatory mechanisms such as Investigational New Drug (IND) applications, Emergency Use Authorization (EUA) requests, and Investigational Device Exemptions (IDEs) required for deployment and use of medical countermeasures are in place. RA also provides regulatory expertise to CDC subject matter experts and principal investigators regarding use of medical products (e.g., drugs, biologics, devices) for both nonresearch and research purposes.

At a Glance

Synopsis: The emergency preparedness and response activities of three pharmacists from the Regulatory Affairs program (RA) at the Centers for Disease Control and Prevention (CDC) are described. RA helps ensure availability and use of medical countermeasures that are essential to preparedness and emergency response programs at CDC by ensuring regulatory compliance of medical countermeasures against potential threats from natural, chemical, biological, radiological, or nuclear events. RA responded to the 2009 pandemic influenza A (H1N1) outbreak by submitting multiple Emergency Use Authorization (EUA) requests to the Food and Drug Administration, including those for medical countermeasures to be deployed from the Strategic National Stockpile, and developing the CDC EUA website.

Analysis: *Pharmacists interested in emergency response and preparedness activities that strengthen national, state, and local efforts to prevent or respond to emergencies are encouraged to visit http://emergency.cdc.gov. For those interested in furthering their knowledge of regulatory compliance, the authors suggest enrolling in graduate education programs that focus on regulatory affairs.*

Background

Following the attacks of September 11, 2001, and the 2001 anthrax events, the U.S. Department of Health and Human Services (HHS) increased efforts for the procurement and development of medical countermeasures for CBRN threats. Consequently, CDC's role as the lead agency responsible for preparedness and response to public health emergencies involving bioterrorism Category A agents (e.g. smallpox, botulism, anthrax, plague, viral hemorrhagic fevers, tularemia) and other emerging public health threats (e.g. avian influenza, 2009 pandemic influenza A [H1N1], monkeypox, severe acute respiratory syndrome) also expanded. One of the notable expansions has been the management of medical countermeasures for these CBRN and emerging threats. The medical countermeasures stockpiled in CDC's Strategic National Stockpile consist of drugs, biologics, and devices. These medical countermeasures can be used for the treatment, mitigation, or prevention of serious or life-threatening conditions/diseases resulting from CBRN or other potential public health threats. Many of these medical countermeasures are considered investigational products (i.e., unapproved products or unapproved uses of approved products) by the Food and Drug Administration (FDA). Moreover, additional medical countermeasures for CBRN and public health threats that are under development or are being considered for procurement are investigational and are not anticipated to have FDA approval prior to stockpiling. Therefore, these investigational medical countermeasures require FDA-regulated mechanisms such as IND applications, IDE applications, EUA requests, or other FDA-regulated applications for receipt into stockpile and for deployment and use in response to a potential or actual public health event. As a result of this expansion, it became essential for CDC to prepare and submit, in a timely manner, high-quality IND and IDE documents to FDA. RA is the entity within CDC responsible for centralizing and ensuring CDC's consistency in submissions and communications with FDA. RA fulfills its responsibilities of ensuring appropriate regulatory mechanisms for stockpiling, deployment, and use of investigational medical countermeasures. Additionally, RA ensures compliance with laws and regulations (applicable parts under Code of Federal Regulations Title 21) enforced by FDA, which are delivered through the specific activities of but not limited to coordinating, drafting, reviewing, submitting, and maintaining the applications regulated by FDA [e.g., IND, IDE, EUA, 510(k)]. These activities ensure that the deployment and use of Strategic National Stockpile investigational medical countermeasures and other medical countermeasures only available through CDC (e.g., therapeutics for rare diseases in the United States such as parasitic and tropical diseases) adhere to FDA regulations.

The first member of RA was a pharmacist (Debra Yeskey, PharmD). Currently, the RA staff consists of nine individuals from various backgrounds, including regulatory, pharmacy, immunology, microbiology, and public health, among others. The RA staff functions as a team and collaboratively develops the protocols and applications for submission to FDA. Three of the nine members of RA are pharmacists and bring unique

perspectives to the development of protocols by providing guidance for drug therapy and special considerations for adverse event and patient monitoring.

Roles in disaster preparedness

CDC has been tasked by HHS with the critical oversight of ensuring availability and use of medical countermeasures against CBRN and emerging threats. RA, in coordination with CDC subject matter experts, supports this task by initiating and developing protocols, executive summaries, fact sheets and related supportive documents required for regulatory mechanisms, such as INDs, EUAs, and IDEs. RA serves as CDC's authorized representative on submissions to FDA and as CDC's representative at HHS Integrated Product Team Meetings (i.e., smallpox, anthrax, botulism, radiation/nuclear) and participates at HHS EUA Working Group meetings.

To better prepare for large-scale emergencies, the Project BioShield Act of 2004 included language for section 564 of the Federal Food, Drug, and Cosmetic Act, which establishes the EUA in a provision titled Authorization for Medical Products for Use in Emergencies. The provision permits the FDA commissioner, upon a declaration of an emergency by the Secretary of HHS, to authorize the use of unapproved products or unapproved uses of approved products for the diagnosis, treatment, or prevention of serious or life-threatening diseases caused by CBRN agents and for which no adequate, approved, or available alternatives exist. The following is a recent example of RA's use of the EUA mechanism.

Role in 2009 H1N1 emergency

In response to the 2009 H1N1 virus, on April 24, 2009, RA mobilized quickly to initiate, draft, and submit multiple EUA requests for deployment and use of medical countermeasures, including those from the Strategic National Stockpile and CDC Influenza Division. Consequently, RA convened with Subject Matter Experts in the CDC Emergency Operations Center to initiate and develop five EUA requests. Each EUA request required submission of an executive summary, which includes a justification for clinical use, a fact sheet for health care providers, and a fact sheet for patients and parents/caregivers. The declaration of a public health emergency involving 2009 H1N1 was made by the Secretary of HHS on April 26, 2009. In the span of 48 hours, RA submitted the five EUA requests that were authorized by FDA for emergency use: N95 respirators (various models), oseltamivir capsules and oral suspension (Tamiflu—Hoffman-La Roche), zanamivir inhalation powder (Relenza—GlaxoSmithKline), and two CDC-developed diagnostic devices. The EUAs issued by the FDA Commissioner allowed the initial deployment of 25% pro rata of Strategic National Stockpile products to affected states in order to augment the state supply of these medical countermeasures[1] and allowed CDC to distribute the diagnostic devices to public health and other qualified laboratories. Furthermore, the FDA-authorized fact sheets provided tangible education materials to health care providers and recipients for each medical countermeasure used.

Under the EUA for N95 respirators, FDA authorized four models of respirators for use by the general public to help reduce the wearer's exposure to airborne germs during the public health medical emergency. ("General public" is a broad term and includes people performing work-related duties.) If respirators are used for people performing work-related duties, employers must comply with the Occupational Safety and Health Administration's Respiratory Protection Standard (29 CFR 1910.134; see www.osha.gov for more information). The EUAs for oseltamivir and zanamivir allow the approved products to be used for unapproved indications. The EUAs allow these products to be used in patients who are symptomatic for more than 2 days and in patients who have complicated illness requiring hospitalization. The EUA for oseltamivir also extended product use to include an unapproved population by authorizing and providing dosing recommendations for pediatric patients younger than 1 year of age. Additionally, given the potential product shortage, the EUAs allowed extended use of certain lots of oseltamivir and zanamivir products beyond their labeled expiry dates based on FDA review of supportive stability and potency data (additional details regarding expired product available at www.fda.gov/NewsEvents/PublicHealthFocus/ucm154962.htm). When 2009 H1N1 virus appeared, no FDA-approved/cleared tests were available in the United States that identified the existence of 2009 H1N1 virus in clinical specimens. The EUA for the CDC Swine Influenza Virus Real-time RT-PCR Detection Panel allowed for the diagnosis of 2009 H1N1 virus. In addition, an EUA for another diagnostic test, the CDC Human Influenza Virus Real-time RT-PCR Detection and Characterization Panel for Respiratory Specimens (NPS, NS, TS, NPS/TS, NA) and Viral Culture allows for the in vitro qualitative detection of influenza types A and B and influenza A H1 (seasonal) and H3 subtypes in nasopharyngeal swabs (NPS), nasal swabs (NS), throat swabs (TS), and/or dual NPS/TS swab specimens and nasal aspirates (NA) from patients with signs and symptoms of respiratory infection and/or from viral culture. Further detail describing each EUA, including copies of the FDA-authorized fact sheets, can be found at www.cdc.gov/h1n1flu/eua.

Given the absence of an FDA-licensed intravenous neuraminidase inhibitor for teating severe, complicated influenza, on October 23, 2009, FDA authorized emergency use of peramivir. The EUA allows peramivir, an investigational product under development by the manufacturer, to be used for treating certain hospitalized adult and pediatric patients with suspected or confirmed cases of 2009 H1N1. The EUA also allows health care providers to use peramivir, subject to specified conditions (shown at www.cdc.gov/h1n1flu/eua/peramivir.htm). CDC is the sponsor of this EUA and is responsible for the distribution of peramivir under the EUA. This EUA is the sixth request that CDC submitted to FDA in response to the 2009 H1N1 outbreak.

In addition to the development and submission of the above EUA requests, RA created the CDC EUA website (www.cdc.gov/h1n1flu/eua) to provide essential information relating to FDA-issued EUAs and to organize all of the EUA-related materials for educating outside audiences such as state/local health de-

partments, health care personnel, and the general public about EUAs. At the time of this writing, it has received more than 360,000 visits and was still being viewed daily.

Applicability to pharmacists

Of particular interest to pharmacists, RA monitored the need to implement revisions to oseltamivir fact sheets for health care providers and patients and parents/caregivers because of potential dosage administration errors for oseltamivir oral suspension in pediatrics.[2] In addition, because a potential shortage of oseltamivir suspension existed, compounding instructions were also considered.

Given the lack of a general awareness and understanding of an EUA before the 2009 H1N1 public health emergency declaration, the CDC EUA website serves as an educational resource for health care providers and the general public by posting essential information regarding legal and regulatory aspects of an EUA, specific product-related information, and answers to potential questions regarding acquisition and administration of product. RA was also involved in the development of an electronic system through which health care providers may request peramivir under the EUA, which has facilitated access to this medical countermeasure for hospitals around the nation.

Although influenza activity caused by the 2009 H1N1 or seasonal influenza viruses may rise and fall, incidence is expected to persist for several more months.[3] If this occurs, RA response efforts during this public health emergency would continue to be used because new states/local health department personnel, clinicians, and patients affected by the virus may be receiving medical countermeasures under EUA and turn to the website for EUA-specific materials. Also, RA will continue its response to the pandemic by requesting additional EUAs for medical countermeasures procured for distribution by CDC.

Opportunities for pharmacists

Pharmacists can learn more about emergency response and preparedness activities that help strengthen national, state, and local efforts to prevent or respond to emergencies at http://emergency.cdc.gov. In addition, those interested in furthering their knowledge of regulatory compliance can seek graduate education programs that focus on regulatory affairs.

Additional information

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