Contains Nonbinding Recommendations

GUIDANCE

Emergency Use Authorization of Medical Products

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GUIDANCE[1]

Emergency Use Authorization of Medical Products

This guidance document represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You may use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, please contact the appropriate FDA staff.

I. INTRODUCTION

This guidance explains FDA's policies for authorizing the emergency use of medical products under section 564 of the Federal Food, Drug, and Cosmetic Act (FD&C Act) (21 U.S.C. 360bbb-3), which was amended by the Project BioShield Act of 2004 (Public Law 108-276).[2] Section 564 permits the FDA Commissioner to authorize the use of an unapproved medical product or an unapproved use of an approved medical product during a declared emergency involving a heightened risk of attack on the public or U.S. military forces, or a significant potential to affect national security.

[1] This guidance was prepared by the Emergency Use Authorization (EUA) Principals Group and the EUA Working Group. The EUA Working Group (WG) is composed of members with expertise in public health, medical, regulatory, legal, ethical, and risk communication areas. The WG, on an ongoing basis, examines issues related to issuance and implementation of an EUA. This group provides expert advice to both the Commissioner of the Food and Drug Administration (FDA Commissioner) and the Secretary of Health and Human Services (the Secretary).

[2] Section 903 of the FD&C Act and existing delegations of authority, found in the FDA Staff Manual Guide 1410.10, permit the authority of the Secretary to issue an EUA under section 564 of the FD&C Act to be delegated to the FDA Commissioner. The Secretary has delegated his authority to issue an EUA under section 564 to the FDA Commissioner. Thus, in this document the FDA Commissioner is identified rather than the Secretary except where the Secretary retains the authority.

21 The Emergency Use Authorization (EUA) authority recently granted by Congress allows the
22 FDA Commissioner to strengthen the public health protections against biological, chemical,
23 radiological, and nuclear agents that may be used to attack the American people or the U.S.
24 armed forces. Under section 564, the FDA Commissioner may allow medical countermeasures
25 to be used in an emergency to diagnose, treat, or prevent serious or life-threatening diseases or
26 conditions caused by such agents, when there are no adequate, approved, and available
27 alternatives.
28
29 The document is intended to inform industry, government agencies, and FDA staff of the
30 Agency's general recommendations and procedures for issuance of EUAs.[3] FDA expects that
31 requests for consideration for an EUA would be submitted by government agencies (e.g., the
32 Department of Health and Human Services or the Department of Defense (DoD)) or private
33 entities. FDA may seek additional data and information on a case-by-case basis to ensure that
34 the statutory criteria for issuance of an EUA are met.
35
36 Additionally, the Secretary of Health and Human Services (the Secretary) will establish a
37 permanent Emergency Use Authorization Working Group (EUA WG), headed by the Assistant
38 Secretary for Preparedness and Response (ASPR), with representatives from FDA, the Centers
39 for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), the
40 Department of Defense (DoD), the Department of Homeland Security (DHS), the Department of
41 Veterans Affairs and, as appropriate, participants from other Federal agencies, to identify and

[3] FDA Centers (i.e., the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Devices and Radiological Health (CDRH)) may issue subsequent guidance providing greater detail on these recommendations and procedures.

42 provide expert consultation on potential EUA candidates prior to and during declared
43 emergencies.
44
45 FDA's guidance documents, including this guidance, do not establish legally enforceable
46 responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should
47 be viewed only as recommendations, unless specific regulatory or statutory requirements are
48 cited. The use of the word *should* in Agency guidances means that something is suggested or
49 recommended, but not required.
50

51 **II. DECLARATION OF EMERGENCY**

52
53 Section 564(b)(1) of the FD&C Act provides that, before an EUA may be issued, the Secretary
54 must declare an emergency based on one of the following grounds:
55 (1) a determination by the Secretary of Homeland Security that there is a domestic
56 emergency, or a significant potential for a domestic emergency, involving a heightened risk of
57 attack with a specified biological, chemical, radiological, or nuclear agent or agents;
58 (2) a determination by the Secretary of Defense that there is a military emergency, or a
59 significant potential for a military emergency, involving a heightened risk to United States
60 military forces of attack with a specified biological, chemical, radiological, or nuclear agent or
61 agents; or
62 (3) a determination by the Secretary of a public health emergency under section 319 of
63 the Public Health Service Act (PHS Act) that affects, or has the significant potential to affect,
64 national security, and that involves a specified biological, chemical, radiological, or nuclear

65 agent or agents, or a specified disease or condition that may be attributable to such agent or
66 agents.
67
68 Once the Secretary has declared an emergency justifying an authorization under section 564 to
69 use an unapproved medical product or an approved product for an unapproved use, the ASPR
70 may convene the EUA Working Group to provide expert consultation to the FDA.[4] Based on his
71 review of the information and data submitted to the Agency and input from the EUA WG (if
72 convened) and after consulting with the Director of NIH and the Director of CDC (to the extent
73 feasible and appropriate given the circumstances of the emergency), the FDA Commissioner
74 may authorize the emergency use of a particular product, assuming other statutory criteria and
75 conditions are met.[5]
76
77 Section 564(b)(2) states that a declaration of emergency will terminate one year after issuance or
78 earlier if the Secretary determines, in consultation (as appropriate) with the Secretary of
79 Homeland Security or the Secretary of Defense, that the circumstances that precipitated the
80 declaration have ceased. Before a declaration terminates, the Secretary must provide, under
81 section 564(b)(3), advance notice that is sufficient to allow for disposition of unapproved product
82 or any labeling or other information provided related to an unapproved use of an approved
83 product. Section 564(b)(2)(B) also authorizes the Secretary to renew a declaration.

---

[4] The FDA Commissioner may issue one or more EUAs on the basis of a single declaration of emergency, under section 564(b)(1), provided that the EUAs are intended for use in the same emergency involving the same biological, chemical, radiological, or nuclear agent or agents.

[5] For purposes of this document, an "unapproved" product refers to a product that is not approved, licensed, or cleared for commercial distribution under sections 505, 510(k), or 515 of the FD&C Act or section 351 of the Public Health Service Act (PHS Act); an "unapproved use of an approved product" refers to a product that is approved, licensed, or cleared under such provisions but which use is not an approved, licensed, or cleared use of the product (21 U.S.C. 360bbb-3).

84

85 **Publication:** The Secretary will promptly publish in the Federal Register notice of each
86 determination of actual or potential emergency, the Secretary's declaration of emergency,
87 advance notice of termination, and renewal of a declaration issued under section 564(b).[6] The
88 FDA Commissioner will promptly publish in the Federal Register a notice of each authorization,
89 including an explanation of the reasons for issuance, a description of the intended use of the
90 EUA product, and its indications and contraindications. The FDA Commissioner also will
91 promptly publish in the Federal Register each termination or revocation of an authorization and
92 an explanation of the reasons for the decision.[7] In addition, FDA plans to provide notice of an
93 emergency use authorization on the Agency's website, at *www.fda.gov*, and through
94 announcements disseminated to the media.[8]

95

96 **III. ELIGIBILITY FOR AN EUA**

97

98 Section 564 permits the FDA Commissioner to authorize the introduction into interstate
99 commerce of a drug, device, or biological product intended for use in an actual or potential
100 emergency during the effective period of a declaration. EUA candidates include products and
101 uses that are not approved, cleared, or licensed under sections 505, 510(k), and 515 of the FD&C
102 Act or section 351 of the PHS Act. The FDA Commissioner may issue an EUA only if, after

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[6] To the maximum extent feasible given the circumstances, Federal Register publication of the notice will occur prior to the action that is the subject of the notice.
[7] *See supra* note 6.
[8] In publicly releasing information on an EUA, FDA will take necessary steps to protect classified information and information otherwise protected by law, as appropriate.

103 consultation with the Director of NIH and the Director of CDC (to the extent feasible and
104 appropriate given the circumstances of the emergency), the FDA Commissioner concludes—
105 1) that the agent specified in the declaration of emergency can cause a serious or life-
106 threatening disease or condition;
107 2) that, based on the totality of scientific evidence available, including data from
108 adequate and well-controlled clinical trials, if available, it is reasonable to believe that the
109 product may be effective in diagnosing, treating, or preventing--(a) the serious or life-
110 threatening disease or condition referred to in paragraph (1); or (b) a serious or life-
111 threatening disease or condition caused by a product authorized under section 564, or
112 approved, cleared, or licensed under the FD&C Act or PHS Act, for diagnosing, treating,
113 or preventing the disease or condition referred to in paragraph (1) and caused by the
114 agent specified in the declaration of emergency;
115 3) that the known and potential benefits outweigh the known and potential risks of the
116 product when used to diagnose, prevent, or treat the serious or life-threatening disease or
117 condition that is the subject of the declaration; and
118 4) that there is no adequate, approved, and available alternative to the product for
119 diagnosing, preventing, or treating such serious or life-threatening disease or condition.
120
121 **Categories of Products:** The range of potential EUA products includes drugs, biological
122 products (e.g., vaccine, blood products, and biological therapeutics), and devices (e.g., *in vitro*
123 diagnostics). (Throughout this document, the term "drugs" includes biological products.)
124 Candidate products include those products that have not been approved or cleared under the
125 FD&C Act or the PHS Act ("unapproved products"), as well as unapproved uses of approved

126 drugs and approved or cleared devices ("unapproved uses of approved products"). Examples of
127 "unapproved uses of approved products" may include: 1) use of an approved antibiotic as
128 prophylaxis for exposure to, or treatment of disease caused by a bacterium that is not included on
129 the approved labeling for the antibiotic; and 2) distribution of a prescription drug by a non-
130 licensed provider (e.g., delivery of oral antibiotics by U.S. postal carriers). Section 564 does not
131 require that an investigational new drug application (IND) or investigational device exemption
132 (IDE) be filed for EUA candidate products, although FDA anticipates that many of the
133 unapproved products already will have been under evaluation through such mechanisms.
134
135 **Effectiveness:** Products and uses that are eligible for authorization are those that "may
136 be effective" to prevent, diagnose, or treat in humans serious or life-threatening diseases or
137 conditions that can be caused by the specified biological, chemical, radiological, or nuclear
138 agent(s) that led to or caused the declared emergency. Eligible products and uses also include
139 those that may be effective to mitigate a disease or condition caused by an FDA-regulated
140 product (including an EUA product, or an approved, cleared, or licensed product) used to
141 diagnose, treat, or prevent a disease or condition caused by such agent. The "may be effective"
142 standard for EUAs provides for a lower level of evidence than the "effectiveness" standard that
143 FDA uses for product approvals.[9]
144

[9] The terminology "may be effective" also appears in 21 CFR 312.34(b)(3)(A), where it states that a request for a Treatment IND (tIND) for a drug intended to treat an immediately life-threatening disease may be denied due to a lack of evidence that the drug "may be effective for its intended use in its intended population." Nevertheless, the Agency's decisions on requests for EUAs and tINDs involve product-specific and circumstance-dependent determinations of risks and benefits.

145 FDA intends to assess the potential effectiveness of an EUA product on a case-by-case
146 basis. The Agency has significant experience assessing effectiveness where clinical information
147 is limited, including experience with treatment INDs and IDEs and humanitarian device
148 exemptions. However, the amount, kind, and quality of evidence available to support an EUA
149 may not always be the same as that required for treatment INDs, IDEs, and humanitarian device
150 exemptions under the FD&C Act and Agency regulations. If, based on the totality of the
151 scientific evidence available, including adequate and well-controlled clinical trials, if they are
152 available, it is reasonable to believe that the product may be effective for the specified use, the
153 FDA Commissioner may authorize its emergency use--provided that other statutory criteria (e.g.,
154 relating to the risk-benefit analysis and alternatives) also are met.
155
156 **Risk-Benefit Analysis:** Products are eligible for emergency use authorization if FDA
157 determines that the known and potential benefits of the product, when used to diagnose, prevent,
158 or treat the identified disease or condition, outweigh the known and potential risks of the
159 product. In determining whether the known and potential benefits of the product outweigh the
160 known and potential risks, FDA intends to assess the quality and quantity of the evidence, given
161 the current state of scientific knowledge, of risks and benefits. The Agency intends to use this
162 information to make an overall risk-benefit determination. To accomplish this, FDA plans to
163 look at the totality of the scientific evidence, which could arise from a variety of sources. The
164 Agency intends to review and consider all evidence, including results of domestic and foreign
165 clinical trials, animal data, and *in vitro* data, available for Agency consideration. FDA
166 anticipates that, for some candidate products, data from controlled clinical trials will be
167 available. For others, the Agency expects to consider clinical experience from other than a

168 controlled trial if the circumstances warrant. For yet others, *in vivo* efficacy data may only be
169 available from animal models. The FDA Commissioner will consult with the Director of NIH
170 and the Director of CDC (to the extent feasible and appropriate given the circumstances of the
171 emergency) and will evaluate all the evidence in light of the specific circumstances of the
172 emergency, including potential risks of not receiving treatment with the candidate product, in
173 determining whether to issue an EUA.[10] If the risk-benefit analysis does not support issuance of
174 an EUA or if the product does not otherwise meet the statutory criteria for issuance, patient
175 access to the investigational product may be available under other regulatory mechanisms (e.g.,
176 IND or IDE).
177
178 **Alternatives to the Product:** The FDA Commissioner may issue an EUA if he
179 determines that there is no adequate, approved, and available alternative to the candidate product.
180 A potential alternative product may be considered "unavailable" if there are insufficient supplies
181 to meet fully the emergency need. A potential alternative product may be considered
182 "inadequate" if there are contraindicating data for special circumstances or populations (e.g.,
183 immunocompromised individuals or individuals with a drug allergy) or if the agent is or may be
184 resistant to approved and available alternative products.
185
186 **IV. REQUEST FOR CONSIDERATION FOR AN EUA**
187
188 Although an EUA may not be issued until after an emergency has been declared by the
189 Secretary, FDA recognizes that during such exigent circumstances, the time available for the

[10] Such evidence includes the possible consequences of not taking or using the candidate product (e.g., possible

190 submission and review of an EUA request may be severely limited. Therefore, the Agency
191 strongly encourages an entity with a possible candidate product, particularly one at an advanced
192 stage of development, to contact the FDA Center responsible for the candidate product even
193 before a determination of actual or potential emergency. This guidance offers recommendations
194 for both "pre-emergency" activities to be conducted prior to the determination of actual or
195 potential emergency and "emergency" activities to be performed once the determination has been
196 issued. In addition, this section of the guidance sets out the types of information FDA believes
197 are important to allow an assessment of safety and effectiveness and to make an adequate risk-
198 benefit determination to support issuance of an EUA.
199
200 **Pre-Emergency Activities:** Such activities may include discussions with FDA about a
201 prospective EUA product and the appropriate vehicle to use, such as an IND, IDE, or Master
202 File, when submitting data on the product prior to a determination of actual or potential
203 emergency.[11] The Agency strongly recommends that an entity submitting data during a "pre-
204 emergency" period follow the recommendations for data submission contained in "Submission of
205 a Request for Consideration," below. If, prior to the declaration of an emergency, FDA believes
206 that a candidate product may meet the criteria for an EUA, the Agency may share appropriate
207 information on such product with the Secretary's EUA WG.[12]
208

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health effects and the need for quarantine).

[11] FDA anticipates that the appropriate mechanism to use for submitting data on a candidate product during the pre-emergency period will vary depending on the circumstances.

[12] Disclosures of information by FDA to the Secretary's EUA WG will be consistent with applicable laws and regulations protecting trade secrets and confidential commercial or financial information,

209 **Emergency Activities:** Once a determination of actual or potential emergency has been
210 made under section 564(b)(1), the Secretary may declare an emergency justifying the
211 authorization to use an unapproved medical product or an approved medical product for an
212 unapproved use. The Secretary will consult with the EUA WG; other technical experts from
213 FDA, NIH, and CDC; and other agencies and private entities, where appropriate, to identify
214 products that may be eligible for an EUA in light of the circumstances of the emergency and to
215 facilitate timely submission of the EUA request by an appropriate entity.
216
217 **Submission of a Request for Consideration:** Section 564(c) requires that the data to
218 support authorization demonstrate that, based on the totality of scientific evidence available to
219 the FDA Commissioner (including data from adequate and well-controlled clinical trials, if
220 available), it is reasonable to believe that the product may be effective in diagnosing, treating, or
221 preventing the serious or life-threatening disease or condition. The exact type and amount of
222 data needed to support an EUA may vary depending on the nature of the declared emergency and
223 the nature of the candidate product. To facilitate FDA review of such data, the Agency
224 recommends that a request for consideration for an EUA include a well-organized summary of
225 the available scientific evidence that evaluates the product's safety and effectiveness, including
226 the adverse event profile when used for diagnosis, treatment, or prevention of the serious or life-
227 threatening disease or condition, as well as data and other information on safety, effectiveness,
228 risks and benefits, and (to the extent available) alternatives.
229
230 The chart below summarizes the types of data that FDA recommends be submitted to
231 support a request for consideration for an EUA.

Summary of Recommended Data to Support a Request for Consideration:

For FDA to evaluate a request for consideration for an EUA, the Agency recommends that the following information be submitted:

1. a description of the product and its intended use (e.g., identification of the serious or life-threatening disease or condition for which the product may be effective);

2. identification and an explanation of what unmet need(s) would be addressed by issuance of the EUA;

3. a description of the product's approval or clearance status, if any, under the FD&C Act or licensure status under the PHS Act, and whether the product is under an investigational application (e.g., whether the product is unapproved or whether it is approved but the EUA is for an unapproved use; whether an IND or IDE is in effect or has been submitted); whether the product is licensed for either the proposed or another use in a foreign country; information on the use of the medical product by either a foreign country or an international mutual defense organization such as NATO;

4. a list of each site where the product, if authorized, would be (or was) manufactured and the Good Manufacturing Practices (GMP) status of the manufacturer;

5. identification of any approved alternative products, including their availability and adequacy for the proposed use (if known);

6. available safety and effectiveness information for the product;

7. a discussion of risks and benefits;

8. a description of the information for health care providers or authorized dispensers and recipients of the product, (e.g., two separate "Fact Sheets"), and the feasibility of providing such information to health care providers or authorized dispensers and recipients in emergency situations;

9. information on chemistry, manufacturing, and controls;

10. instructions for use of the EUA product (e.g., if follow-up treatment is required); and

11. proposed labeling (if applicable).

12. right of reference (if applicable).

285

286 **Recommended Safety Data**

287

288 *In general*: The amount and type(s) of safety data that FDA recommends be submitted as
289 part of a request for consideration for an EUA will differ depending upon a number of factors,
290 including whether the product is approved for another indication and, in the case of an
291 unapproved product, the product's stage of development. FDA expects to interpret safety
292 information in light of the seriousness of the clinical condition, alternative therapies (if any), and
293 the specific circumstances of the emergency. FDA strongly encourages any person or entity with
294 a candidate product to discuss with the Agency at the earliest possible time (even before a
295 determination of actual or potential emergency) the nature and type of safety data that might be
296 appropriate to submit to FDA.

297

298 *Previously approved products*: If the new indication uses a similar dose, duration, route
299 of administration, and/or mechanism of action (as appropriate given the nature of the product),
300 and the intended patient population is similar to that for which the product is approved, FDA
301 recommends that the request for consideration for an EUA reference the approved application if
302 the requester submitted the approved application or has a right of reference. If the new use poses
303 a different risk to the patient population (e.g., suggesting the possibility of increased toxicity),
304 the Agency recommends that information from relevant *in vitro* studies, animal toxicology
305 studies, and (if available) human clinical data and experience be provided to support such a use.

306

307 *Products under development*: The range of available data for such products will differ
308 widely. FDA recommends that any request for consideration for an EUA include available
309 preclinical testing data, such as *in vitro* and animal toxicology data. The Agency also strongly
310 encourages that safety information in humans from clinical trials and individual patient
311 experience be provided, if available. FDA further recommends that data submitted in the request
312 attempt to link the likely patient exposure to any relevant existing preclinical data. Similarly,
313 where animal data are used, sufficient information should be provided to link the results of these
314 data to expected exposures related to the proposed use in humans. Any information on safety
315 associated with use in humans of this or related compounds or devices of a similar design also
316 should be submitted.
317
318 **Recommended Effectiveness Data**
319
320 *In general*: FDA recognizes that comprehensive effectiveness data are unlikely to be
321 available for every EUA candidate product, and the information necessary to authorize
322 emergency use of a product will depend on the circumstances of the declared emergency, as well
323 as available knowledge about the product's safety profile. FDA plans to assess the sufficiency of
324 the effectiveness data and the risk-benefit profile of each candidate product on a case-by-case
325 basis.
326
327 FDA recommends that requests for consideration for EUAs include (or, for products that
328 are developed under IND or IDE or have Drug or Device Master Files, refer to the appropriate
329 document containing) any available relevant scientific evidence regarding the following:

330 (a) mechanism(s) of the product's action to diagnose, treat, or prevent the disease
331 or condition underlying the request;
332 (b) preclinical testing data, such as *in vitro* evidence of effect of the product in
333 preventing or reducing the toxicity of the specified agent;
334 (c) for drugs, demonstration of effectiveness in diagnosing, treating, or preventing
335 the subject disease or condition in at least one animal species expected to react
336 with a response predictive for humans, where the animal study endpoint is clearly
337 related to the desired benefit in humans (e.g., enhancement of survival or
338 prevention of major morbidity);[13]
339 (d) evidence of effect in humans (e.g., in published case reports, uncontrolled
340 trials, controlled trials, if available, and any other relevant human use experience);
341 (e) for drugs, data to support the proposed dosage (including pharmacokinetics
342 and pharmacodynamics data, and for vaccines or antibody therapies,
343 immunogenicity and/or achievement of protective levels of relevant parameters of
344 immunity) for the intended use; and
345 (f) for devices, clinical testing data to support the proposed intended use, as
346 necessary and appropriate.
347
348 **Other Data Considerations**
349
350 *In general:* FDA recommends that the request for consideration include the following
351 types of data, as appropriate and to the extent feasible given the exigencies of the circumstances:

352

353 (a) Well-organized study reports that provide a complete assessment and analysis
354 of available safety and effectiveness data and an interpretation of the findings. If
355 final study reports are not yet available, any available interim study reports should
356 be provided and clearly identified as such;
357 (b) Any relevant statistical analyses; and
358 (c) Source data for clinical studies, nonclinical laboratory studies, and any animal
359 studies demonstrating activity or effectiveness of the product in the treatment of
360 the underlying disease or condition or a closely related disease or condition, such
361 as case report tabulations for key studies; case report forms for all patients who
362 died during the clinical studies and for all persons who did not complete the study
363 due to an adverse event, regardless of causality; relevant reports in the published
364 literature; and translations of source materials in a language other than English.
365

366 *Data quality*: The Agency recommends that requests for consideration for EUAs include
367 statements on whether the nonclinical laboratory studies were conducted in compliance with
368 applicable Good Laboratory Practice requirements in 21 CFR part 58 and whether the clinical
369 studies were conducted in compliance with applicable Good Clinical Practice standards.
370

371 *Data updates:* FDA recommends that any data from any ongoing testing (e.g., longer
372 term stability data) or other data or information that may change the Agency's evaluation of the
373 product's safety or effectiveness that become available during the period of review or the term of

[13] See, e.g., Food and Drugs; Applications for FDA Approval to Market a New Drug; Approval Based on Evidence

374 the EUA (to the extent that such data are not required to be submitted under a condition of
375 authorization) be submitted to the Agency when such data become available.
376
377 **Discussion of Risks and Benefits:** FDA recommends that a request for consideration for
378 an EUA include a discussion of the candidate product's known and potential risks and benefits,
379 which includes a synthesis of the data and information requested above, including:
380 (a) Measures taken to mitigate risk or optimize benefit;
381 (b) Limitations, uncertainty, and data gaps; and
382 (c) A description of circumstances, if any, under which the product should not be
383 used (e.g., contraindications).
384
385 **Format of Submissions:** Submissions may be provided in paper or electronic format.
386 Specific information for electronic format may be obtained by reviewing guidance from the
387 appropriate FDA Center (CBER--www.fda.gov/cber/esub/esubguid.htm; CDER--
388 www.fda.gov/cder/regulatory/ersr; and CDRH--www.fda.gov/cdrh/elecsub.html). Where a paper
389 submission is filed, FDA recommends that a minimum of three copies be provided.
390
391 The Agency recommends that each submission begin with a section that describes the
392 contents and organization of the included materials. The submitter of the original application or
393 anyone with a right of reference may refer to data or other information previously submitted to
394 the Agency in a marketing application, investigational application, or Master File.
395

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of Effectiveness from Studies in Animals, 21 CFR 314.610(a)(2) and (3).

396 FDA expects material to be provided in a reviewable form and sufficiently complete to
397 permit substantive review. Nevertheless, the Agency recognizes that, in rapidly developing or
398 unexpected emergency circumstances, or when previously unanticipated or unavailable medical
399 countermeasures are being considered, it may not be possible for an entity to provide all of the
400 requested data or to provide it in the format suggested in a timely manner. In such
401 circumstances, the Agency will accept and evaluate the request for consideration for an EUA
402 based on data in the form an entity is able to submit. However, a request for consideration that is
403 missing data or that is otherwise incomplete or poorly documented will make determination of
404 whether the product's benefits outweigh its risks more difficult and may, for that reason, be more
405 likely to result in a request for additional information, the need for a longer time period for
406 review, or a decision not to authorize emergency use of the candidate product.
407
408 The addresses for submission of a request for consideration for an EUA are as follows:
409
410 For the Center for Biologics Evaluation and Research:

411 Food and Drug Administration
412 Center for Biologics Evaluation and Research
413 Document Control Center, HFM-99, Suite 200N
414 1401 Rockville Pike
415 Rockville, MD 20852-1448
416 ATTN: EUA
417

418 For the Center for Devices and Radiological Health:

419 Document Mail Center (HFZ-401)
420 Center for Device and Radiological Health
421 Food and Drug Administration
422 9200 Corporate Boulevard
423 Rockville, MD 20850

424 ATTN: EUA
425
426 For the Center for Drug Evaluation and Research:

427 Food and Drug Administration
428 Center for Drug Evaluation and Research
429 Central Document Room
430 5901-B Ammendale Road
431 Beltsville, MD 20705-1266
432 ATTN: EUA

433

434 **V. PROCESSING OF AN EUA**

435

436 This section discusses FDA's role in pre-emergency activities for candidate EUA products, as
437 well as the procedures the Agency will follow in processing a request for consideration for an
438 EUA once the Secretary has issued a declaration of emergency.

439

440 **Prioritization of Pre-Emergency Activities:** The Agency intends to establish priorities
441 for the activities it undertakes, prior to a determination of actual or potential emergency, on
442 candidate products. Such prioritization may be based on the circumstances, such as:

443 (a) the seriousness of the clinical condition;

444 (b) the incidence of the clinical condition;

445 (c) the effect use of the product may have in ensuring national security;

446 (d) whether the product is included in government (Federal, State, or local)
447 stockpiles or whether there is a significant likelihood that the product will be
448 included in government stockpiles if an EUA is granted;

449 (e) whether the product could be used by a large population or is limited to
450 subpopulation(s);
451 (f) request of another government agency;
452 (g) the extent to which the product would serve a significant unmet medical need
453 in a special population (e.g., pregnant women, infants and children, and
454 immunocompromised persons);
455 (h) the availability and, where known, safety and effectiveness of other
456 countermeasures;
457 (i) the urgency of the treatment need (i.e., the window of opportunity for
458 treatment can vary between different medical conditions);
459 (j) the available information concerning the likelihood that the product may be
460 safe and effective in treating the condition;
461 (k) the adequacy of the supporting nonclinical and clinical information; and
462 (l) the quantity of product available.
463
464 FDA intends to establish priorities for its pre-emergency activities at the Division level or
465 higher and, as appropriate and feasible, will consult with the Secretary's EUA WG and may
466 consult other agencies on its priority setting.
467
468 **Review of Pre-Emergency Submissions:** To allow FDA review to begin before a
469 determination of actual or potential emergency, the Agency recommends that a pre-emergency
470 submission be filed using existing processes (e.g., IND or IDE), to the extent feasible and
471 appropriate. The extent of, and timelines for, review of such submission will be determined on a

472 case-by-case basis and will depend on the nature of the submission (e.g., whether an IND or IDE
473 for the product already is on file) and the workload of the reviewing Center. Subject to those
474 considerations and other exigent circumstances beyond Agency control, FDA anticipates that
475 pre-emergency submissions for high priority activities may be reviewed in a matter of weeks to
476 months.
477
478 **Prioritization of Requests for Consideration for an EUA During a Declared**
479 **Emergency:** Once the Secretary has declared an emergency justifying the authorization to use
480 an unapproved product or an unapproved use of an approved product, the Agency intends to
481 prioritize its review of requests for consideration for an EUA based on factors such as:
482 (a) the seriousness of the clinical condition;
483 (b) the incidence of the clinical condition;
484 (c) the likelihood that the product may be effective in treating the condition;
485 (d) the effect use of the product may have in ensuring national security;
486 (e) whether the product is included in government (Federal, State, or local)
487 strategic stockpiles;
488 (f) whether the product could be used by a large population or is limited to
489 subpopulation(s) (unless such use may be critical in managing a public health
490 threat or in protecting a subpopulation with no other suitable measures available);
491 (g) request of another government agency;
492 (h) the extent to which the product would serve a significant unmet medical need
493 in a special population (e.g., pregnant women, infants and children, and
494 immunocompromised persons);

495 (i) the availability and, where known, safety and effectiveness of other
496 countermeasures;
497 (j) the urgency of the treatment need (i.e., the window of opportunity for
498 treatment can vary between different medical conditions);
499 (k) the adequacy of the supporting nonclinical and clinical information; and
500 (l) the quantity of product available.
501
502 FDA intends to establish priorities for its review of requests for consideration at the
503 Division level or higher and, as appropriate and feasible, will consult with the EUA WG and may
504 consult with other agencies on its priority setting.
505
506 **Review Process for a Request for Consideration for an EUA**: The relevant FDA
507 Center will be responsible for the overall coordination of the Agency's disposition of the request
508 and will interact directly with the entity submitting the request for consideration. The Office of
509 the Commissioner will arrange for the consultations with the Director of NIH and the Director of
510 CDC to occur, to the extent that such consultations are feasible and appropriate given the
511 circumstances of the emergency.[14] The Commissioner's Office also will work with the ASPR to
512 coordinate interactions with the EUA Working Group, if convened, although technical input
513 from the EUA WG will be communicated directly to the appropriate FDA review division. The
514 review division also may consult with other countermeasures working groups and expert
515 technical groups within the Agency and, depending on the complexity of the issues presented

[14] The authority of the Commissioner of Food and Drugs to perform consultations under section 564 of the Act has been delegated to the Assistant Commissioner of Counterterrorism Policy, the CBER Director, the CDER Director, and the CDRH Director (FDA Staff Manual Guide 1410.21).

516 and the nature of the declared emergency, may seek additional scientific and technical input from
517 outside experts or advisory committees.
518
519 FDA recognizes that the exact type and amount of data needed to support an EUA may
520 vary depending on the nature of the declared emergency and the nature of the candidate product.
521 The Agency intends to evaluate each request in light of the circumstances and the statutory
522 criteria for issuance.
523
524 FDA expects that the responsible FDA Center, in coordination with internal and external
525 technical experts (as appropriate and feasible), will perform its review of the information and
526 data included in the request for consideration and make recommendations to the Commissioner.
527 FDA anticipates that the letter authorizing, or not authorizing, a specific emergency use or uses
528 of the candidate product will be issued by the Office of the Commissioner. The letter
529 authorizing emergency use of a product will include a description of the intended use, as well as
530 the indications and contraindications of the product. FDA anticipates that when an EUA is
531 issued, the relevant Center will work with the Office of the Commissioner in drafting the Federal
532 Register notice of the EUA for publication by the Office of the Commissioner. In addition, FDA
533 plans to post information about the EUA on the Agency website (*www.fda.gov*).
534
535 **Timelines for Review:** The timelines for FDA review and action on a request for
536 consideration for an EUA will depend on the product profile; the existence, if any, of pending
537 applications for the product; the nature of the emergency; and other relevant factors. Although
538 the length of time required for FDA action will vary, the Agency recognizes that it is likely that,

539 in an emergency situation that is occurring or believed imminent, a request for consideration for
540 an EUA will be acted upon within a matter of hours or days.
541
542 **VI. CONDITIONS OF AUTHORIZATION**
543
544 Under section 564, the FDA Commissioner may establish conditions on an EUA. Section 564(e)
545 requires the FDA Commissioner (to the extent practicable given the circumstances of the
546 emergency) to establish certain conditions on an EUA authorization that the Commissioner finds
547 necessary or appropriate to protect the public health, and permits the Commissioner to establish
548 other conditions that he finds necessary or appropriate to protect the public health. Conditions
549 authorized by section 564(e) include, for example: requirements for information dissemination
550 to health care providers or authorized dispensers and product recipients; adverse event
551 monitoring and reporting; data collection and analysis; recordkeeping and records access;
552 restrictions on product advertising, distribution, and administration; and limitations on GMP
553 requirements. Some conditions, the statute specifies, are mandatory to the extent practicable for
554 authorizations of unapproved products and discretionary for authorizations of unapproved uses
555 of approved products. Moreover, some conditions may apply to manufacturers of an EUA
556 product, while other conditions may apply to any person who carries out any activity for which
557 the authorization is issued. Section 564 also gives the FDA Commissioner authority to establish
558 other conditions on an authorization that he finds to be necessary or appropriate to protect the
559 public health.
560

561 **Conditions of Authorization for Emergency Use of an Unapproved Product:** Section
562 564(e)(1) describes certain requirements with respect to the emergency use of an unapproved
563 product. For example, requirements to disseminate certain information to health care providers
564 or authorized dispensers and recipients and to perform adverse event monitoring and reporting
565 are mandatory under section 564(e)(1)(A) on any person who carries out any activity for which
566 an authorization for an unapproved product is issued, unless the FDA Commissioner determines
567 that such conditions are not practicable given the circumstances of the emergency. Section
568 564(e)(1)(A) further provides that the FDA Commissioner shall establish appropriate conditions
569 with respect to manufacturers' recordkeeping, reporting, and records access, to the extent that
570 such conditions are practicable. The FDA Commissioner also may, under section 564(e)(1)(B),
571 impose comparable records conditions on any person (other than a manufacturer) who carries out
572 any activity for which an authorization is issued. In addition, the Commissioner may impose,
573 under section 564(e)(1)(B), the following requirements on any person (including a manufacturer)
574 who carries out any activity for which the authorization of an unapproved product is issued:
575 restrictions on distribution of the EUA product and on who may administer it, as well as
576 requirements to collect and analyze safety and effectiveness data on the product. Additionally,
577 section 564(e)(3) authorizes the FDA Commissioner to waive or limit (as appropriate) existing
578 GMP requirements, and section 564(e)(4) permits the Commissioner to establish conditions for
579 advertising and other promotional descriptive printed matter relating to the unapproved product.
580 Each of the conditions described in section 564(e) is summarized below.
581
582 **Conditions of Authorization for Emergency Use of an Approved Product for an**
583 **Unapproved Use:** Section 564(e)(2) describes certain requirements with respect to the

584 emergency use of an unapproved use of an approved product. For example, the requirements of
585 section 564(e)(1)(A)(i) and (ii) -- to impose conditions with respect to the dissemination of
586 information to health care providers or authorized dispensers and recipients – are mandatory
587 under section 564(e)(2)(A), to the extent practicable given the circumstances of the emergency,
588 if a manufacturer of an approved product authorized for an unapproved use carries out any
589 activity for which an EUA is authorized. The FDA Commissioner also may, if he chooses under
590 section 564(e)(2)(A), impose on such manufacturers requirements for adverse event monitoring
591 and reporting as well as recordkeeping, reporting, and records access.

592 Under section 564(e)(2)(B), with respect to an EUA that authorizes a change in labeling
593 of an approved product, but for which the manufacturer chooses not to make such labeling
594 change, the EUA may not authorize the product's distributor or any other person to alter or
595 obscure the manufacturer's labeling. However, under such conditions, the FDA Commissioner
596 must authorize, to the extent practicable given the circumstances of the emergency, any person
597 (other than the manufacturer) acting pursuant to such EUA to provide appropriate information, in
598 addition to the manufacturer's labeling, with respect to the product.[15]

599

600 In addition, section 564(e)(2)(C) allows the FDA Commissioner to establish, with respect
601 to the distribution and administration of the product, conditions that are no more restrictive than
602 those established with respect to the distribution and administration of the product for the
603 approved use.

604

[15] Additional information required under section 564(e)(2)(B)(ii) as a condition of authorization is not considered "labeling" for purposes of section 502 of the FD&C Act while the EUA for the product is effective.

605 **Additional Conditions of Authorization:** Section 564 also permits the FDA
606 Commissioner to establish other conditions on an EUA. For example, section 564(e)(3)
607 authorizes the FDA Commissioner to waive or limit, as appropriate, existing GMP requirements,
608 and section 564(e)(4) permits the Commissioner to establish conditions for advertising and other
609 promotional descriptive printed matter relating to the unapproved use. These and other
610 conditions are described below.
611
612 *Information for Health Care Providers or Authorized Dispensers*: Under section
613 564(e)(1)(A)(i) (for an unapproved product) and section 564(e)(2)(A) (for a manufacturer
614 carrying out any activity concerning an unapproved use of an approved product), the FDA
615 Commissioner must establish conditions on an authorization (to the extent practicable given the
616 circumstances of the emergency) to ensure that health care providers or authorized dispensers
617 who administer the EUA product are informed that the FDA Commissioner has authorized the
618 emergency use of the product, of its significant known and potential benefits and risks and the
619 extent to which such benefits and risks are unknown, as well as the available alternatives and
620 their benefits and risks. FDA recommends that the request for consideration for an EUA include
621 a "Fact Sheet" for the health care provider or authorized dispenser that would include essential
622 information about the product. FDA plans to review submitted Fact Sheets for accuracy and
623 completeness. A sample "Fact Sheet for the Health Care Provider or Authorized Dispenser"
624 template is provided at the end of the guidance as Appendix A. FDA recommends that the Fact
625 Sheet include, at a minimum, the information listed on the first page of the sample template.
626 FDA further recommends that the Fact Sheet target the health care provider or authorized
627 dispenser who has the most basic level of training, recognizing that such individuals may have

628 different levels of training (nurse, doctor, other), could come from a variety of backgrounds
629 (state, local, military, civilian), and may have different types of experience. FDA recommends
630 that the Fact Sheet accompany the EUA product when the product is distributed, and be in a form
631 that is readily accessible to the health care provider or authorized dispenser. To the extent
632 consistent with other conditions of authorization, information on the EUA product also may be
633 disseminated to providers through media, videos/DVDs, the Internet, and direct communication
634 from public health agencies.
635
636 *Information for Recipients*: Although informed consent under part 50 of FDA
637 regulations (21 CFR part 50) is not required for administration of an EUA product and the
638 information dissemination requirements of section 564 are mandatory only to the extent
639 conditions establishing such requirements are practicable, FDA recommends that recipients be
640 given as much appropriate information as possible given the nature of the emergency and the
641 conditions of the authorization. Under section 564(e)(1)(A)(ii)(III) (for an unapproved product)
642 and section 564(e)(2)(A) (for a manufacturer carrying out any activity concerning an unapproved
643 use of an approved product), recipients must be informed that the FDA Commissioner has
644 authorized emergency use of the product, of the significant known and potential benefits and
645 risks of the EUA product, and of the extent to which such benefits and risks are unknown.
646 Recipients must have an opportunity to accept or refuse the EUA product and must be informed
647 of any consequences of refusing administration of the product.[16] Recipients also must be
648 informed of available alternatives to the product and of their risks and benefits under section

[16] However, Congress authorized the President to waive, under certain circumstances, the option for members of the armed forces to accept or refuse administration of an EUA product (10 U.S.C. 1107a).

649 564(e)(1)(A)(ii)(III) (for an unapproved product) and section 564(e)(2)(A) (for a manufacturer
650 carrying out any activity concerning an approved product for an unapproved use).
651
652 Ordinarily, FDA expects that some form of written information will be given to
653 recipients, similar to the Fact Sheet for health care providers or authorized dispensers. To assure
654 that individuals of all educational levels comprehend the information provided, FDA
655 recommends that it be written in the simplest language possible and using other techniques to
656 improve health literacy.[17] The Agency recommends that the written information include the
657 significant known and potential risks and benefits of the product and the extent to which the
658 potential risks and benefits are unknown, specific instructions for home use (if necessary), and
659 adverse event information, including contact information should adverse events occur. A sample
660 "Fact Sheet for Recipients" template is provided at the end of the guidance as Appendix B. FDA
661 recommends that the Fact Sheet include the information in the template and be submitted to the
662 Agency as part of the request for consideration for an EUA. Furthermore, the Agency
663 recommends that the Fact Sheet or other written information for recipients be tested (e.g., by
664 focus groups) for clarity, particularly regarding messages on uncertainty and relative risks. FDA
665 acknowledges, however, that exigent circumstances may dictate the use of other, more
666 appropriate, dissemination methods. Therefore, FDA expects that recipient information would be
667 disseminated in the most effective and expeditious way possible to reach the intended audience.
668 Methods of dissemination may include media (e.g., public service announcements),
669 videos/DVDs, the Internet, and direct communication from health care providers and public
670 health agencies. Section 564(e)(1)(A)(ii) (for an unapproved product) and section 564(e)(2)(A)

671 (for a manufacturer carrying out any activity concerning an unapproved use of an approved
672 product) contemplates that the Fact Sheet or other recipient information will be provided to
673 recipients before administration of an EUA product. If, however, taking the time needed to
674 provide such information would diminish or negate the effectiveness of the product for the
675 recipient, the FDA Commissioner may include as part of the condition that the information be
676 provided to the recipient as soon as practicable afterward.
677
678 *Monitoring and Reporting of Adverse Events*: Section 564(e)(1)(A)(iii) (for an
679 unapproved product) and section 564(e)(2)(A) (for a manufacturer carrying out any activity
680 concerning an unapproved use of an approved product) provide for adverse event monitoring and
681 reporting for EUA products. FDA expects that the primary focus of such conditions will be on
682 capturing serious adverse events and identifying the appropriate mechanism(s) to be used for the
683 collection of follow-up clinical information, the size of the safety database, and the types of data
684 needed. Predefined mechanisms to capture adverse event data are preferred, where feasible (e.g.,
685 MEDWATCH and VAERS). In certain circumstances, other mechanisms also may be
686 considered, such as using postage-paid postcards or stickers added to the product, labeling, and
687 any other information that refers the health care provider or authorized dispenser and recipient to
688 a toll-free number and Internet site to report adverse events (such information could be included
689 as part of a Fact Sheet, as described above).
690
691 *Records*: Section 564(e)(1)(A)(iv) requires (to the extent practicable given the
692 circumstances of the emergency) that manufacturers of an unapproved product be required to

[17] See, e.g., http://www.health.gov/communication/literacy/quickguide/healthinfo.htm.

693 maintain records and to grant to the Agency access to records concerning the EUA product. The
694 FDA Commissioner may impose comparable records requirements on any person other than a
695 manufacturer who carries out any activity for an unapproved product under section
696 564(e)(1)(B)(iv) and on the manufacturer of an approved product for an unapproved use under
697 section 564(e)(2)(A). The Agency anticipates that such records requirements may, for
698 manufacturers, relate to the number of doses, devices, etc. (including lot number identification)
699 that have been shipped or sold under an EUA; the name and addresses of the facilities where the
700 EUA product was shipped; and may, for persons other than manufacturers, relate to the
701 monitoring of patients who have been administered a product under an EUA. The FDA
702 Commissioner also may impose conditions regarding other matters the Agency determines are
703 appropriate and practicable given the circumstances of the emergency.
704
705 *Additional Conditions for Unapproved Products*: To the extent feasible given the
706 circumstances of the emergency, the FDA Commissioner may establish additional conditions for
707 unapproved products, such as the following:
708 *Restricted distribution under the EUA*--conditions may be placed on which
709 entities may distribute the product and how distribution is to be performed.[18]
710 *Personnel*--conditions may be placed on who may administer the product, and on
711 the categories of individuals to whom, and the circumstances under which, the
712 product may be administered.
713 *Information*–conditions may be placed on the collection and analysis of
714 information on the safety and effectiveness of the EUA product.

715 The FDA Commissioner will establish these conditions on a case-by-case basis.

716

717 *Additional Conditions for an Unapproved Use of an Approved Product*: Under section
718 564(e)(2)(B), with respect to an EUA that authorizes a change in labeling of an approved
719 product, but for which the manufacturer chooses not to make such labeling change, the EUA
720 may not authorize a product distributor or any other person to alter or obscure the manufacturer's
721 labeling. However, under such conditions, the FDA Commissioner must authorize, to the extent
722 practicable under the circumstances of the emergency, any person (other than the manufacturer)
723 acting pursuant to such EUA to provide appropriate information, in addition to the
724 manufacturer's labeling, with respect to the product.[19]

725

726 The FDA Commissioner may, under section 564(e)(2)(C), establish conditions for
727 distribution and administration of an approved product for an unapproved use that are no more
728 restrictive than those established by the Agency for the distribution and administration of the
729 product for an approved use. Any such additional conditions will be established by the
730 Commissioner on a case-by-case basis, depending on the circumstances of the emergency and
731 the nature of the approved product authorized for an unapproved use.

732

733 *Compliance with GMPs or Alternative Approaches*: The Agency expects that EUA
734 products will be produced in compliance with GMP; however, limits or waivers may be granted

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[18] FDA anticipates that distribution of EUA products will be performed according to existing response plans, as practicable and appropriate.
[19] *See supra* note 13.

735 under section 564(e)(3), on a case-by-case basis, after consideration of the circumstances and of
736 any alternative proposed approach.
737
738 *Advertising*: Section 564(e)(4) allows the FDA Commissioner to establish conditions on
739 advertisements and other promotional descriptive printed matter relating to the use of an EUA
740 product, such as, for drugs (including biologics), requirements applicable to prescription drugs
741 under section 502(n) of the FD&C Act and, for devices, requirements applicable to restricted
742 devices under section 502(r) of the FD&C Act.
743
744 **Summary of Conditions Described in Section 564(e):** The following chart sets out
745 conditions described in section 564(e) that may be imposed on an EUA for unapproved products
746 and for unapproved uses of approved products, respectively. A condition is identified as
747 "mandatory" in the chart below if section 564(e) requires the FDA Commissioner, to the extent
748 practicable given the circumstances of the emergency, to establish such condition when it is
749 necessary or appropriate to protect the public health. A condition identified as "discretionary" in
750 the chart below is one that the FDA Commissioner may, under section 564(e), impose as he finds
751 necessary or appropriate to protect the public health. In addition to the conditions described as
752 "mandatory" and "discretionary" in the chart below, section 564 allows the FDA Commissioner
753 to establish other conditions on an authorization that he finds to be necessary or appropriate to
754 protect the public health.

755

CONDITION OF AUTHORIZATION	UNAPPROVED PRODUCT	UNAPPROVED USE OF AN APPROVED PRODUCT
Information for Health Care Providers and Authorized Dispensers	Mandatory for manufacturers and others*	Mandatory for manufacturers[20]
Information for Recipients	Mandatory for manufacturers and others*	Mandatory for manufacturers[21]
Adverse Event Monitoring/Reporting	Mandatory for manufacturers and others*	Discretionary for manufacturers
Recordkeeping/Access	Mandatory for manufacturers; discretionary for others*	Discretionary for manufacturers
Compliance with GMPs	Discretionary for manufacturers and others*	Discretionary for manufacturers and others*
Advertising	Discretionary for manufacturers and others*	Discretionary for manufacturers and others*
Restricted Distribution	Discretionary for manufacturers and others*	Discretionary for manufacturers and others*
Restricted Administration	Discretionary for manufacturers and others*	Discretionary for manufacturers and others*
Data Collection/Analysis	Discretionary for manufacturers and others*	

756 * Others may include, for example, the U.S. government.

757

[20] Under section 564(e)(2)(B), with respect to an EUA that authorizes a change in labeling of an approved product, but for which the manufacturer chooses not to make such labeling change, the EUA may not authorize a product distributor or any other person to alter or obscure the manufacturer's labeling. However, under such conditions, the FDA Commissioner must authorize, to the extent practicable under the circumstances of the emergency, any person (other than the manufacturer) acting pursuant to such EUA to provide appropriate information, in addition to the manufacturer's labeling, with respect to the product.

[21] *See supra* note 17.

758 **Option To Carry Out Authorized Activities:** Section 564(l) requires the manufacturer
759 of a sole-source unapproved product authorized for emergency use to inform the FDA
760 Commissioner, within a reasonable time after authorization, that the manufacturer does not
761 intend to carry out any activity under the EUA. Although the Commissioner does not have the
762 authority under section 564 to require a person to carry out any activity for which an EUA is
763 issued, section 564(l) does not limit the Commissioner's authority to impose conditions on
764 persons who choose to carry out any activity pursuant to an EUA.
765
766 **Rules of Statutory Construction:** Section 564(j) provides that nothing in section 564
767 impairs the authority of the President as Commander in Chief of the Armed Forces under the
768 Constitution. In addition, section 564(j) indicates that nothing in section 564 impairs the
769 authority of the Secretary of Defense with respect to the Department of Defense (including the
770 armed forces), under other provisions of Federal law. Section 564(j) also provides that nothing
771 in section 564, including any action by a manufacturer with respect to an unapproved use of an
772 approved product, impairs the authority of the United States to use or manage quantities of a
773 product that are owned or controlled by the United States (including products maintained in the
774 stockpile managed under section 319F-2 of the PHS Act).
775
776 **VII. REVOCATION OR TERMINATION OF AN EUA**
777
778 Section 564(f) provides that an EUA will be in effect for the duration of the declaration under
779 which it was issued (see Section II, "Declaration of Emergency," above), unless the EUA is
780 revoked because the criteria of issuance (see Section III, "Eligibility for an Emergency Use

781 Authorization," above) are no longer met or revocation is appropriate to protect public health or
782 safety.
783
784 **Revocation:** The FDA Commissioner will periodically review the circumstances and
785 appropriateness of an EUA, including circumstances that might warrant revocation of the EUA.
786 Such circumstances may include significant adverse inspectional findings (e.g., where an
787 inspection of the manufacturing site and processes have raised significant questions regarding the
788 purity, potency, or safety of the EUA product that materially affect the risk/benefit assessment
789 upon which the EUA was based); reports of adverse events (number or severity) linked to, or
790 suspected of being caused by, the EUA product; product failure; product ineffectiveness (such as
791 newly emerging data that undermine the Agency's conclusion that the product "may be effective"
792 against a particular agent); and availability of a preferred product.
793
794 **Termination:** Upon termination of the declaration, unapproved product or labeling and
795 product information for an unapproved use must be disposed of pursuant to section 564(b)(2)(C)
796 and (b)(3). A manufacturer may choose to have unapproved product returned after termination.
797 Notwithstanding any such termination, under section 564(f)(2) an authorization shall continue to
798 be effective to provide for continued use in any patient who began treatment before termination
799 (to the extent found necessary by the patient's attending physician).
800
801 **Continued Use:** Any use of an EUA product beyond the term of a declaration is subject
802 to investigational product regulations (e.g., IND regulations), except for use by patients who

803 began treatment when the declaration was in effect, to the extent found necessary by such
804 patient's attending physician.
805
806 **VIII. PREEMPTION**
807
808 FDA anticipates that preemption issues may arise when an EUA is issued to the extent that states
809 have existing requirements governing the dispensing, administration, or labeling of unapproved
810 medical products or approved medical products for unapproved uses. The Supremacy Clause
811 can operate to nullify both state legislative requirements and state common-law duties.
812 *Medtronic v. Lohr*, 518 U.S. 470, 503 (1996) (Breyer, J., concurring in part and concurring in the
813 judgment); *id.* at 510 (O'Connor, J., joined by Rehnquist, C.J., Scalia, J., and Thomas, J.,
814 concurring in part and dissenting in part); *Cipollone v. Liggett Group, Inc.*, 505 U.S. 504, 521
815 (1992) (plurality opinion); *id.* at 548-49 (Scalia, J., joined by Thomas, J., concurring in judgment
816 in part and dissenting in part). Under the principles of implied conflict preemption, courts have
817 found state law preempted where it is impossible to comply with both federal and state law or
818 where the state law "stands as an obstacle to the accomplishment and execution of the full
819 purposes and objectives of Congress." *See English v. General Electric Co.*, 496 U.S. 72, 79
820 (1990); *Florida Lime & Avocado Growers, Inc.*, 373 U.S. 132, 142-43 (1963); *Hines v.*
821 *Davidowitz*, 312 U.S. 52, 67 (1941). Consistent with this case law, section 4(a) of Executive
822 Order 13132 states that "[a]gencies shall construe . . . a Federal statute to preempt State law only
823 where the statute contains an express preemption provision or there is some other clear evidence
824 that the Congress intended preemption of State law, or where the exercise of State authority
825 conflicts with the exercise of Federal authority under the Federal statute."

826

827 FDA believes that the terms and conditions of an EUA issued under section 564 preempt state
828 law--legislative requirements and common-law duties--imposing different or additional
829 requirements on the medical product for which the EUA was issued in the context of the
830 emergency declared under section 564. To the extent state law may impose requirements
831 different from or in addition to those imposed by the EUA for a particular medical product
832 within the scope of the declared emergency, e.g., requirements on prescribing, dispensing,
833 administering, or labeling of the medical product, such state law "stands as an obstacle to the
834 accomplishment and execution of the full purposes and objectives of Congress," *See Hines*, 312
835 U.S. at 67, and "conflicts with the exercise of Federal authority under [§ 564]." Executive Order
836 13132. Affected state laws may include, but are not limited to, laws governing the
837 administration of investigational medical products, such as informed consent laws and laws
838 requiring Institutional Review Board approval, and laws governing the prescribing or dispensing
839 of medical products, such as laws limiting who may prescribe or dispense medical products and
840 under what circumstances. FDA anticipates consulting state officials when the terms and
841 conditions of an EUA may preempt state law.

842

843 In an emergency, it is critical that the conditions that are part of the EUA--those that the
844 Commissioner has determined to be necessary or appropriate to protect the public health--be
845 strictly followed, and that no additional conditions be imposed. To the extent there may be
846 circumstances in which FDA would like people carrying out activities under an EUA also to
847 comply with requirements contained in preempted state law, FDA anticipates that the
848 Commissioner will incorporate such requirements into the terms and conditions of the EUA.

849 **IX. LIABILITY PROTECTION AND COMPENSATION UNDER OTHER STATUTES**

850

851 Apart from any applicable preemption principles, section 564 of the FD&C Act does not
852 establish a liability protection scheme for manufacturers or others who carry out any activity for
853 which an EUA is issued. However, certain persons or certain products may be eligible for
854 compensation or liability protection under other statutes and programs, such as the Federal
855 Employees' Compensation Act (5 U.S.C. 8101 *et seq.*); the Federal Tort Claims Act (28 U.S.C.
856 1346(b)); the Smallpox Vaccine Injury Compensation Program and the liability protections of
857 section 304 of the Homeland Security Act , as amended by Smallpox Emergency Personnel
858 Protection Act of 2003 (42 U.S.C. 233(p)); the National Vaccine Injury Compensation Program
859 (42 U.S.C. 300aa-10 *et seq.*); the Support Anti-terrorism by Fostering Effective Technologies
860 Act of 2002 (SAFETY Act); and the Public Readiness and Emergency Preparedness Act of 2005
861 (Pub. L. 109-148). Contact information for these statutes and programs is provided in Appendix
862 C.

863 APPENDIX A

864 **FACT SHEET for the Health Care Provider or Authorized Dispenser**

865

866 [PRODUCT for INTENDED USE]

867

868 1. An emergency has been declared by the Secretary of Health and Human Services.

869

870 2. [INCLUDE A BRIEF DESCRIPTION (1-2 sentences) OF THE EMERGENCY].

871

872 3. The FDA Commissioner has authorized the emergency use of [PRODUCT] for a use
873 [IDENTIFY THE INTENDED USE] that has not yet obtained FDA approval by usual FDA
874 processes. This authorization will terminate on [DATE 1 YEAR FROM THE DATE OF
875 DECLARATION], or when the emergency has ceased to exist, whichever is earlier.

876

877 4. The information in this Fact Sheet is the minimum necessary to inform you of the
878 significant known and potential risks and benefits of emergency use of [PRODUCT].

879

880 5. The significant known and potential risks and benefits of emergency use of [PRODUCT]
881 are: [LIST]. The extent to which such risks and benefits are unknown is [EXPLAIN].

882

883 6. The available alternatives to [PRODUCT] are: [LIST]. The risks and benefits of
884 [ALTERNATIVES] are: [LIST]. [If there is no alternative, provide an explanation of outcomes

885 of exposure or of any special public health measures (e.g., quarantine or monitoring) that an
886 individual who does not receive the EUA product may face.]
887
888 7. [INCLUDE NAME, ADDRESS, AND TELEPHONE NUMBER FOR
889 MANUFACTURER.]
890
891 As the health care provider or authorized dispenser administering [PRODUCT], please
892 communicate the significant known and potential risks and benefits, and the extent to which such
893 risks and benefits are unknown, to the recipient of [PRODUCT].
894
895 Please inform the recipient that he or she has the option to accept or refuse administration of
896 [PRODUCT], and of the consequences of refusing administration. Please inform the recipient of
897 any available alternatives to [PRODUCT], and of their risks and benefits. Please provide the
898 "Fact Sheet for Recipients" to the recipient of [PRODUCT].
899
900 If providing this information before administration would delay the administration [PRODUCT]
901 to a degree that would endanger the lives of exposed or affected individuals, the information
902 must be provided to the recipient as soon as practicable after [PRODUCT] is administered.
903
904 If you follow these instructions when administering or using [PRODUCT], you do not need to
905 comply with state laws imposing different or additional requirements on use of the product in
906 this emergency situation.

907 FDA also recommends that EUA applicants include the following additional information in the
908 Fact Sheet for Health Care Providers or Authorized Dispensers, if it is available:
909
910 - **Instructions for use.**
911 - How to administer the product (including dose, route of intake or infusion, how long to
912 use the product, how to take care of the infusion site), how to store the product, how it is
913 supplied/forms that it comes in, how to constitute;
914
915 - If it is an *in vitro* diagnostic (IVD): what type of specimens should be collected for
916 testing with the product, how to store the specimens, how the laboratory should use the
917 product (procedure), how to interpret the results; and
918
919 - Instructions for use for special populations (e.g., pregnant women, infants and children,
920 and immunocompromised individuals), including special dosing instructions (e.g.,
921 weight-based dosing), special precautions.
922
923 - **Known major interactions** with other products or substances, including drug interactions,
924 cross reactivity for IVDs.
925
926 - **Known efficacy information or performance characteristics** (for IVDs)
927
928 - **Adverse events.** Significant known adverse event information (e.g., what are the significant
929 known side effects? Under what conditions should the recipient stop taking product?),

930 instructions for follow up in case of an adverse event, how to report an adverse event, what
931 to do in case of an adverse event (stop using the product? seek treatment?), whom to contact
932 for professional advice if an adverse event occurs or if the product does not work. Health
933 care providers or authorized dispensers also may report adverse events to MEDWATCH at
934 www.fda.gov/medwatch/report/hcp.htm or 1-800-FDA-1088, or to VAERS (for vaccines) at
935 www.vaers.org or 1-800-822-7967.
936
937 • **Alternatives.** If other agents (approved/licensed/cleared products or EUA products) may
938 treat or prevent the same or closely related condition for [INTENDED USE], this
939 information should be stated. If available, the relative or expected safety and effectiveness of
940 the alternative should be provided, particularly for use in different populations or settings.
941 Such information may include:
942
943 ➢ When an alternative product may be more appropriate, e.g., in the treatment of the
944 pregnant women, infants and children, and immunocompromised individuals, or other
945 special populations.
946
947 ➢ For preventive treatments, the time needed for [PRODUCT] to be administered in
948 advance of the exposure to be effective, and alternatives that may be more effective if
949 that time is exceeded.
950
951 • **Significant known and potential risks and benefits** may include relevant information about
952 the manufacturer (e.g., a waiver of Good Manufacturing Practices compliance), if known.

953

954 • **Consequences** of not taking/using [PRODUCT], including possible health effects and
955 quarantine, and of stopping the use of [PRODUCT] against the recommendation of the
956 health care provider.

957

958 • **New findings.** A statement about the fact that any significant new findings observed during
959 or after the course of widespread use will be made available.

960

961 • **Approved products.** For approved products being used for unapproved indications, the Fact
962 Sheet also may include critical elements from the package insert.

963

964 • **Contacts.** Whom to contact if you have any questions or concerns (other than an adverse
965 event report) about the product.

966

967 # APPENDIX B

968

969 **FACT SHEET for the Recipient**

970

971 [PRODUCT for INTENDED USE]

972

973 1. An emergency has been declared by the Secretary of Health and Human Services.

974

975 2. [INCLUDE A BRIEF DESCRIPTION (1-2 sentences) OF THE EMERGENCY].

976

977 3. The FDA Commissioner has authorized the emergency use of [PRODUCT] for
978 [IDENTIFY THE INTENDED USE]. This authorization will terminate on [DATE 1 YEAR
979 FROM THE DATE OF DECLARATION], or when the emergency has ceased to exist,
980 whichever is earlier.

981

982 4. The information in this Fact Sheet is the minimum necessary to inform you of the
983 significant known and potential risks and benefits of emergency use of [PRODUCT].

984

985 5. The significant known and potential risks and benefits of emergency use of [PRODUCT]
986 are: [LIST]. The extent to which such risks and benefits are unknown is [EXPLAIN].

987

988 6. The available alternatives to [PRODUCT] are: [LIST]. The risks and benefits of
989 [ALTERNATIVES] are: [LIST]. [If there is no alternative, provide an explanation of outcomes

990 of exposure or of any special public health measures (e.g., quarantine or monitoring) that an
991 individual who does not receive the EUA product may face.]
992
993 7. [INCLUDE NAME, ADDRESS, AND TELEPHONE NUMBER FOR
994 MANUFACTURER.]
995
996 You have the option to accept or refuse administration of [PRODUCT]. The consequences of
997 refusing administration of [PRODUCT] are [LIST].
998
999 Available alternatives to [PRODUCT] are: [LIST]. The risks and benefits of these alternatives
1000 are: [LIST].
1001
1002 Potential adverse events for [PRODUCT] include [LIST]. Should you experience an adverse
1003 event, [INCLUDE INSTRUCTIONS].
1004
1005 Any significant new findings observed during the course of emergency use of [PRODUCT] will
1006 be made available [STATE HOW FINDINGS WILL BE MADE AVAILABLE].

1007 APPENDIX C

1008

1009 LIABILITY AND COMPENSATION PROGRAMS

1010 CONTACT INFORMATION

1011

1012

1013 **Federal Employees' Compensation Act**

1014 U.S. Department of Labor

1015 Office of Workers' Compensation Programs

1016 200 Constitution Avenue, NW

1017 Washington, DC 20210

1018 (202) 693-0031

1019 *www.dol.gov/esa/owcp_org.htm*

1020

1021 **Federal Tort Claims Act (DHHS Program)**

1022 Department of Health & Human Services

1023 Public Health Service

1024 FTCA

1025 5600 Fishers Lane, Room 5C-10

1026 Rockville, Maryland 20857

1027 FTCA Help Line: 1-866-FTCA-HELP (382-2435

1028 *http://bphc.hrsa.gov/risk/default.htm*

1029

1030 **Smallpox Vaccine Injury Compensation Program**

1031 Health Resources and Services Administration

1032 Smallpox Vaccine Injury Compensation Program Office

1033 5600 Fishers Lane, Room 16C-17

1034 Rockville, MD 20857

1035 (888) 496-0338

1036 *www.hrsa.gov/smallpoxinjury*

1037

1038 **National Vaccine Injury Compensation Program**

1039 Health Resources and Services Administration

1040 National Vaccine Injury Compensation Program Office

1041 5600 Fishers Lane, Room 11C-26

1042 Rockville, Maryland 20857

1043 (800) 338-2382

1044 *www.hrsa.gov/vaccinecompensation*

1045

1046 **SAFETY ACT:**

1047 Department of Homeland Security

1048 ATTN: SAFETY ACT

1049 245 Murray Lane, Bldg. 410

1050 Washington, DC 20528

1051 (866) 788-9318

1052 *www.safetyact.gov*

1053

1054 **PREP Act**

1055 Department of Health and Human Services

1056 Office of Public Health Emergency Preparedness

1057 200 Independence Ave., SW, Room 638-G

1058 Washington, DC 20201

1059 (202) 205-2882

1060 *www.hhs.gov/ophep*

1061