DISPENSING MEDICAL COUNTERMEASURES: EMERGENCY USE AUTHORITIES AND LIABILITY PROTECTIONS

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The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) enhances emergency use authorities with respect to both approved and unapproved medical countermeasures (MCMs). PAHPRA authorities can also be critical to preserving tort liability protections for public health stakeholders, since these protections are often contingent upon appropriate authorizations for the MCMs utilized. This article details the evolution of emergency use authorities and liability protections, analyzes how these separate legal doctrines can intersect in practice, and discusses implications for facilitating preparedness and response activities and for protecting associated personnel.

MEDICAL COUNTERMEASURE (MCM) DISPENSING is a core public health preparedness capability.¹ Modalities for mass dispensing in an emergency inevitably raise legal concerns among personnel designated to participate in dispensing operations. Effectively addressing these concerns as a component of training for individuals tasked to dispense MCMs or assist with related activities, such as supporting a point of dispensing (POD), can help bolster the readiness of response staff and thereby enhance community preparedness for emergencies involving emerging infectious diseases or chemical, biological, radiological, or nuclear (CBRN) agents.

While legal considerations vary according to the dispensing modality used and the category of individuals mobilized to support the process, 2 recurring issues often elicit anxiety among participants in mass dispensing schemes. These concerns involve the authority to dispense specified MCMs and the attendant tort liability assumed by members of the dispensing team. This article provides an overview of these dual legal concepts and an explanation of how they can intersect. It also analyzes how recently enacted legislation has strengthened certain preparedness and response authorities regarding the use of MCMs for emergencies.

EMERGENCY USE OF MCMs

Historically, the sole mechanisms for the large-scale use of drugs, devices, and biological products regulated by the Food and Drug Administration (FDA) were traditional FDA approval, clearance, or licensure or, alternatively, an investigational new drug (IND) application or investigational device exemption (IDE).² Over the past decade, 2 other legal pathways have emerged to facilitate emergency uses of MCMs: Emergency Use Authorizations (EUAs) and additional emergency use authorities for certain activities involving FDA-approved products.³ This section explains the current statutory and regulatory framework for the use of MCMs during emergencies (Table 1).

Expanded Access to Investigational Products

As a general rule, the use of an investigational drug, biologic, or medical device, or the investigational use of an approved product, requires authorization from FDA via an

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Table 1. Legal Paradigms for Emergency Use of MCMs

Category	Context	Authority
Investigational drugs and devices	Expanded access for ill patients to experimental products	21 CFR 312.300-320 (IND) 21 CFR 812.36 (IDE)
Emergency use authorization	Actual or potential emergency involving specified agents justifying the use of an unapproved medical product or the unapproved use of an approved medical product	21 USC 360bbb-3
Emergency use of medical products	Preparedness and response activities involving approved, cleared, or licensed medical products before or during an emergency involving specified agents	21 USC 360bbb-3a 21 USC 355-1

Note. MCM, medical countermeasure; CFR, Code of Federal Regulations; IND, Investigational New Drug application; IDE, Investigational Device Exemption; USC, United States Code.

IND or IDE.⁴ An investigational new drug is a drug or biologic “that is used in a clinical investigation,”⁵ while an investigational device is a device that is “the object of an investigation.”⁶ Investigational use of an approved product denotes its use “in the context of a clinical study protocol.”⁴ Investigational use differs from the “off-label” use of an approved product by a physician, in the course of medical practice, for an unapproved indication or in unapproved doses or patient populations. Off-label use on a patient-by-patient basis is part of the practice of medicine, which FDA does not typically regulate.⁷ In contrast, FDA’s broad regulatory authority encompasses, among other responsibilities, “assuring the safety, efficacy and security” of human and veterinary drugs, medical devices, and biological products.⁸

In the context of investigational drugs, expanded access—also referred to as *treatment use*—refers to their use “when the primary purpose is to diagnose, monitor, or treat a patient’s disease or condition,”⁹ rather than “to obtain information about [their] safety or effectiveness.”¹⁰ Under FDA regulations published in 2009,¹¹ there are currently 3 categories of expanded access, depending on the size of the patient population (Table 2). These are: expanded access for individual patients, including for emergency use;¹² expanded access for intermediate-size patient populations (ie, more than one patient);¹³ and expanded access for large patient populations under a treatment IND or protocol.¹⁴ “For administrative purposes,” FDA further breaks down the 3 expanded access categories into 8 subcategories of access submissions.¹⁰

Each expanded access category for investigational drugs includes its own special requirements.¹²⁻¹⁴ With respect to access for an individual patient, the patient’s physician must conclude that “the probable risk” posed by the drug is “not greater than” that posed by the person’s disease or condition, and FDA must find that the patient cannot obtain the drug under an existing clinical trial or expanded access program.¹² Thus, regardless of who sponsors the expanded access submission for an individual patient, that patient “can obtain access to the investigational drug only through a licensed physician.”¹⁰ Treatment use for an intermediate-size group requires “enough evidence” of the

drug’s safety to justify a clinical trial in a similar-size patient population, along with “at least preliminary clinical evidence” of the drug’s effectiveness or plausible effect to render it a “reasonable therapeutic option” in its anticipated expanded access use.¹¹ Widespread treatment use is predicated on specific conditions regarding the drug’s trial and marketing status, as well as the state of evidence on its safety and effectiveness.¹²

Moreover, for all 3 types of expanded access, FDA must determine that 3 criteria are met. First, the patient population must have “a serious or immediately life-threatening disease or condition” and no other comparable or satisfactory therapeutic alternatives. Second, FDA must conclude that “the potential patient benefit justifies the potential risks of the treatment use,” which are deemed not to be “unreasonable in the context of the disease or condition to be treated.”¹⁵ Finally, providing expanded access to the investigational drug for the requested use must not interfere with anticipated or ongoing clinical investigations that could support marketing approval of the product or otherwise compromise its potential development.¹⁵ To ensure these general criteria are met—along with the criteria specific to each type of expanded access—the requirements for all expanded access categories specify that the submission must include “information adequate” to demonstrate to FDA’s satisfaction that the regulatory prerequisites are satisfied.¹²⁻¹⁴

The treatment use of both investigational drugs and investigational devices is designed to facilitate the availability of experimental products for patients with “serious or immediately life-threatening” ailments^{15,16} (ie, “desperately ill”¹⁶ patients) who lack other viable therapeutic options. A “serious” disease or condition is defined as one “associated with morbidity that has substantial impact on day-to-day functioning.”⁹ “Immediately life threatening” means a stage of disease with a “reasonable likelihood that death will occur within a matter of months or in which premature death is likely without early treatment.”^{9,16}

In some cases, these expanded access mechanisms may provide an appropriate route for use of an unapproved or investigational product during a public health emergency. The IND process has been used in the past in preparation

Table 2. Categories of Expanded Access to Investigational Drugs for Treatment Use

<i>Patient Population Size</i>	<i>Criteria</i>	<i>Authority</i>
Individual patients, including for emergency use	<i>FDA determinations:</i>	21 CFR 312.310
	Patient cannot obtain drug under another IND/protocol; Serious/immediately life-threatening disease/condition; No comparable/satisfactory alternative therapy; Potential patient benefit justifies potential risks; Potential risks not unreasonable re: disease/condition; Not impede investigations or compromise development. <i>Physician determination:</i> Probable risk (drug) not greater than probable risk (disease/condition).	21 CFR 312.305
Intermediate size	<i>FDA determinations:</i>	21 CFR 312.315
	Enough safety evidence to justify a similar-size clinical trial; Reasonable therapeutic option per effectiveness evidence; Serious/immediately life-threatening disease/condition; No comparable/satisfactory alternative therapy; Potential patient benefit justifies potential risks; Potential risks not unreasonable re: disease/condition; Not impede investigations or compromise development.	21 CFR 312.305
Treatment IND or treatment protocol	<i>FDA determinations:</i>	21 CFR 312.320
	Drug being investigated under IND or trials completed; Sponsor actively pursuing approval with due diligence; For serious disease/condition— Sufficient clinical evidence of safety and effectiveness; For immediately life-threatening disease/condition— Available scientific evidence affords reasonable basis that drug may be effective & would not pose unreasonable/significant risk; Serious/immediately life-threatening disease/condition; No comparable/satisfactory alternative therapy; Potential patient benefit justifies potential risks; Potential risks not unreasonable re: disease/condition; Not impede investigations or compromise development.	21 CFR 312.305

Note. FDA, US Food and Drug Administration; CFR, Code of Federal Regulations; IND, Investigational New Drug application.

for certain contingencies, particularly by the Department of Defense (DoD) in the lead-up to the Persian Gulf War and the Centers for Disease Control and Prevention (CDC) with respect to assembling the Strategic National Stockpile.¹⁷ No emergency determination or declaration is required to invoke the expanded access procedures.¹⁸ For example, “when little or no safety data exist” to enable the risk-benefit assessment required for FDA to issue an EUA (discussed in the next subsection), an expanded access submission may present the most viable option for facilitating the availability of needed products.^{3,18} However, as the size of the population contemplated for treatment use of an investigational drug increases from an individual patient to intermediate and large groups, the preauthorization requirements for evidence of demonstrated safety and efficacy ratchet up correspondingly.¹²⁻¹⁴

The IND paradigm can prove unwieldy and ill-suited to public health preparedness because of its inherent nature as a clinical research tool.¹⁷ Even outside a clinical trial in the context of treatment use, the aim of compassion in facilitating access for those in need must be balanced with the imperative both to “protect patients and preserve the ability

to develop meaningful data about the use of the drug.”¹⁰ All expanded access categories, including for individual patients, require full Institutional Review Board (IRB) review, informed consent documentation, and FDA reporting.¹⁹ These vital safeguards are appropriately geared toward the protection of human research subjects rather than the rapid deployment of MCMs, and they can be difficult to satisfy under emergency conditions.¹⁸

The application and approval process for sponsors and investigators is not tailored to meet the exigencies of a national emergency because it was not developed for that purpose. Leveraging expanded access to respond to public health emergencies is, when possible, therefore “typically most appropriate for smaller-scale events.”¹⁸ In contrast to its public health connotation, the concept of “emergency use” of investigational drugs is a subset of expanded access for individual patients,¹² wherein a life-threatening situation provides insufficient time to obtain prospective IRB approval for “use of a test article on a human subject.”²⁰ The exigent situation justifying emergency procedures¹² centers on the threat to one person, rather than a risk posed to the public at large.

Genesis and Modification of the EUA Authority

In his 2003 State of the Union address, President George W. Bush proposed Project Bioshield, “a major research and production effort” to field MCMs against CBRN threats.²¹ The Project Bioshield Act of 2004, enacted by Congress in response, instituted several measures to encourage MCM development.²² Among these initiatives was an alternative legal pathway to facilitate MCM availability during public health emergencies, alongside the aforementioned steady-state mechanisms of traditional approval and IND or IDE applications. Specifically, the 2004 statute amended Section 564 of the Federal Food, Drug, and Cosmetic (FD&C) Act to enable the secretary of the Department of Health and Human Services (HHS) to permit the emergency use of FDA-regulated products that are either unapproved or approved only for other uses.²³

The issuance of such an Emergency Use Authorization (EUA) requires a 3-step approach (Table 3).² The first action is a relevant determination, whereby the secretary of the Department of Homeland Security (DHS), DoD, or HHS pronounces the existence of (or significant potential for) a qualifying domestic, military, or public health emergency, respectively. The DHS or DoD determination of a domestic or military emergency, or significant potential thereof, must involve a “heightened risk” of attack with a CBRN agent or agents against either the United States or its military forces. The HHS determination of an actual or potential public health emergency must involve either a CBRN agent or agents, or a “disease or condition that may be attributable” to such agent(s).²³ The Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) amended the EUA authority so that the determination of a public health emergency by the HHS secretary no longer requires a full-fledged public health emergency declaration under Section 319 of the Public Health Service (PHS) Act.^{24,25} Moreover, the HHS determination can now take into account either “national security or the health and security of United States citizens

living abroad.”²³ Together, these recent changes increase secretarial flexibility with regard to the determinations required for EUA issuance.²⁵

In addition, PAHPRA included a Material Threat Determination (MTD) by the DHS secretary as another type of determination that can satisfy the EUA prerequisites.²⁴ In issuing an MTD as authorized by the Project Bioshield Act, the DHS secretary assesses and identifies—in consultation with the HHS secretary and other agencies as appropriate—which CBRN agents present a material threat against the country “sufficient to affect national security.”²⁶ For purposes of EUA issuance, PAHPRA expands the scope of material threats to also include those affecting “the health and security” of US citizens “living abroad.”²⁴ The MTD authority, which is still used to prioritize MCM procurements,²⁶ can now also constitute a basis for invoking the EUA process.

The second step required for EUA issuance is a declaration from the HHS secretary, based on a relevant determination discussed above, that circumstances exist justifying an EUA for a particular product. The declaration references both the relevant threat determination and a product for which emergency use is justified.² Such declarations used to last for a maximum of 1 year and require regular renewals if the situation continued to warrant EUA coverage.²² PAHPRA extended the lifespan of EUA declarations until either the circumstances underlying the supporting secretarial determination or the approval status of the product itself render the declaration obsolete.^{24,25}

Finally, the FDA commissioner, acting under delegated authority from the HHS secretary,²⁷ may issue the EUA after satisfying certain criteria and consulting (to the extent feasible) with the director of CDC, the director of the National Institutes of Health (NIH), and the HHS Assistant Secretary for Preparedness and Response (ASPR).²³ In order to issue the EUA, the FDA commissioner must conclude: (1) that an agent referenced in the HHS declaration “can cause a serious or life-threatening disease or condition”; (2) that it is reasonable to believe based on the totality of available scientific evidence that the product may be effective in diagnosing, treating, or preventing such disease or

Table 3. EUA Issuance Process

<i>Action</i>	<i>Agency</i>	<i>Authority</i>
Determination		
Domestic emergency (or significant potential thereof)	DHS	21 USC 360bbb-3(b)(1)(A)
Military emergency (or significant potential thereof)	DoD	21 USC 360bbb-3(b)(1)(B)
Public health emergency (or significant potential thereof)	HHS	21 USC 360bbb-3(b)(1)(C)
Identification of material threat	DHS	21 USC 360bbb-3(b)(1)(D) / 42 USC 247d-6b(c)(2)
Declaration	HHS	21 USC 360bbb-3(b)(1)
Issuance after appropriate consultation with ASPR, NIH, CDC (to the extent feasible and appropriate given circumstances) if criteria for issuance are met	HHS/FDA	21 USC 360bbb-3(c) / HHS delegation to FDA

Note. EUA, Emergency Use Authorization; USC, United States Code; DHS, Department of Homeland Security; DoD, Department of Defense; HHS, Department of Health and Human Services; ASPR, HHS Assistant Secretary for Preparedness and Response; NIH, National Institutes of Health; CDC, Centers for Disease Control and Prevention; FDA, US Food and Drug Administration.

condition, or one caused by an authorized or approved product used for that disease or condition; (3) that it is similarly reasonable to believe in light of the available evidence that “the known and potential benefits of the product” when used for the anticipated purpose “outweigh the known and potential risks of the product,” taking into account (if applicable) the material threat identified by DHS; and (4) “that there is no adequate, approved, and available alternative” for the intended purpose.²³

Further requirements may be prescribed by regulation, but thus far HHS has not published additional regulatory criteria for EUA issuance.² FDA has, however, disseminated guidance—now scheduled to be updated in light of PAHPRA—explaining its policies on the EUA authority.²⁸ The guidance recommends that certain safety and effectiveness data be submitted as part of a request for consideration for an EUA by government agencies or private entities; it notes that scientific evidence “could arise from a variety of sources,” including domestic and foreign clinical trial results, animal data, and in vitro data. The agency considers all available evidence and evaluates it “in light of the specific circumstances of the emergency.”²⁸

If issued once all statutory criteria are met, the resulting EUA enables authorized individuals and entities to use the unapproved medical product, or to use the otherwise approved product for unapproved CBRN indications, in accordance with the EUA’s conditions without running afoul of the FD&C Act. The EUA must state each disease or condition for which the product may be used, along with FDA’s aforementioned conclusions about safety, potential effectiveness, known and potential benefits and risks, and, to the extent practicable under the emergency circumstances, “an assessment of the available scientific evidence.”²³ In order to “protect the public health,” FDA is required to establish certain conditions on EUAs to the extent practicable, and it is empowered to levy other discretionary conditions as appropriate. EUAs for unapproved products are subject to more mandatory conditions than those for unapproved uses of approved products, although FDA may elect to establish certain additional conditions of authorization for both EUA categories.²³

In the context of the 2014 Ebola outbreak in West Africa, FDA has thus far issued 8 EUAs for assays intended for detecting the Ebola virus. Three of the EUAs were requested by federal agencies (2 by CDC and 1 by DoD), and 5 were requested by industry.²⁹ The EUA issuances for Ebola MCMs have utilized the PAHPRA changes to the EUA authority. Specifically, the underlying determination serving as the starting point for the EUA process was an MTD³⁰—a new basis included in PAHPRA for the HHS secretary to declare an emergency justifying an EUA for a product.²⁴ In 2006, DHS identified the Ebola virus as a material threat against the US population sufficient to affect national security. This MTD enabled HHS to declare in August 2014 that circumstances justified the emergency authorized use of in vitro diagnostics for detection of the

Ebola virus.³¹ In light of PAHPRA’s EUA language, no further threat determination from DHS, DoD, or HHS was required to support the HHS declaration necessary for EUA issuance. Such newfound flexibility has worked to augment the efficiency of the 3-part EUA process but does not change the criteria that FDA must conclude are met before issuing an EUA with appropriate conditions.

EUAs for Preparedness Purposes

The recently enacted PAHPRA legislation modified the existing EUA authority to better “support rapid responses to public health emergencies.”³² In particular, by eliminating the requirement under the original Project Bioshield Act that an HHS secretarial determination in support of an EUA always take the form of an official public health emergency declaration, PAHPRA is designed to facilitate preparation for both actual and potential public health emergencies. As such, FDA now has clearer authority to issue EUAs for preparedness purposes before a CBRN or emerging infectious disease emergency occurs.³³ Although the criteria for issuance remain unchanged—the FDA commissioner must still conduct a risk-benefit analysis²⁸ “based on the totality of scientific evidence”²³—the ability to promulgate preevent authorizations can help support preparedness and planning initiatives by the public health community.²⁵ FDA can still engage in pre-EUA activity to begin reviewing data on prospective EUA products in advance of an emergency determination and declaration.^{2,18} However, these efforts to ensure timely MCM availability in the event of an actual public health emergency may no longer be as critical, given the ability of the HHS secretary to base a determination on either an actual or potential public health emergency.

Governmental Pre-Positioning

In addition to amending the EUA mechanism, PAHPRA established streamlined authorities to bolster certain preparedness and response activities without the requirement to have an EUA in place (Table 4). Specifically, PAHPRA allows government entities—at the federal, state, local, and tribal levels—and those acting on their behalf to pre-position MCMs in anticipation of later regulatory permission for use via traditional approval, an IND or IDE, or an EUA.³⁴ Governments now have explicit statutory authorization to stockpile MCMs regardless of their approval status, so long as the stockpiled products are not actually used until appropriate FDA action is taken. The ability to pre-position products without an EUA can help governments prepare for rapid dispensing once an EUA is issued.

New MCM Authorities

PAHPRA also created significant efficiencies by authorizing certain types of emergency use of currently FDA-approved

Table 4. PAHPRA MCM Authorities

<i>Action</i>	<i>Applicability</i>	<i>Authority</i>
Governmental pre-positioning	Any status of product (held and not used) Federal, state, local, tribal government or agent In anticipation of approval, IND, IDE, EUA Held and not used until approval, IND, IDE, EUA	21 USC 360bbb-3b
Expiration dating extension	Approved, cleared, or licensed product Intended for use during CBRN emergency Supported by appropriate scientific evaluation	21 USC 360bbb-3a(b)
CGMP deviation authorization	Approved, cleared, or licensed product Intended for use during CBRN emergency Warranted by circumstances in secretarial determination	21 USC 360bbb-3a(c)
Emergency dispensing (no prescription) As permitted by state law, <i>or</i> Per FDA emergency dispensing order	Approved, cleared, or licensed product Intended for use during CBRN emergency Dispensed in circumstances of secretarial determination	21 USC 360bbb-3a(d)
Emergency use instructions Used during emergency response, <i>or</i> Used by government entities/agents in preparation for emergency response	Approved, cleared, or licensed product Intended for use during CBRN emergency	21 USC 360bbb-3a(e)
REMS waiver	Approved, cleared, or licensed product Intended for use during CBRN emergency To mitigate circumstances in secretarial determination	21 USC 355-1(k)

Note. PAHPRA, Pandemic and All-Hazards Preparedness Reauthorization Act of 2013; MCM, medical countermeasure; IND, Investigational New Drug application; IDE, Investigational Device Exemption; EUA, Emergency Use Authorization; USC, United States Code; CBRN, Chemical, biological, radiological, or nuclear, including emerging infectious diseases; CGMP, Current good manufacturing process; FDA, US Food and Drug Administration; REMS, Risk evaluation and mitigation strategies.

MCMs without the need for an EUA altogether (Table 4). Before PAHPRA's enactment, even uses of approved products for approved indications in an emergency could necessitate an EUA to the extent that emergency use contemplated deviation from FD&C Act requirements pertaining to labeling, prescribing, or storage.²⁵ EUAs were needed when envisioned MCM emergency uses, such as dispensing via a POD and handing out emergency information, could be interpreted as FD&C Act violations.¹⁸ For example, in 2011 CDC requested and received an EUA from FDA for the emergency use of oral formulations of doxycycline products for the postexposure prophylaxis (PEP) of inhalational anthrax.³⁵ Although doxycycline was already approved for this indication, certain stakeholders responsible for responding to a potential anthrax incident required additional flexibility for preparedness and response purposes. Among the activities authorized by the EUA were issuing emergency fact sheets, dispensing without individual prescriptions and as partial supplies, and storing for mass dispensing.^{25,35}

In such cases, where FDA-approved MCMs are intended for use in CBRN emergencies, PAHPRA's provisions now provide a simplified alternative. In lieu of seeking emergency fact sheets through an EUA, the CDC director has delegated authority to issue emergency use instructions to be used either during an actual emergency response or by government entities or their agents in preparation for such a response. Similarly, the FDA commissioner can exercise

delegated authority to permit deviations from applicable current good manufacturing practice (CGMP) requirements pertaining to storage and handling, extend shelf-life, issue emergency dispensing orders,³⁶ and waive Risk Evaluation and Mitigation Strategies (REMS) requirements.³⁷ These expedited authorities apply only to FDA-approved MCMs intended for approved uses to counter qualifying CBRN threats, including certain emerging infectious diseases. Moreover, the exercise of these authorities still presumes that the affected products are intended for use during circumstances in which an appropriate baseline determination has been made by the DHS, DoD, or HHS secretary related to a CBRN or disease threat.

Unlike the EUA process, however, PAHPRA's new emergency use authorities require neither a further declaration from the HHS secretary nor certain criteria of EUA issuance that may be duplicative in the context of FDA-approved products. Thus, although the doxycycline mass dispensing EUA remains in effect,³⁵ it would not have been required in the post-PAHPRA environment to facilitate the contemplated uses for inhalational anthrax postexposure prophylaxis in a CBRN emergency.²⁵ Ciprofloxacin—another antibiotic approved for inhalational anthrax postexposure prophylaxis, but for which there is no mass dispensing EUA—is now also eligible for the new PAHPRA mechanisms that enable emergency-related activities,²⁵ if intended for use during the circumstances under which the current DHS determination related to *Bacillus anthracis*³⁸

applies or another requisite threat determination has been made.

As a result of PAHPRA, therefore, CDC may issue emergency use instructions about approved anthrax MCMs that deviate from FDA-approved labeling without rendering those products adulterated or misbranded under the FD&C Act if used by appropriate parties. FDA, among other actions, may promulgate an emergency dispensing order permitting approved anthrax MCMs to be dispensed without individual prescriptions and/or by non-healthcare professionals without resulting in the products being deemed unapproved, adulterated, or misbranded; emergency dispensing may also occur as permitted under relevant state law.³⁶ To foster emergency response, FDA can take further steps to waive current good manufacturing practice requirements for approved products in support of temporary storage at dispensing sites, as well as extend expiration dating when supported by “appropriate scientific evaluation.”³⁶ These actions no longer necessitate an EUA for approved MCMs intended for use in a CBRN emergency (Table 1).

Overall, the MCM provisions of PAHPRA aim to strike a balance by streamlining preparedness and response authorities without meaningfully eroding safeguards for emergency use. Although the statutory criteria for invoking the new MCM authorities in PAHPRA are substantially less burdensome than those for issuing an EUA, any resulting risk is largely mitigated by the fact that the only products eligible for these authorities are already approved, cleared, or licensed for their intended CBRN-related indications.³⁶ These provisions are completely distinct from the EUA authority and are focused on accommodating minor changes needed to facilitate emergency distribution, dispensing, and use of approved MCMs.³⁹ With respect to PAHPRA’s amendments to the EUA mechanism, the criteria for FDA issuance are the same as before.²⁵ Thus, although the changes effected by PAHPRA with respect to the EUA determination language and other factors have enhanced the flexibility of the EUA process, they have not lowered the bar for issuing an EUA.

TORT LIABILITY CONSIDERATIONS

In late 2005, Congress passed the Public Readiness and Emergency Preparedness (PREP) Act to promote innovation across the MCM enterprise by providing liability protections to a spectrum of activities associated with their development and delivery.⁴⁰ In addition to addressing the liability concerns of MCM manufacturers and distributors, Congress sought to allay anxieties over legal risk among personnel involved in MCM dispensing, prescribing, and administration.⁴¹ Once triggered, PREP Act protections can cover “the full range of MCM actors.”¹⁸ Specifically, the PREP Act empowers the HHS secretary to issue a declaration that provides qualified immunity from tort liability for all claims of loss with a causal relationship to the administration or use

of a specified MCM for a specified health concern. This grant of immunity precludes all suits seeking tort damages under federal or state law for loss incurred by the MCM recipient, except in rare cases of death or serious physical injury caused by “willful misconduct.”⁴²

A PREP Act declaration is specifically geared toward providing targeted liability protections for priority MCMs and is distinct from other types of edicts in the HHS secretary’s purview, such as a public health emergency declaration or a declaration supporting an EUA.⁴³ In order to promulgate a PREP Act declaration, the secretary must determine that a disease, health condition, or health threat either constitutes a public health emergency or poses a credible risk of constituting such an emergency in the future. Based on this threat, the secretarial declaration may recommend one or more MCMs, specifying the category of health concerns for which such MCM is advised, the effective time period of the legal protections, and the population of individuals receiving the product, along with any geographic limitations on administration or use (Table 5). The declaration may further delineate any limitations on the means of distribution, as well as additional categories of persons qualified to prescribe, administer, or dispense the MCM (if not already authorized to do so under applicable state law).⁴²

Thus, the PREP Act’s liability protections are afforded to “covered persons” working with “covered countermeasures.” The contents of the specific PREP Act declaration define each term for the purpose of scoping its protections.⁴¹ “Covered countermeasures” may include products that are approved, cleared, or licensed; covered by an IND or IDE; authorized for emergency use under an EUA;²³ or FDA-approved and used under PAHPRA emergency use authorities.³⁶ In the context of administration and use of a covered MCM, “covered persons” may include both a licensed healthcare provider authorized to prescribe or dispense by the relevant state, along with additional populations specified by the declaration itself.⁴²

Returning to the example of anthrax, the applicable PREP Act declaration, issued in 2008, defines “covered countermeasures” broadly as encompassing any vaccine, antibiotic, or other drug or device used with respect to anthrax and subject to appropriate regulatory approval. The categories of “covered persons” in the context of MCM administration were extended beyond licensed healthcare providers to include personnel authorized by DoD, by appropriate public health and medical emergency response authorities following an emergency declaration, or by an EUA or other mechanism.⁴⁴ Given that the aforementioned doxycycline mass dispensing EUA explicitly recognized that non-healthcare providers might be involved in mass dispensing operations in response to a suspected anthrax event, such responders would benefit from the liability protections of the anthrax PREP Act declaration so long as they comply with the conditions of the EUA.³⁵ The same does not automatically hold true for the administration of ciprofloxacin, since there is no EUA in effect; however, given ciprofloxacin’s approval for

Table 5. Contents of a PREP Act Declaration Issued by the HHS Secretary

<i>Element</i>	<i>Authority</i>
Determination that a disease, health condition, or health threat constitutes a public health emergency or a credible risk thereof	42 USC 247d-6d(b)(1)
Recommendation for manufacture, testing, development, distribution, administration, or use of one or more covered MCMs	42 USC 247d-6d(b)(1)
Statement that liability protections are in effect with respect to the recommended activities	42 USC 247d-6d(b)(1)
Category or categories of diseases, health conditions, or health threats for which the administration or use of the MCM(s) is recommended	42 USC 247d-6d(b)(2)(A)
Effective time period(s) of the declaration, delineated by dates, milestones, or events	42 USC 247d-6d(b)(2)(B)
Population(s) of individuals receiving the MCM(s)	42 USC 247d-6d(b)(2)(C)
Geographic limitations (if any) on the area(s) for which liability protections are in effect with respect to administration or use of the MCM(s); may specify no geographic limitation	42 USC 247d-6d(b)(2)(D)
Limitations (if any) on the means of distribution for obtaining the MCM(s)	42 USC 247d-6d(b)(2)(E)
Extended time period for manufacturers to dispose of the MCM(s) and for others to limit administration and use; HHS secretary determines a “reasonable period”	42 USC 247d-6d(b)(3)(B)
Identification of additional categories (if any) of persons qualified to prescribe, dispense, or administer the MCM(s)	42 USC 247d-6d(i)(8)(B)
Other conditions as the HHS secretary may specify	42 USC 247d-6d(b)(1)

Note. PREP Act, Public Readiness and Emergency Preparedness Act of 2005; HHS, Department of Health and Human Services; MCM, medical countermeasure; USC, United States Code.

inhalational anthrax postexposure prophylaxis, action by FDA and CDC under PAHPRA’s streamlined provisions could potentially provide such dispensing authorization and instructions to additional categories of responders in a time-efficient manner.²⁵

Along with its provision of limited tort immunity, the PREP Act also authorized the Treasury to establish a compensation fund to furnish an administrative means of redress for eligible individuals suffering serious physical injuries or death from covered MCMs.⁴⁵ The Countermeasures Injury Compensation Program (CICP) is managed by the Health Resources and Services Administration (HRSA) of HHS.⁴⁶ For individuals deemed eligible by HRSA, the CICP provides an alternative remedy “for covered injuries directly caused by the administration or use of a covered countermeasure” pursuant to a PREP Act declaration.⁴⁵ Compensation provided through the CICP is the exclusive remedy for such injuries, with the exception of a federal cause of action for injuries sustained due to the willful misconduct of covered persons under a declaration.^{42,45} In the latter case, the injured party must elect either to accept compensation under the CICP or pursue a willful misconduct action in the federal district court for the District of Columbia.^{42,45}

Given that willful misconduct constitutes “a very high legal standard”⁴¹ and is the “sole exception” under the PREP Act to immunity for covered persons,⁴² the liability protections provided by a declaration can be sweeping. In 2012, a New York appellate court dismissed a negligence and battery complaint filed against a county public health department for lack of parental consent in administering the H1N1 vaccine to a child during a school vaccination clinic held several years before.⁴⁷ During the relevant timeframe, the H1N1 influenza vaccine was covered under a PREP Act declaration promulgated in response to the

2009 outbreak of the swine flu virus.⁴⁸ The health department was acting under the authority of an executive order issued by the governor “to implement a statewide vaccination campaign to protect New Yorkers from H1N1 influenza.”⁴⁹ The crux of the case was whether PREP Act coverage extended to claims for lack of informed consent. The court concluded that it did, given Congress’s intent “to preempt all state law tort claims arising from the administration of covered countermeasures by a qualified person pursuant to a declaration by the [HHS] secretary, including one based upon a defendant’s failure to obtain consent.”⁴⁷

The court presumed that the breadth of PREP Act immunity reflected Congress’s determination that “potential tort liability must give way to the need to promptly and efficiently respond to a pandemic or other public health emergency.”⁴⁷ In implementing the statute, HHS has thus far limited the liability immunity provided in its declarations to 2 kinds of MCM programs designed to facilitate preparedness and response. These are: (1) recommended activities related to federal contracts, transactions, and agreements; and (2) initiatives aligned with the public health and medical response of the authority having jurisdiction to respond to an incident following an applicable emergency declaration.¹⁸ The former category lessens the need for federal contractors involved in priority countermeasure development to seek contractual indemnification,⁵⁰ which exposes the government to significant financial uncertainties outside the structure of an administrative compensation program like the CICP.⁴¹ The latter type of PREP Act coverage supports the response activities of federal, state, local, and tribal authorities related to the administration and use of covered countermeasures.

It is important to note that the PREP Act did not displace other legal protections that may be available to certain

categories of individuals in the public health community. For example, a provision of the Federal Tort Claims Act generally makes a claim against the US government—as opposed to individual federal employees—the exclusive remedy for most negligent or wrongful actions committed by those employees while acting within the scope of their federal employment.⁵¹ Some types of federal employees, such as healthcare providers working for the Public Health Service, benefit from tort immunity statutes specifically targeted to their agency.⁵² Moreover, certain volunteers may be eligible for liability protections under federal⁵³ or state⁵⁴ law, depending on the circumstances under which their services are rendered. For such individuals, a relevant PREP Act declaration can serve as an added and robust layer of protection particular to a given set of MCMs.

In the homeland security domain, the Support Anti-terrorism by Fostering Effective Technologies (SAFETY) Act—enacted as part of the Homeland Security Act of 2002⁵⁵—provides certain liability protections to sellers of qualified antiterrorism technologies (QATTs).⁵⁶ The term “QATT” means any technology “designed, developed, modified, procured, or sold for the purpose of preventing, detecting, identifying, or deterring acts of terrorism or limiting the harm such acts might otherwise cause.”⁵⁷ QATTs must be designated as such by the DHS undersecretary for science and technology, under authority delegated by the DHS secretary.⁵⁸ Designation as a QATT confers upon its sellers numerous protections, including (but not limited to) exclusive jurisdiction in federal court for lawsuits against them, a prohibition on punitive damages and joint and several liability, and—perhaps most advantageously—a cap on tort liability not to exceed the amount of insurance coverage determined by DHS as part of the designation process.⁵⁹ When a designated QATT has been shown to perform as intended, conform to the seller’s specifications, and be safe for use as intended, it may also be issued a DHS certification.⁶⁰ Certification offers the additional advantage of creating a rebuttable presumption that the seller is entitled to assert the “government contractor defense” in product liability and other lawsuits,⁶⁰ which essentially immunizes defendants against state tort claims.⁶¹

The liability limitations emanating from SAFETY Act designation and certification apply exclusively to sellers because they are the only parties subject to suit. The federal cause of action authorized under the law⁵⁶ is exclusive and “may not be brought against the buyers, the buyers’ contractors, or downstream users of the technology, the seller’s suppliers or contractors, or any other person or entity.”⁵⁹ Thus, users of the technology benefit from SAFETY Act coverage.

However, the law’s liability protections are limited in scope, extending only to claims “arising out of, relating to, or resulting from an act of terrorism” when the relevant QATT has been deployed.⁵⁹ To qualify as terrorism for this purpose, the act must be unlawful, cause harm (including financial harm), and employ “instrumentalities, weapons or

other methods designed or intended to cause mass destruction, injury or other loss to citizens or institutions of the United States.”⁵⁷ This standard differs from PREP Act immunity, which applies to “all claims for loss caused by, arising out of, relating to, or resulting from the administration to or the use by an individual of a covered countermeasure” in accordance with a relevant declaration.⁴² The analysis of PREP Act coverage therefore looks to whether the claim is directly connected to the administration or use of a covered countermeasure, and whether the covered persons have abided by the declaration’s conditions.^{41,62} The PREP Act provides discretion to the HHS secretary to specify any limitations on the protections in a declaration. It is the declaration itself, along with the conditions delineated therein, that activate the statute’s immunity provisions.^{41,42}

Much as the PREP Act was designed to stimulate the manufacture and delivery of MCMs by limiting the liability exposure associated with products that are needed for public health emergencies but have limited market opportunities,⁴¹ the purpose of the SAFETY Act protections is “to facilitate and promote the development and deployment of anti-terrorism technologies that will save lives.”⁶³ There certainly can be a role for the SAFETY Act in MCM development and use when particular MCMs qualify as a QATT. For example, DHS has provided SAFETY Act designation to co-packaged sodium nitrite and sodium thiosulfate injections for the treatment of life-threatening cyanide poisoning in accordance with FDA approval. It also issued SAFETY Act designation and certification (since expired) to an atropine auto-injector for the treatment of chemical nerve agent exposure.⁶⁴ To garner these SAFETY Act protections, the MCM technologies must meet the criteria for QATT designation⁶⁵ and, where applicable, certification.⁶⁰ The liability limitations afforded by the SAFETY Act apply in the antiterrorism context, acting as a homeland security tool. Reflecting a public health mindset, the PREP Act enables HHS to extend limited tort immunity for preparedness and response activities related to both terrorism and infectious diseases.⁴¹ Thus in December 2014, the HHS secretary issued a PREP Act declaration to help combat the Ebola epidemic in West Africa by encouraging the development and potential use of experimental Ebola vaccines.⁶⁶

LYNCHPINS FOR LIABILITY PROTECTION

The legal mechanisms for allowing medical products to be used and for imbuing their use with liability immunity stem from separate authorities and depend on distinct administrative actions. However, these different areas of the law often come together whenever PREP Act coverage is contingent upon the exercise of emergency use authorities with respect to a specified MCM. Where the product at issue is neither FDA-approved nor authorized for investigational use—or where its intended use will deviate from FD&C requirements—the issuance of an EUA or action under

PAHPRA can help to ensure its inclusion as a “covered countermeasure” under the PREP Act and thereby preserve applicable liability protections. In this sense, immunity from tort liability may hinge on the appropriate permission to administer the product in the manner contemplated.

Of course, FDA continues to possess the ability to exercise its enforcement discretion concerning potential violations of the FD&C Act. Such enforcement discretion could extend to unapproved products or unapproved uses that might otherwise necessitate an EUA, or to certain emergency uses of approved products that can now be addressed via action under PAHPRA. However, for MCMs covered by a PREP Act declaration, mere abstention from enforcement under the FD&C Act can create uncertainty as to the viability of the liability protections provided.²⁵ The issuance of an EUA, or the exercise of PAHPRA emergency use authorities, can thereby help ensure PREP Act liability protections, both by clarifying that the MCM remains “covered” and by indicating (where applicable) legitimate emergency dispensing models outside the construct of individual prescriptions. This is especially so where the PREP Act declaration itself identifies additional categories of qualified persons empowered to administer the MCM, contingent upon authorization to do so by means of an EUA or other emergency authority (Table 6). For products “that do not otherwise comply with the FDA regulatory scheme,” applicable PREP Act protections may only be available upon the exercise of EUA or PAHPRA authorities and if used in accordance with the relevant EUA or PAHPRA action.²

Again, the example of anthrax postexposure prophylaxis is instructive. The considerations that prompted CDC to request the doxycycline mass dispensing EUA included a concern among public health stakeholders that certain preparedness and response activities for CBRN emergencies risked violating elements of the FD&C Act as interpreted by FDA. Although these stakeholders intended to use doxycycline for its approved anthrax indications, they anticipated potentially having to do so through PODs that

stored and dispensed the product in an unapproved manner. While FDA could to some extent address the anxiety over FD&C Act compliance by exercising its enforcement discretion to effectively permit these activities, further action was required to make certain that aspects of emergency use—such as dispensing partial supplies as an initial start-up regimen—did not jeopardize any of the tort liability protections provided by the PREP Act declaration for anthrax MCMs.²⁵ As such, the doxycycline mass dispensing EUA³⁵ served the dual purpose of both authorizing certain emergency activities and helping ensure tort liability protections through PREP Act coverage.²⁵

At the time, the sole mechanism for accomplishing this objective was issuing an EUA under the process established by the Project Bioshield Act. Since then, PAHPRA has helped clarify that certain emergency activities involving an approved MCM for its approved CBRN indications do not constitute an unapproved use necessitating an EUA. In such cases involving FDA-approved MCMs “intended for use in certain CBRN scenarios,” FDA and CDC can elect to exercise their respective emergency use authorities under PAHPRA.²⁵ These administrative actions can expressly authorize the kind of preparedness and response activities envisioned by the doxycycline mass dispensing EUA.²⁵ In so doing, the new PAHPRA authorities can prove instrumental in preserving applicable liability protections, such as those afforded by the PREP Act.

In the context of mass dispensing, PAHPRA therefore helps address potential vulnerabilities with respect to PREP Act coverage by providing another vehicle, outside of the EUA process, to support certain aspects of emergency use of approved MCMs. Emergency dispensing of approved MCMs at a POD or other dispensing modality, to include dispensing without individual prescriptions or by non-healthcare providers, can be authorized via either the conditions of an EUA²³ or action under PAHPRA.³⁶ In the latter case, emergency dispensing must occur during an actual CBRN emergency and be either in accordance with

Table 6. PREP Act Coverage and Emergency Use Authorities

<i>Coverage</i>	<i>Definition</i>	<i>Caveat</i>
Covered MCMs	Generally must be— Approved, cleared or licensed by FDA, <i>or</i> Authorized under an IND or IDE, <i>or</i> Authorized under an EUA, <i>or</i> Otherwise authorized for emergency use (PAHPRA)	Liability protections may be affected by noncompliance with terms and conditions of FDA authorization
Covered persons	May include— US government Manufacturers Distributors Program planners Qualified persons who prescribe/administer/dispense Officials/agents/employees thereof	“Qualified persons” include licensed health professionals or other individuals authorized by the relevant state, <i>or</i> categories of persons identified in the PREP Act declaration itself

Note. PREP Act, Public Readiness and Emergency Preparedness Act of 2005; MCM, medical countermeasure; FDA, US Food and Drug Administration; CFR, Code of Federal Regulations; IND, Investigational New Drug application; IDE, Investigational Device Exemption; EUA, Emergency Use Authorization; PAHPRA, Pandemic and All-Hazards Preparedness Reauthorization Act of 2013.

an FDA emergency dispensing order or as permitted by applicable state law.³⁶

While the cost of closing this potential gap in PREP Act coverage is to more completely foreclose tort recovery for MCM recipients injured through negligent dispensing operations, such action is consistent with the underlying rationale of the PREP Act to ensure the availability of MCMs to the public during a possibly catastrophic event.⁴¹ Access to MCMs for emergency response depends not only on the deployment of needed products, but also the presence of personnel, including volunteers, trained in applicable mass dispensing plans. Concerns about tort liability can undermine the recruitment and readiness of such responders. Ultimately, the coherence and fairness of the PREP Act regime rests on the balance between promoting MCM availability and affording “timely, uniform, and adequate compensation” to harmed individuals.⁴⁵ The viability of the alternative remedy established by the PREP Act in turn depends on continuing and adequate funding of the CICP by Congress.⁶⁷

CONCLUSION

Individuals and entities on the front lines of the medical response to emergencies involving CBRN threats and emerging infectious diseases need to know both their authority to participate in dispensing operations and the concomitant liability protections that accompany their activities. Where an MCM or its intended use is neither approved, cleared, or licensed by FDA, nor authorized for investigational purposes, the issuance of an EUA can facilitate its use for actual or potential emergencies involving specified agents. For FDA-approved MCMs anticipated for use in CBRN emergencies, actions authorized under PAHPRA can permit practices that might otherwise render the product unapproved, adulterated, or misbranded.²⁵

Separately, a PREP Act declaration can provide vital immunity from most tort claims stemming from the administration and use of designated MCMs. Oftentimes, an EUA or PAHPRA action can help ensure PREP Act coverage where a relevant declaration has been issued, both by reinforcing that the MCM is covered under the PREP Act declaration and by acknowledging that responders and volunteers who are not healthcare providers may be involved in dispensing activities. When this scenario occurs, it is important that stakeholders dispense the MCM in strict accordance with the scope and conditions of the relevant authorization, so as not to jeopardize both their underlying authority to undertake these responsibilities and the liability protections provided by the PREP Act.

Proactive vetting of emergency plans by local counsel can help ensure that appropriate FDA authorizations and applicable liability protections are in place, and that anticipated operations comply with the pertinent conditions therein. Incorporating discussion of the terms and conditions of rel-

evant EUAs, PAHPRA authorities, and/or PREP Act declarations into training modules for preparedness and response personnel can help cut through confusion and ease anxiety over perceived legal uncertainties. Additional guidance planned by FDA²⁵ on the implementation and interpretation of PAHPRA’s MCM provisions will aid in this endeavor.

The MCM language in PAHPRA provided a legislative fix to perceived inefficiencies in both the EUA authority and the emergency use of approved MCMs. The experiences of public health stakeholders in leveraging these authorities for their MCM activities will indicate whether future reforms to the existing panoply of federal legal preparedness tools are needed. In particular, the consistent application by courts of PREP Act targeted immunity for qualified persons who prescribe, administer, or dispense MCMs in accordance with an EUA or with PAHPRA authorities is vital to achieving the fundamental goal of alleviating liability concerns associated with MCM delivery. Outside of a willful misconduct action authorized under the PREP Act itself, piercing the qualified immunity shield for responders, volunteers, and authorized MCM dispensers will vitiate the statute’s protections and undermine its public health rationale. To ensure MCM availability in a public health emergency, those tasked with delivering MCMs to the public must be assured a predictable measure of legal protection.

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