Federal Legal Preparedness Tools for Facilitating Medical Countermeasure Use during Public Health Emergencies

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Introduction
Law can greatly facilitate responses to public health emergencies, including naturally-occurring infectious disease outbreaks and intentional or accidental exposures to chemical, biological, radiological, or nuclear (CBRN) agents. At the federal level, the Secretary of the Department of Health and Human Services (HHS), as the lead for federal public health and medical responses to public health emergencies and incidents, has a range of authorities to support federal, state, tribal, local, and territorial responses. For example, under the Public Health Service (PHS) Act, the Secretary may provide temporary assistance to States to meet health emergency needs or deploy medicine and supplies from the Strategic National Stockpile. The Secretary also may determine that a disease or disorder presents a public health emergency, which may be the first step in triggering other critical legal authorities for response. Since the 2001 anthrax attacks, one focus of public health preparedness has been on developing, distributing, and rapidly dispensing medical countermeasures (MCMs) for CBRN emergencies and pandemics. MCMs include drugs, biologics (e.g., vaccines), and devices (e.g., diagnostics) “used to prevent, mitigate, or treat the adverse health effects of an intentional, accidental, or naturally occurring public health emergency.” Planning for and responding to emergencies involving MCMs raise often complex legal questions among government and private sector actors, including concerns about emergency legal authorities, liability, emergency use of regulated medical products, and regulations that might enhance or hinder public health response goals.

This article addresses federal legal authorities used to facilitate MCM development, distribution, and use in a public health emergency, including liability protections under the Public Readiness and Emergency Preparedness (PREP) Act and emergency use under the Food and Drug Administration’s (FDA) Investigational New Drug (IND) and Emergency Use Authorization (EUA) mechanisms. Conditions for using these tools and examples of how they have been used to support pre-event (e.g., mass dispensing preparedness) and intra-event (e.g., 2009 H1N1 influenza pandemic) response activities are also discussed.

PREP Act Liability Protections for MCM Activities
Enacted in 2005, the PREP Act amended the PHS Act to address liability concerns related to the manufacture, testing, development, distribution, administration, and use of MCMs for diseases, health conditions, or threats to health that constitute a public health emergency or credible risk of a future health emergency. To trigger PREP Act protections, the Secretary must issue a PREP Act declaration recommending manufacture, testing, development, distribution, administration, or use of an MCM and stating that liability immunity is in effect for those activities under conditions stated in the declaration. A PREP Act declaration is distinct from a public health emergency determination, and may be made in advance of
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including death; physical, mental, or emotional injury, or fear of such injury; property damage or loss; or business interruption. The full range of MCM actors are protected: manufacturers; distributors; program planners (State, local, and tribal governments and others who supervise or administer MCM programs, including the private sector); qualified persons (licensed health professionals and others identified by the Secretary to prescribe, administer, or dispense MCMs, including volunteers); officials, agents, and employees of the above; and the United States. Covered MCMs include qualified pandemic or epidemic products; security countermeasures for CBRN agents; and products to address adverse effects of or enhance use and effect of such drugs, biological products, or devices and must be: (1) approved, cleared, or licensed under the Federal Food, Drug, and Cosmetic (FD&C) Act or the PHS Act; (2) allowed for investigational use under the FD&C Act; or (3) authorized under an EUA.

Seven PREP Act declarations are currently in effect, covering pandemic influenza vaccines, antivirals, diagnostics, and respiratory protection and support devices; and countermeasures for anthrax, smallpox, acute radiation syndrome, and botulism. Each declaration provides liability immunity for two types of MCM initiatives: recommended activities related to a federal award or arrangement; or any activity that is part of the public health and medical response of the federal, State, local, tribal, or other authority having jurisdiction to respond following any federal, State, local, or other declaration of an emergency. In this way, the declarations support preparedness, such as federally-supported clinical trials and the National Postal Model (NPM), and emergency response, such as mass dispensing through points of dispensing (PODs) and school vaccination clinics. The PREP Act declarations for pandemic influenza MCMs were the first to be used broadly, providing protections in preparation for an outbreak for manufacturers and developers conducting testing and clinical trials of vaccines, and to a broad array of responders who administered H1N1 vaccines and antivirals, including States, local governments, private health care providers, and volunteers.

The PREP Act also authorized the Countermeasures Injury Compensation Program (CICP). When the HHS Secretary issues a PREP Act declaration, and Congress appropriates funds, HHS may provide compensation to individuals for serious physical injuries or deaths directly caused by administration or use of covered MCMs, including medical expenses, lost wages, and survivor death benefits. The CICP received funding in 2009. Current claims predominantly relate to H1N1 pandemic influenza vaccination.

Emergency Use of Medical Countermeasures

For public health emergencies necessitating MCMs, approved MCMs ideally would be available without the need to use unapproved products. However, even with approved products, response challenges can emerge, especially when large populations are impacted and the timing of MCM provision is critical. For example, approved MCMs might be accompanied by emergency use instructions that are not part of the product’s approved labeling, have extended expiry dating, or be dispensed without an individual prescription. In other circumstances, MCMs might be intended to be used during emergencies in ways that are beyond their FDA-approved indications (e.g., for a new age group). Or, some countermeasures needed for the response might not be approved for any use. In such cases, special legal preparedness mechanisms, including INDs and EUAs, are needed to help ensure that MCMs can be rapidly distributed and dispensed to impacted populations, while also ensuring that appropriate patient safeguards and legal protections (including PREP Act protection, when applicable) are available.

Investigational New Drug Application

To be used in human testing, in most cases a drug must be covered by an IND and a device must be cov-
Due to the investigational status of such products, specific patient safeguards, including institutional review board (IRB) approval, informed consent, and protocols for use, are required. INDs and IDEs can also be used during public health emergencies to facilitate access to investigational and unapproved products needed for responses, such as when little or no safety data exist to enable FDA to make the risk-benefit assessment needed for EUA issuance. Several mechanisms can provide patients with serious or immediately life-threatening diseases or conditions expanded access to investigational products outside of a clinical trial under an IND, depending in part on the patient population size. An emergency declaration is not needed to use these mechanisms, which are typically most appropriate for smaller-scale events.

**Emergency Use Authorization**

Another legal tool FDA can use to facilitate MCM use during emergencies is the EUA. Under the FD&C Act, the FDA Commissioner may, after certain statutory criteria are met, authorize for emergency use: (1) unapproved medical products; or (2) unapproved uses of FDA-approved medical products. An EUA is an authorization for certain uses of MCMs during specified emergencies and is not a form of product approval.

The reasons for using the EUA mechanism vary. Investigational products or unapproved indications of approved drugs might be the best available MCMs for the emergency. However, certain FDA requirements for investigational products, such as informed consent under an IND, might be difficult to meet in emergency scenarios. Also, certain MCM emergency uses, such as dispensing without a prescription at a POD or providing emergency information not part of the product’s approved labeling, might be interpreted as violating the FD&C Act. Further, the PREP Act may provide important liability protections that could be jeopardized if the product is not used as approved or as authorized under an EUA.

FDA leads EUA efforts in close collaboration with federal partners. Typically, the issuance process begins with FDA receiving an EUA request from a federal partner or manufacturer. Before the FDA Commissioner can issue an EUA, three steps are required: (1) one of three emergency determinations related to CBRN agents or the identification of a specified material threat must be made; (2) the HHS Secretary must declare that an emergency or threat exists justifying the emergency authorized use of the product; and (3) criteria for issuance of the EUA itself must be met (including existence of a serious or life-threatening disease or condition caused by a CBRN agent; reasonable belief the product may be effective and its known and potential benefits outweigh its known and potential risks; and no adequate, approved alternative to the product being available).

Each EUA includes “conditions of authorization” unique to the product being authorized. For example, the conditions might require that specific product information be provided to recipients. They might also waive certain regulatory requirements (e.g., by allowing specified deviations in storage temperatures during a response) that otherwise could render the product’s distribution illegal. EUAs may be amended after issuance, and are effective until revoked or the HHS declaration justifying the authorization is terminated.

Most EUA activity occurred during the 2009 H1N1 influenza pandemic, when FDA issued numerous EUAs for antiviral drugs (including the first EUA for an unapproved product), diagnostic devices, and personal protective equipment; all of these EUAs have terminated. An EUA was not needed for H1N1 vaccine because it was licensed. In 2011, FDA issued two EUAs for doxycycline for inhalational anthrax...
post-exposure prophylaxis (PEP). These EUAs could be issued in advance of an actual anthrax emergency because of an existing anthrax emergency determination and declaration justifying emergency use of the product. While doxycycline is approved for inhalational anthrax PEP, these EUAs were needed at the time because certain aspects of emergency distribution, dispensing, and use could have been interpreted as violating the FD&C Act's adulteration and misbranding provisions.

FDA issued the doxycycline mass dispensing EUA to support a range of anthrax preparedness and response activities. It covers all oral formulations of doxycycline products and incorporates planning and response flexibilities, including storing product pre-event and dispensing partial supplies (e.g., 10 days) without a prescription. To ensure appropriate oversight for these activities, this EUA specifically defines the "stakeholders" who may act under the authorization. The other EUA supports the NPM, whereby volunteer Postal employees would deliver antibiotics to households in response to an anthrax attack. The authorization, which covers pre-positioned kits containing 10-day supplies of doxycycline in unit-of-use bottles in a special bag with emergency instructions that are not part of the approved labeling, further demonstrates the flexibilities an EUA can allow.

Because timely MCM access is often a critical component of public health emergency responses, FDA is also engaged with its partners in pre-EUA activity. This involves FDA review of submitted product data prior to a formal EUA request. Pre-EUA efforts are important for preparedness since an EUA cannot be issued until the requisite emergency determination and declaration are in place and criteria for issuance are met.

Conclusion

Significant strides in public health legal preparedness have been made since 2001. The 2009 H1N1 pandemic response and other preparedness efforts (e.g., anthrax) have served as the first major tests of public health preparedness tools will continue to evolve to meet such challenges.

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References

2. 42 U.S.C. §§ 243(c), 247d-6b(a); §§ 311 and 319F-2 of the PHS Act.
6. Liability immunity means that no legal claim can be filed. Both federal and State claims are precluded, as the PREP Act contains an express preemption of State law. 42 U.S.C. § 247d-6d(b)(8); § 319F-3(b)(8) of the PHS Act. The declaration must include provisions describing the scope of liability immunity provided, including the following: the category of disease, health condition, or threat to health for which the Secretary recommends MCM; effective time period that the declaration is in effect; target population; geographic area for administration; any limitations on means of distribution; and additional persons qualified to prescribe, administer, or dispense the MCM. 42 U.S.C. § 247d-6d(b)(2), (i)(8); § 319F-3(b)(2), (i)(8) of the PHS Act.
7. Administration includes actual provision of an MCM to a patient and activities directly related to management and operation of programs or facilities for MCM delivery, distribution, and dispensing. This definition appears in declarations issued by the HHS Secretary. See U.S. Department of Health and Human Services, Public Readiness and Emergency Preparedness Act, available at <http://www.phe.gov/Preparedness/legal/prepare/Pages/default.aspx> (last visited January 3, 2013). Although the term is not defined in the Act, the Secretary interprets the term to mean that, when a declaration is in effect, the Act precludes, for example, liability claims alleging negligence by a manufacturer in creating a vaccine, or negligence by a health care provider in prescribing the wrong dose, absent willful misconduct. Likewise, the Act precludes a liability claim relating to the management and operation of a countermeasure distribution program or site, such as a slip-and-fall injury or vehicle collision by a recipient receiving a countermeasure at a retail store serving as an administration or dispensing location that alleges, for example, lax security or chaotic crowd control. However, a liability claim alleging an injury occurring at the site that was not directly related to the countermeasure activities is not covered, such as a slip and fall
with no direct connection to the countermeasure's administration or use. In each case, whether immunity is applicable will depend on the particular facts and circumstances. U.S. Department of Health and Human Services, “Pandemic Influenza Vaccines – Amendment," Federal Register 77 (March 6, 2012): 13329. The only exception to this broad protection is when claims arise from willful misconduct, a standard more stringent than any form of negligence or recklessness. 42 U.S.C. § 247d-6(d); § 319F-3(c) of the PHS Act.

8. 42 U.S.C. § 247d-6(d); § 319F-3(1) of the PHS Act as amended by section 402(g) of the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013.


10. Two lawsuits challenging PREP Act coverage of H1N1 pandemic influenza vaccination have been filed in state courts. In Parker v. St. Lawrence County Public Health Department, 554 N.Y.S. 2d 239 (November 21, 2012), the plaintiff claimed that a nurse employed by the county committed negligence and battery by vaccinating her child during a school vaccination clinic without parental informed consent. The trial court upheld the plaintiff’s claims, asserting that Congress had not intended to preclude informed consent claims under the PREP Act. The appellate court dismissed the case for lack of subject matter jurisdiction, finding that the preemption provision and public liability protections under the PREP Act preempted such claims. The court observed that the PREP Act provides alternate remedies under the Countermeasures Injury Compensation Program and a federal cause of action for willful misconduct claims. The court noted that “we must presume that Congress fully understood that errors in administering a vaccination program may have physical as well as emotional consequences, and determined that such potential tort liability must give way to the need to promptly and efficiently respond to a pandemic or other public health emergency.”Id. In Kehlery v. Hood, 2012 WL 1945952 (E.D. Mo) 4:11CV1416 (May 30, 2012), the U.S. district court dismissed third-party claims against the H1N1 pandemic vaccine manufacturer for lack of subject matter jurisdiction, noting that the parties agreed that the PREP Act precluded such claims and pointing out that the statute provides exclusive jurisdiction to hear federal claims under the PREP Act to the U.S. District Court for the District of Columbia. The district court remanded to state court remaining negligence claims against the physician who administered the vaccine to the adult plaintiff. A decision on that case was still pending as of the date of this article.


12. “The CICP covers only the monovalent version of the 2009 H1N1 vaccine. The 2009 H1N1 virus was included in the 2010-11 seasonal flu vaccine, which is covered by the VICP [Vaccine Injury Compensation Program].” Claims have also been filed for other countermeasures, including anthrax and smallpox vaccines. R. Roos, “HHS: 386 Injury Claims Filed over H1N1 Countermeasures," CIDRAP News, March 16, 2011, available at <http://www.cidrap.umn.edu/cidrap/content/influenza/swine-flu/news/mar1611claims.html> (last visited January 3, 2013).

13. FDAs authorities to regulate medical products, including reviewing and approving products, enforcing FDAs laws and regulations, and communicating important product information to the public and health care practitioners, are derived from the FD&C Act and the PHS Act. See 21 U.S.C. § 301 et seq.; 21 C.F.R. (Food and Drugs); 42 U.S.C. § 262; 21 C.F.R. § 601.2(a).


15. 21 C.F.R. Part 312 (2011). “Current Federal law requires that a drug be the subject of an approved marketing application before it is transported or distributed across state lines. Because a sponsor will probably want to ship the investigational drug to clinical investigators in many states, it must seek an exemption from that legal requirement. The IND is the means through which the sponsor technically obtains this exemption from the FDA. During a new drug’s early preclinical development, the sponsor’s primary goal is to determine if the product is reasonably safe for initial use in humans, and if the compound exhibits pharmacological activity that justifies commercial development.” Food and Drug Administration, Investigational New Drug (IND) Application, available at <http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ ApprovalApplications/InvestigationalNewDrugINDApplication/default.htm> (last visited January 3, 2013).


18. The HHS Secretary may make a declaration that the circumstances exist justifying a product’s emergency authorization based on: (1) a determination by the Secretary of Homeland Security that there is a domestic emergency, or a significant potential for a domestic emergency, involving a heightened risk of attack with a CBRN agent or agents; or (2) a determination by the Secretary of Defense that there is a military emergency, or a significant potential for a military emergency, involving a heightened risk to United States military forces of attack with a CBRN agent or agents; or (3) a determination by the HHS Secretary that there is a public health emergency.
or a significant potential for a public health emergency, that affects, or has a significant potential to affect, national security or the health and security of United States citizens living abroad, and that involves a CBRN agent or agents, or a disease or condition that may be attributable to such agent(s); or (4) the identification of a material threat pursuant to section 319F–2 of the PHS Act sufficient to affect national security or the health and security of United States citizens living abroad.


22. “The term ‘stakeholder(s)’ means the public agency or its delegate that has legal responsibility and authority for responding to an incident, based on political or geographical, e.g., city, county, tribal, State, or Federal boundary lines, or functional, e.g., law enforcement or public health range or sphere of authority to prescribe, administer, deliver, distribute, or dispense doxycycline in an emergency situation.” See Food and Drug Administration, “Authorization of Emergency Use of Oral Formulations of Doxycycline; Availability,” supra note 20.


24. Provision of kits is limited to eligible United States Postal Service (USPS) employees and their household members. See Food and Drug Administration, supra note 22.

25. FDA, for example, has been working to address these challenges, primarily through the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013, Public Law 113-5, which was signed into law by the President on March 13, 2013. For recent FDA developments on this law and EUAs, see Food and Drug Administration, Medical Countermeasures Initiative, available at <http://www.fda.gov/medical-countermeasures> (last visited March 19, 2013).