



INTERAGENCY AGREEMENT

CPSC-IAG-02-1300

1. IAG NO. (FDA) 224-02-3005	2. TYPE OF AGREEMENT <input checked="" type="checkbox"/> New <input type="checkbox"/> Mod <input type="checkbox"/> Administrative <input type="checkbox"/> No Cost Ext.	3. MODIFICATION NO.
---------------------------------	--	---------------------

4. TITLE OF PROJECT
National Surveillance of Injury & Death Related to Drugs and Medication Errors Pilot

5. DESCRIPTION OF WORK - ATTACHED	6. AMOUNT \$44,750.00
-----------------------------------	--------------------------

7. NAME AND ADDRESS OF PARTICIPATING FEDERAL AGENCY US Consumer Product Safety Commission 4330 East-West Highway, Room 604 Bethesda, MD 20814	LIAISON NAME Art McDonald	PHONE NO. () 301 504-0539 X1249
--	------------------------------	--

8. NAME AND ADDRESS OF PARTICIPATING FDA UNIT FDA/CDER/OPSS/Office of Drug Safety 5600 Fishers Lane, Room 15B-33 Rockville, MD 20857	LIAISON NAME Diane Wysowski	PHONE NO. (301) 827-3165
---	--------------------------------	------------------------------

9. PERIOD OF AGREEMENT FROM From the date of signature THROUGH FY2002

This agreement may be terminated by either party upon a thirty day advance written notice.

10. AUTHORITY (FDA)

Economy Act approved June 30, 1932, as amended by 31 USC 1535

Section 301 of the Public Health Service Act (42 USC 241)

Other (specify) _____

11. AUTHORITY (Other Agency)

12. FDA FUNDING INFORMATION

Increase from \$0 by \$44,750.00 to \$44,750.00

Decrease from _____ by _____ to _____

7520600
2-699210-D-78015
25.38 ↓ (699 2910 - D -

13. Administrative billing requirements will comply with GAO Policy and Procedures, Title 7, Section 8.4

Billing: see Sec. H OPAC system; FDA ALC 75080029 Other Agency ALC 61-00-0001

_____ SF 1050 - FDA Accounting (NFA-120) 5600 Fishers Lane, Rockville, MD 20857

14. PARTICIPATING AGENCY FUNDING INFORMATION (This block must be completed if funding is being provided to the FDA)

a. Legal authority for the acquisition of supplies/services exists within your agency.
b. This action does not conflict with any other agency's authority or responsibility.

15. PARTICIPATING AGENCY IS

Required to sign Not required to sign

16. FDA ACCEPTANCE

NAME: Peggy Jones
Peggy Jones

TITLE: Grants Management Officer

DATE: 7/1/02

17. PARTICIPATING AGENCY ACCEPTANCE

NAME: Doris B. Kessler
Doris B. Kessler

TITLE: Contracting Officer

DATE: June 27, 2002

OFACS ACQUISITIONS
2002 JUN 28 3:25

**INTERAGENCY AGREEMENT FOR A PILOT STUDY BETWEEN THE
OFFICE OF DRUG SAFETY, FDA, AND THE U.S. CONSUMER PRODUCT
SAFETY COMMISSION**

A. Introduction and Background

The Office of Drug Safety, Food and Drug Administration, agrees to provide funds to the U.S. Consumer Product Safety Commission (CPSC) for the services described in this pilot project in accordance with the terms and conditions set forth under Section D, Statement of Work, below.

The Office of Drug Safety of the FDA conducts ongoing national surveillance of injury and death related to drugs and medication errors. Surveillance of drug-related injury and death is primarily accomplished through analysis of adverse event reports in which the adverse event is suspected of being caused by a drug. Reporters who include physicians, pharmacists, other health professionals, lawyers, and consumers submit the reports to the FDA's Adverse Event Reporting System (AERS). Serious outcomes, especially death, are priorities for review and analysis.

A major limitation of this reporting system is underreporting. Underreporting is believed to be especially egregious for older drugs with known reactions. Also, the reporting of serious reactions and deaths related to use of over the counter drugs is poor. Underreporting hampers our efforts to determine the incidence, etiology, and risk factors associated with drug-related deaths, thereby also affecting risk management strategies and ultimately, public health.

Surveillance of serious reports in AERS is often supplemented by searches of the medical literature. Sometimes individual case reports, a case series, and clinical or epidemiological studies are published that can aid in risk assessment. However, such literature is not always available, and when it is, it is often about new medications with novel and/or relatively rare reactions. Important drug safety issues involving well-known reactions of older drugs are not usually priorities for ongoing risk assessment and risk management.

All deaths in the United States are required to be registered on death certificates and are entered into the national vital statistics system of the United States. If FDA staff had access to death certificates for deaths attributed to drugs, the information could supplement and validate the reports from AERS and case reports in the medical literature. The information from death certificates could help provide rates, trends, and demographic factors for drug-attributed deaths.

This interagency agreement would set up a mechanism for the FDA to obtain and analyze certificates for deaths attributed to certain drugs causing adverse effects in therapeutic use. This is being set up as a pilot study to assess its utility for FDA's drug risk assessment and regulatory action.

B. Need

A primary mission of the Center for Drug Evaluation and Research of the FDA is the approval of safe and effective drugs. Prior to approval, drug experiments are conducted on a relatively small number of persons. Persons with various characteristics including significant illness are usually excluded from participation in these drug trials. In the post-marketing phase, the drug's safety profile becomes more evident through the accumulation, review, and analysis of adverse event reports submitted to the FDA and through case reports, case series, and studies published in the medical literature.

A priority for analysis of adverse event reports at the FDA is those with a fatal outcome. Unfortunately, the reporting system is limited by underreporting so that estimates of incidence of adverse events are unknown. To more reliably estimate the incidence of death attributed to specific drugs and drug categories, it would be desirable to have access to death certificates in which drugs were attributed by the physician as the underlying or contributing cause of death. Since death registration is national in scope and is required and ongoing, accessing death certificates would provide a resource to track mortality rates for specific drugs and drug categories. Unlike the FDA's system of adverse event reports that contains duplicate records, the death registration system includes only one death certificate per deceased person. In addition, death certificates provide the specific cause of death and demographic information for the decedent so that age- and sex-specific mortality rates can be obtained and compared with the age- and sex-specific use of the drug. Persons at risk of death due to drugs can thus be characterized.

However, as with underreporting in AERS, there is also likely to be under-attribution of drugs as causes of death. Drugs that exert acute and direct effects are most likely to be attributed as causes of death on certificates. Examples of these drugs include hypoglycemics, intravenous contrast media, drugs that cause anaphylaxis, and anticoagulants. As a result, we have targeted some of these codes for collection of death certificates for drug classes with the highest likelihood of being detected and coded on death certificates.

The Division of Medical Imaging and Radiopharmaceutical Drug Products of the FDA would like to know whether ionic contrast agents are associated with more deaths and higher rates of death than nonionic contrast agents. We may be able to answer this question by analyzing the death certificate data in which contrast agents are mentioned as the underlying or contributing cause of death by collecting those with the ICD-10 code Y57.5, adverse effects in therapeutic use of x-ray contrast media. From NCHS multiple cause of death mortality statistics, the number of deaths attributed to Y57.5 in 1999 was 53.

Codes that could provide data on the drugs associated with anaphylaxis include T88.6, Anaphylactic shock due to adverse effects of correct drug or medicament properly administered and T88.7, allergic reaction NOS to correct medicinal substance properly administered. NCHS statistics indicate that there were 36 deaths attributed to T88.6 and 312 attributed to T88.7 in 1999.

According to the NCHS 1999 multiple cause of death file, deaths attributed to adverse effects of androgens and anabolic congeners in therapeutic use (code Y42.7) increased from 7 deaths in 1998 to 389 deaths in 1999. Because of this increase, we believe it would be important to obtain death certificates for this code to investigate this trend further.

C. Choice of Instrument

The Consumer Product Safety Commission (CPSC) has arrangements with each of the fifty states for the purchase of specific death certificates. Through this interagency agreement, their scope of work would be expanded to include death certificates in which drugs (i.e., those described above) have been attributed as the underlying or contributing cause. Death certificates would be identified by the codes of interest and forwarded by each state to the CPSC. Information would be abstracted from each certificate and coded to a data file that would be sent to the FDA for data analysis. We believe that this would be an efficient way to gather the information for FDA to describe deaths attributed to certain drugs or drug categories in the U.S. To test the feasibility and desirability of this approach, we propose this Interagency Agreement as a pilot project. This pilot project will test the ability of CPSC to obtain death certificates with the designated codes from the state health departments. To do this, CPSC will have to modify the contract that they have with each state health department. Obtaining the desired death certificates will depend on the ability of the state health department to retrieve them.

D. Statement of Work

This Agreement provides funds from the FDA to CPSC for the purchase and coding of death certificates in which the ICD-10 codes for drugs causing adverse effects in therapeutic use appear as causes of death (either underlying or contributing cause) on the death certificate. Specifically this agreement provides for the following:

1. The CPSC will request death certificates from all 50 states for deaths that occurred during the period from January 1, 1999 through December 31, 1999 with mention on the certificate as underlying cause or contributing cause the following codes: Y57.5, T88.6, T88.7, and Y42.7.
2. The death certificates will be processed and coded by CPSC in accordance with their present coding practices. The standard variables coded by CPSC include the following: certificate number, age, sex, race, products (drug names) associated with the death, date of death, date of incident leading to death, and location of death (city, state, zip code). FDA will supply up to 30 drug names that would be coded in the product field if they appear on the death certificate. The narrative that CPSC captures includes the causes of death (including specific drug names) recorded verbatim from the death certificate. The narrative also includes whether the decedent had an autopsy. The narrative is limited to 4 lines of 69 characters per line. Using NCHS 1999 multiple cause of death data, we are

able to estimate that about 790 death certificates will be collected and coded under this request.

3. CPSC will provide to FDA the coded record including the narrative and a scanned copy (pdf) of the original certificate.

4. CPSC will prepare a SAS data set of the death certificate data with documentation. Documentation will be submitted by CPSC staff to FDA staff for approval before coding is initiated. FDA staff understands that with the exception of the product field, CPSC coding is standardized and is not able to be amended for customized coding of variables. FDA will supply to CPSC up to 40 drug names that would be coded in the product field. CPSC will answer any questions FDA staff have concerning the data set and documentation and will provide guidance as requested.

5. Researchers from the Office of Drug Safety of the FDA will be primarily responsible for analyzing the data and preparing a publication to report pertinent findings. It is anticipated that findings would be published in one or more peer reviewed journal articles. Members of the professional staff of FDA and CPSC will jointly author publications of findings.

The costs include an overhead fee of \$25,000 plus \$25 per death certificate retrieved and coded for a total anticipated cost of \$44,750 for 790 death certificates.

E. Deliverables

1. CPSC will provide FDA staff with each coded death certificate including narrative and a scanned copy (pdf) of each original death certificate.
2. CPSC will deliver a SAS data set of the death certificate data with FDA preapproved documentation.

F. Restrictions on Use of Information

The Office of Drug Safety, FDA, will be responsible for the protection of personal information on the death certificates. The FDA shall not use the personal identifiers on the certificates without consent of the CPSC Project Officer and the state issuing the certificate. The FDA shall not release the personal identifiers to any outside party.

G. Period of Performance

We anticipate the entire project period to be from the date of signature through 2003. The initial budget period will be from the date of signature to September 30, 2002.

H. FASA Compliance

As the servicing agency, CPSC agrees to act in full compliance with Section 1074 of the Federal Acquisition Streamlining Act (FASA) of 1994 entitled ECONOMY ACT PURCHASES.

I. Method of Payment

Payment shall be made within 30 calendar days of the billing date set by CPSC through IPAC.

J. Funding

All funds provided by FDA in this agreement must be obligated by the performing agency by the end of the fiscal year in which the funds expire. Any unobligated but expired funds may not be used to fund services in subsequent periods. CPSC will notify FDA of any unobligated funds pertaining to this agreement at least 15 days before the end of the fiscal year so that the agreement can be amended to reduce the obligated amount when appropriate.

K. Resolution of Disagreements

In the event that CPSC and FDA have a disagreement arising under this interagency agreement, the parties shall cooperatively seek to resolve the disagreement. CPSC will make every reasonable effort to accommodate the needs of FDA before making a final decision.

L. Liaison Officers

For FDA:

Diane K. Wysowski, Ph.D.
Epidemiologist, Office of Drug Safety
FDA
Parklawn Building, Room 15B-08
Rockville, Maryland 20857
301-827-3165

Parivash Nourjah, Ph.D.
Epidemiologist, Office of Drug Safety
FDA
Parklawn Building, Room 15B-08
Rockville, Maryland 20857
301-827-3164

For CPSC:

Art McDonald
Director, Division of Hazards and Injury Data Systems

CPSC
4330 East-West Highway, Room 604
Bethesda, Maryland
301-594-0539, ext. 1249

G. Authority

This agreement is entered into under the authority of Section 27(g) of the Consumer Product Safety Act, approved October 27, 1972, U.S.C. 2076 (g) and the Economy Act, 31 U.S.C. 1535.

H. Appropriation Data

For CPSC:

For FDA:

02 PS EXOB 4310 11282 252e (\$44,750)

Attachment

**Variables to be Extracted from Death Certificates for the Following ICD-10 Codes:
Y57.5**

T88.6

T88.7

Y42.7

1. Certificate number
2. Age
3. Sex
4. Race
5. Product--specific drug name (verbatim)
6. Product--specific drug name (verbatim)
7. Date of death
8. Date of adverse drug event leading to death
9. City location of death
10. State location of death
11. Zip code location of death
12. Narrative remarks (free text) include verbatim causes of death and performance of autopsy as noted on death certificate. The narrative is limited to 4 lines of 69 characters per line.