Guidance on Emergency Use Authorization of Medical Products
(OMB Control Number 0910-0595)
SUPPORTING STATEMENT

Terms of Clearance: None

A. Justification

1. Circumstances Making the Collection of Information Necessary

The Food and Drug Administration (FDA) is requesting OMB approval under the Paperwork Reduction Act (5 CFR Part 1320) for a guidance on the Agency's policies for authorizing the use of an unapproved drug, device, or biologic (unapproved product) or an unapproved use of an approved medical product during a declared emergency. The guidance describes the Agency's general recommendations and procedures for issuance of Emergency Use Authorizations (EUAs) under section 564 of the Federal Food, Drug, and Cosmetic (FD&C) Act.

The guidance describes six collections of information: (1) The submission of a request for FDA to issue an EUA or a substantive amendment to an EUA that has previously been issued, assuming the requisite declaration under section 564 of the FD&C Act has been made and criteria for issuance have been met; (2) the submission of a request for FDA to review information/data (i.e., a pre-EUA package) for a candidate EUA product or a substantive amendment to an existing pre-EUA package for preparedness purposes; (3) the submission of reports by a manufacturer of an unapproved EUA product; (4) the submission of reports by State and local public health officials administering an unapproved EUA product; (5) recordkeeping by a manufacturer of an unapproved EUA product; and (6) recordkeeping by State and local public health officials administering an unapproved EUA product.

No burden was attributed to recordkeeping by the Federal Government (e.g., related to the administration of EUA products). In addition, no burden was attributed to reporting or recordkeeping for unapproved uses of approved products because, as approved products, they already are subject to approved collections of information: adverse experience reporting for biological products is approved under OMB control number 0910-0308 through 02/28/18; adverse drug experience reporting is approved under OMB control number 0910-0230 through 12/31/18; adverse device experience reporting is approved under OMB control number 0910-0471 through 05/31/17; investigational new drug (IND) application regulations are approved under OMB control number 0910-0014 through 02/28/19; and investigational device exemption reporting is approved under OMB control number 0910-0078 through 03/31/16. Any additional burden for an unapproved use of an approved product that might be imposed by this collection would be minimal.

Because the guidance provides recommendations for submitting information to FDA in support of an EUA for an unapproved medical product or an unapproved use of an approved product, FDA is requesting OMB approval for the following reporting and recordkeeping recommendations:

- Requests for FDA to issue an EUA or a substantive amendment to an EUA that has previously been issued, assuming the requisite declaration under section 564 of the FD&C Act has been made and criteria for issuance have been met

The guidance provides recommendations for submission of data and information to meet the criteria for issuance of an authorization that are set out in section 564(c) of the Act. Among other things, data supporting an EUA must demonstrate that, based on the totality of the scientific evidence available to the agency, including data from adequate and well-controlled clinical trials (if available), it is reasonable to believe that the product may be effective in diagnosing, treating, or preventing a serious or life-threatening disease or condition; the known and potential benefits of the product outweigh the known and potential risks; and there is no adequate, approved, and available alternative to the product. Although the exact type and amount of data needed to support an EUA may vary depending on the nature of the declared emergency and the nature of the candidate product, the guidance provides recommendations for scientific evidence evaluating the product's safety and effectiveness, including the adverse event profile for diagnosis, treatment, or prevention of the serious or life-threatening disease or condition, as well as data and other information on safety, effectiveness, risks and benefits, and (to the extent available) alternatives.

- Requests for FDA to review information/data (i.e., a pre-EUA package) for a candidate EUA product or a substantive amendment to an existing pre-EUA package for preparedness purposes

Recognizing that during an emergency, the time available for the submission and review of an EUA request may be severely limited, the guidance encourages entities with candidate products to submit data and information on a candidate product prior to a determination of emergency (pre-EUA submissions). The same data recommendations that apply to a Request for Consideration for an EUA also apply to a pre-emergency submission.

- Reporting by a manufacturer of an unapproved EUA product

Section 564(e) of the Act requires the FDA Commissioner (to the extent practicable given the circumstances of the emergency) to establish certain conditions on an EUA that the Commissioner finds necessary or appropriate to protect public health. Those conditions include adverse event monitoring and reporting by manufacturers of an unapproved medical product authorized for emergency use. The statute also gives the FDA Commissioner authority to establish other conditions on an authorization necessary or appropriate to protect the public health.

- Reporting by State and local public health officials of an unapproved EUA product

The requirements to perform adverse event monitoring and reporting are mandatory (to the extent practicable given the circumstances of the emergency) under section 564(e) on any person who carries out any activity for which an authorization for an unapproved product is issued. If unapproved products needed to be used under an EUA, it is likely that State and local public health officials would be involved in the administration of EUA products. Accordingly,

PRA burden is calculated for State and local public health officials who would be required to perform activities related to product administration and information dissemination under the terms of an authorization.

- Recordkeeping by manufacturers of an unapproved EUA product

Section 564(e) provides that the FDA Commissioner shall establish appropriate conditions with respect to manufacturers' recordkeeping, reporting, and records access, to the extent that such conditions are practicable.

- Recordkeeping by State and local public health officials regarding an unapproved EUA product

The FDA Commissioner also may, under section 564(e), impose comparable records conditions on any person (e.g., State and local public health officials) carrying out any activity for which an authorization is issued.

2. Purpose and Use of the Information Collection

The submissions described in the guidance provide the means by which FDA can, among other things, determine whether a candidate product meets the statutory criteria for issuance of an authorization under section 564(c) of the Act. The Agency will use information submitted in compliance with a condition of authorization for the following purposes: to (1) track the distribution and administration of an EUA product; (2) monitor the information being disseminated to health care professionals and other authorized dispensers and potential product recipients regarding the known and potential risks and benefits of an EUA product, an individual's option to refuse the product, and the possible consequences of refusal; (3) obtain timely information on adverse reactions to an EUA product; (4) obtain other information pertinent to determining whether the authorization should be revoked because the statutory criteria for issuance are no longer met; (5) determine whether a manufacturer or other person acting under an EUA has complied with the conditions of the authorization; and (6) prepare pre-EUA packages to be poised for timely issuance should there be a determination of emergency justifying issuance of the EUA.

3. Use of Improved Information Technology and Burden Reduction

Use of Improved Technology and Burden Reduction – FDA has developed several guidances for industry to improve the use of information technology in the submission of marketing applications for human drugs and related reports. These guidance documents and others are available at FDA's web site http://www.fda.gov/Drugs/%20GuidanceComplianceRegulatoryInformation/Guidances/default.htm.

Section 745A(b) of the FD&C Act, added by section 1136 of the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA), provides statutory authority to require eCopies after issuance of final guidance (See Public Law No: 112-144). FDA's

implementing guidance describes how device companies should replace one paper copy of a device application with an eCopy and identify the required format and technical requirements of the eCopy. The eCopy requirement does not require or request any information that is not already submitted to the Agency and/or covered under the existing ICR, and therefore does not change the cost or hour burden.

4. Efforts to Identify Duplication and Use of Similar Information

FDA is the only Agency that has the power, by delegation from the Secretary of Health and Human Services, to issue EUAs for medical products under section 564 of the Act and would be the only Agency that would collect this information.

5. Impact on Small Businesses or Other Small Entities

Although the majority of drug products are developed by large pharmaceuticals, medical countermeasures typically are developed by small companies. Generally the information collection requested under the guidance will apply to small companies. To ensure adequate protection of the public health, FDA's Office of Counterterrorism and Emerging Threats provides ongoing assistance on EUA issues to interested entities. Staff from the three medical product centers, the Center for Biologic Evaluation and Research, the Center for Drug Evaluation and Research, and the Center for Devices and Radiological Health, consult with, and expend considerable resources providing technical assistance to, small businesses and other interested companies regarding EUA submissions.

6. Consequences of Collecting the Information/Less Frequent Collection

Less frequent collection of the information described above would significantly limit the FDA Commissioner's ability to determine whether the statutory criteria for issuance of an authorization of an unapproved product were met and to ensure compliance with the conditions of the authorization. Moreover, the information required by and reported under a condition of authorization is critical to an appropriate public health response should significant adverse events occur once an EUA product is administered widely. It also would provide early warning if a product no longer met the criteria for authorization. Information collected for preparation of pre-EUA packages is critical to the U.S. Government's ability to respond in a timely manner to the relevant medical emergencies.

7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The recordkeeping and reporting requirements set out in the guidance are consistent with the guidelines in 5 CFR 1320.5(d)(2), including the frequency of reporting. However, the Agency recognizes that the FDA Commissioner may, due to the risk-benefit profile of a particular EUA product, require frequent reporting as a condition of authorization.

8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

In accordance with 5 CFR 1320.8(d), FDA published a 60 day notice for public comment in the FEDERAL REGISTER of December 23, 2015 (80 FR 79905). No comments were received.

9. Explanation of any Payment/Gift to Respondents

FDA did not provide any payment or gift to respondents.

10. Assurance of Confidentiality Provided to Respondents

Confidentiality of the information submitted under this guidance is protected under 21 CFR part 20. The unauthorized use or disclosure of trade secrets required in applications is specifically prohibited under section 310(j) of the Act.

11. Justification for Sensitive Questions

There are no questions of a sensitive nature.

12. Estimates of Annualized Hour and Cost Burden

12 a. Annualized Hour Burden Estimate

The total annual burden estimate for this information collection is 1,622 hours. The estimated reporting burden for this collection is 1,152 hours and the estimated recordkeeping burden is 470 hours.

FDA estimates the burden of this collection of information as follows:

Table 1. -- Estimated Annual Reporting Burden

Type of Respondent	No. of Respondents	No. of Responses per Respondent	Total Annual Responses	Average Burden per Response	Total Hours
Requests to Issue an EUA or a Substantive Amendment to an Existing EUA	9	1.33	12	33	396
FDA Review of a Pre-EUA Package or an Amendment Thereto	11	1.45	16	35	560

Manufacturers of an Unapproved EUA Product	5	1.6	8	2	16
Public Health Authorities; Unapproved EUA Product	30	3	90	2	180
Total					1,152

The reporting burden is based on the following:

- Requests to Issue an EUA or a Substantive Amendment to an Existing EUA

Based on the previous three years' experience, which has included two determinations of actual or potential emergencies involving a biological, chemical, radiological, or nuclear agent and declarations justifying EUA submissions, FDA anticipates continued occurrences of such determinations and declarations, and therefore, FDA estimates that 12 Requests for FDA to issue an EUA or to amend a previously issued EUA will be filed annually. In some cases, manufacturers directly submit EUA requests. Often a federal government entity (e.g., CDC, DOD) requests that FDA issue an EUA. In many of these cases, manufacturer respondents inform these requests, which are the activities that form the basis of the estimated reporting burdens. However, in some cases such as with antimicrobial products for which there are multiple generic manufacturers, the federal government is the sole respondent; manufacturers do not inform these requests or submissions. FDA estimates minimal burden when the federal government performs the relevant activities. In addition to variability based on whether there is an active manufacturer respondent, other factors also inject significant variability in estimates for annual reporting burdens. A second factor is the type of product. For example, FDA estimates greater burden for novel therapeutics than for certain unapproved uses of approved products. A third significant factor that injects variability is the type of submission. For example, FDA estimates greater burden for "original" EUA than for amendments to them, and FDA estimates minimal burden to issue an EUA when there is a previously reviewed pre-EUA package or investigational application. For purposes of estimating the reporting burden, FDA has calculated the anticipated burden on manufacturers based on the anticipated types of responses (i.e., estimated manufacturer input), types of product, and types of submission that comprise the described reporting activities. Based on the recommendations in the guidance, FDA estimates the average reporting burden to be 33 hours per Request. This estimate anticipates as few as no hours (i.e., when there is no manufacturer input) to as many as 70 hours (i.e., for novel therapeutic products). Therefore, FDA estimates that a total of approximately 396 hours per year will be required to prepare and submit Requests for FDA to Issue an EUA or a Substantive Amendment to an Existing EUA.

- Requests to Review a Pre-EUA Submission or Substantive Amendment Thereto

Based on the number of pre-EUA submissions that the Agency received in the past three

years, FDA estimates that 16 pre-EUA submissions will be filed annually. As with EUA submissions, a federal government entity (e.g., CDC, DOD) often file pre-EUA submissions, and there is varying degrees to which manufacturer respondents inform these requests. Also as with EUA submissions, there is significant variability in estimates for annual reporting burdens based on the type of product (e.g., novel therapeutic compared to an approved product) and the type of submission (e.g., original pre-EUA submission compared to an amendment to a pre-EUA package). Based on the recommendations in the guidance, FDA estimates the average reporting burden to be 35 hours per Request. As with Requests for an EUA, this estimate anticipates as few as no hours (i.e., when there is no manufacturer input) to as many as 80 hours (i.e., for novel therapeutic products). Therefore, FDA estimates that a total of approximately 560 hours per year will be required to prepare and submit Requests for FDA to Review a pre- EUA submission or a substantive Amendment to an Existing pre-EUA package.

- Manufacturers of an unapproved EUA product

Section 564(e) of the Act sets out certain conditions of authorization that are mandatory for manufacturers of an unapproved product, to the extent that such conditions are practicable. These include, among other things, requirements for information dissemination to health care providers and potential product recipients and adverse event reporting. FDA estimates that it will issue 8 EUAs for unapproved products annually and that 5 manufacturers would need to report under the conditions of an EUA. The Agency estimates that such reporting will require approximately two hours per response. Therefore, FDA estimates that 16 hours per year will be required to prepare and submit manufacturers' reports to the Agency under the conditions of an authorization.

- State and local public health officials; unapproved EUA product

If unapproved products needed to be used under an EUA, it is likely that State and local public health officials would be responsible for the administration of EUA products and would need to report to FDA under the conditions of an authorization. The Agency estimates that 30 jurisdictions each year would be involved in administering three EUAs for unapproved products. FDA anticipates that 6 of the unapproved products authorized of a total of 8 would be for use of an unapproved *in vitro* diagnostic device. While manufacturers would be required to report for each device, a public health official would only be required to report for the one device available to that jurisdiction. Therefore, the FDA estimates that State and local officials will spend approximately 180 hours per year to prepare and submit information under the conditions of an authorization.

Table 2. - Estimated Annual Recordkeeping Burden

Type of Respondent	No. of Recordkeepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Record	Total Hours

Manufacturers of an Unapproved EUA Product	5	1.6	8	25	200
Public Health Authorities; Unapproved EUA Product	30	3	90	3	270
Total					470

The recordkeeping burden is based on the following:

- Manufacturers of an unapproved EUA product

Section 564(e) of the Act sets out certain conditions of authorization that are mandatory for manufacturers of an unapproved product, to the extent that such conditions are practicable. These include, among other things, recordkeeping requirements. FDA estimates that five different manufacturers would need to keep such records for 8 products each year under the conditions of an EUA. The Agency estimates that such recordkeeping will require approximately 25 hours per record. Therefore, FDA estimates that 200 hours per year will be required to prepare such records under the conditions of an authorization.

- State and local public health officials; unapproved EUA product

If an unapproved product is needed to be used under an EUA, it is likely that State and local public health officials would be responsible for the administration of EUA products and would need to report to FDA under the conditions of an authorization. The Agency estimates that 30 jurisdictions each year would be involved in administering three EUAs for unapproved products. FDA anticipates that 6 of the unapproved products authorized of a total of 8 would be for use of an unapproved *in vitro* diagnostic device. While manufacturers would be required to maintain records for each device, a public health official would only be required to maintain records for the one device available to that jurisdiction. Therefore, the FDA estimates that State and local officials will spend approximately 270 hours per year to prepare and submit information under the conditions of an authorization.

12b. Estimated Annualized Burden Costs

In remaining consistent with FDA's current estimates for INDs we estimate an average industry wage rate of $75.00 per hour (including overhead and benefits) for preparing and submitting the information collection requirements under 21 CFR Parts 312 and 601. Assuming an average of $75 per hour to comply with the recommendations and conditions of authorization, the cost would be approximately $81,100.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs

Requests to Issue an EUA or a Substantive Amendment to an Existing EUA	396	$75	$29,700
FDA Review of a Pre-EUA Package or an Amendment Thereto	560	$75	$42,000
Manufacturers of an Unapproved EUA Product	216	$75	$16,200
State and Local Public Health Officials; Unapproved EUA Product	450	$75	$33,750
Total			$121,650

13. Estimates of other Total Annual Cost Burden to Respondents and/or Recordkeepers/Capital Costs

    There are no capital, start-up, operating or maintenance costs associated with this information collection.

14. Annualized Cost to Federal Government

    FDA estimates it would need approximately 35 full-time equivalents (FTEs) to review the information submitted under the EUA guidance. If each FTE equals approximately $110,000, the annualized cost burden to FDA would be $ 3.85 million.

15. Explanation for Program Changes or Adjustments

    There are no program changes or adjustments to the information collection burden.

16. Plans for Tabulation and Publication and Project Time Schedule

    Information collected under this requirement will not be published.

17. Reason(s) Display of OMB Expiration Date is Inappropriate

    The Agency does not seek an exemption from displaying the expiration date.

18. Exceptions to the Certification Statement

    There are no exceptions to the certification.