SUPPORTING STATEMENT

Draft Guidance on Emergency Use Authorization of Medical Products

(OMB Control Number 0910-0595)

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 Act (the Act).

The guidance describes six collections of information: (1) The submission of a request for consideration for an EUA; (2) the submission of data and other information on a candidate EUA product prior to a determination of actual or potential emergency; (3) the submission of reports by a manufacturer of an EUA product; (4) the submission of reports by State and local public health officials administering an EUA product; (5) recordkeeping by a manufacturer of an EUA product; and (6) recordkeeping by State and local public health officials administering an EUA product.

No burden was attributed to recordkeeping by the Federal Government (e.g., related to the administration of EUA products to military personnel). 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 6/30/2010; adverse drug experience reporting is approved under OMB control number 0910-0230 through 11/30/2010; adverse device experience reporting is approved under OMB control number 0910-0471 through 7/31/2011; investigational new drug application regulations (IND) are approved under OMB control number 0910-0014 through 8/31/2010; and investigational device exemption reporting is approved under OMB control number 0910-0078 through 1/31/2010. 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 Consideration for an EUA

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.

- Pre-emergency Submissions

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. Entities submitting data and information prior to an emergency generally will have more time to consult with the Agency and to respond to data or information inquiries.

- Reporting by Manufacturers

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 that he finds to be necessary or appropriate to protect the public health.

- Reporting by State and local public health officials

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 adverse event monitoring and reporting 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 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 information on side effects associated the product; and (5) obtain other information pertinent to determining whether the authorization should be revoked because the statutory criteria for issuance are no longer met. FDA also will use this information to determine whether a manufacturer or other person acting under an EUA has complied with the conditions of the authorization.

3. Use of Improved Information Technology and Burden Reduction

Submissions may be provided in paper or electronic format. Specific information for electronic format may be obtained by reviewing guidance from the appropriate FDA Center (CBER--www.fda.gov/cber/esub/esubguid.htm; CDER--www.fda.gov/cder/regulatory/ersr; and CDRH--www.fda.gov/cdrh/elecsub.html).

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 medical product development typically is an activity completed by large firms, the information collection requested under the guidance applies to small as well as large companies. To ensure adequate protection of the public health, FDA does not believe that it should apply different standards with respect to the authorization and use of these unapproved medical products. The Agency, in its outreach activities and through its participation in workshops, has continually offered its assistance on EUA issues to any 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, continue to consult with, and offer 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. To the extent that such information collection and reporting requirements would be impracticable, section 564(e) of the Act allows the FDA Commissioner not to impose "mandatory" conditions of authorization set out in the statute.

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/Outside Consultation

In the Federal Register of April 20, 2009 (74 FR 17962), FDA invited comments on the collection of information. There were no comments 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

12a. Estimated Annualized Burden Hours

The total annual burden estimate for this information collection is 3,204 hours. The estimated reporting burden for this collection is 2,544 hours and the estimated recordkeeping burden is 660 hours.

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

Table 1. -- Estimated Annual Reporting Burden

Type of Respondent	No. of Respondents	Annual Frequency per Response	Total Annual Responses	Hours per Response	Total Hours
Requests for Consideration; Pending Application on file	5	2	10	15/60	150
Requests for Consideration; No Application pending	4	2	8	50/60	400
Pre-EUA Submissions; Pending Application on file	2	2	4	20/60	80
Pre-EUA Submissions; No Application pending	11	2	22	75/60	1,650
Manufacturers of an Unapproved EUA Product	3	4	12	2/60	24
State and Local Public Health Officials; Unapproved EUA Product	30	4	120	2/60	240
Total					2,544

The reporting burden is based on the following:

- Requests for Consideration for an EUA

Since in the past year, there have been several determinations of actual or potential

emergencies involving a biological, chemical, radiological, or nuclear agent and declarations justifying EUA submissions, FDA anticipates that such determinations and declarations will continue to occur, and therefore, FDA estimates that 18 Requests for Consideration will be filed annually. For 10 of the Requests, the entity will provide reference to pending or approved applications (e.g., an Investigational New Drug application). Based on the recommendations in the draft guidance, the reporting burden for such a Request is estimated to be approximately 15 hours. The other 8 Requests for Consideration will not reference a pending application for the proposed use and, therefore, is estimated to require approximately 50 hours. Therefore, FDA estimates that a total of approximately 620 hours per year will be required to prepare and submit Requests for Consideration for an EUA following a determination of actual or potential emergency.

- Pre-EUA Submissions

Recognizing that a rapid response to an emergency can help mitigate effects, FDA encourages entities to submit data and information on candidate products before a determination of emergency occurs. The number of companies working on medical countermeasures (MCM) to biological, chemical, radiological, or nuclear agents is increasing and FDA anticipates increasing numbers of pre-EUA submissions. Based on the number of pre-EUA submissions that the Agency received in the past year, FDA estimates that 26 pre-EUA submissions will be filed annually. Because most pre-EUA submissions do not reference a pending application, FDA anticipates that 4 of these pre-EUA submissions will reference applications currently pending before the Agency; 22 submissions will not. Because there typically is greater opportunity for an ongoing dialogue to refine pre-EUA submissions, the Agency estimates that a pre-EUA submission referencing a pending application will require approximately 20 hours per response and a pre-EUA submission not referencing a pending application will require an estimated 75 hours per response. Therefore, the Agency estimates that a total of 740 hours will be required to prepare and submit pre-emergency submissions to FDA.

- 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 three EUAs for unapproved products and that three manufacturers would need to report, on a quarterly basis, under the conditions of an EUA. The Agency estimates that such reporting will require approximately two hours per response. Therefore, FDA estimates that 24 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 and would need to file quarterly reports. Therefore, the FDA estimates that State and local officials will spend approximately 720 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	3	4	12	25/60	300
State and Local Public Health Officials; Unapproved EUA Product	30	4	120	3/60	360
Total					660

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 three manufacturers would need to keep such records, on a quarterly basis, under the conditions of an EUA. The Agency estimates that such recordkeeping will require approximately 25 hours per record. Therefore, FDA estimates that 300 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 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 keep records required by the FDA Commissioner as the condition of an authorization. The Agency estimates that 30 jurisdictions each year would be involved in administering an EUA product and would need to keep such records, on a quarterly basis. FDA estimates that each record will require three hours per record. Therefore, the FDA estimates that State and local officials will spend approximately 660 hours per year to prepare records required as a condition of authorization.

12b. Estimated Annualized Burden Costs

Assuming an average of $50 per hour (labor plus overhead) to comply with the recommendations and conditions of authorization, the cost would be approximately $160,200.

Type of Respondent	Total Burden Hours	Hourly Wage Rate	Total Respondent Costs
Requests for Consideration	550	$50	$27,500
Pre-EUA Submissions	1,730	$50	$86,500
Manufacturers of an Unapproved EUA Product	324	$50	$16,200
State and Local Public Health Officials; Unapproved EUA Product	600	$50	$30,000
Total			$160,200

13. Estimates of other Total Annual Cost Burden to Respondents 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 85 full-time equivalents (FTEs) to review the information submitted under the EUA guidance. If each FTE equals approximately $100,000, the annualized cost burden to FDA would be $8.5 million.

15. Explanation for Program Changes or Adjustments

The adjustment/increase in burden is a result of the agency determining that we will receive more declarations supporting the issuance of EUAs as a result of the 2009 H1N1 public health emergency. As a result of this increased activity, the likelihood of a continued increase in the number of EUA and pre-EUA submissions, as well as data on the number of past reports received, FDA is estimating an increase in 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.