[4] Total applications submitted during FY 95
[5] New Drug Application (includes applications for new antibiotic drugs)
[6] Abbreviated New Drug Application
[7] Abbreviated Antibiotic Drug Application
[8] Establishment License Application
[9] Product License Application

In FY 95, CDER received a total of 10,232 submissions and CBER received 1,905 submissions that would require use of this application form. FDA estimates that 40 hours would be required for an industry regulatory affairs specialist to fill out the harmonized form, collate the documentation, and submit the application to CDER or CBER.

Dated: September 25, 1996.

William B. Schultz,

Deputy Commissioner for Policy.

[FR Doc. 96–25076 Filed 9–30–96; 8:45 am]

BILLING CODE 4160–01–F

[Docket No. 96D–0236]

International Conference on Harmonisation; Draft Guideline on Data Elements for Transmission of Individual Case Safety Reports

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is publishing a draft guideline entitled ''Data Elements for Transmission of Individual Case Safety Reports.'' The draft guideline was prepared under the auspices of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH). The draft guideline is intended to standardize the data elements for the electronic transmission of individual case safety reports for both preapproval and postapproval reporting periods.

DATES: Written comments by December 30, 1996.

ADDRESSES: Submit written comments on the draft guideline to the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857. Copies of the draft guideline are available from the Drug Information Branch (HFD–210), Center for Drug Evaluation and Research, Food and Drug Administration, 7500 Standish Pl., Rockville, MD 20855, 301–594–1012, or written requests for single copies of the ICH documents can be submitted to the Manufacturers Assistance and Communication Staff (HFM–42), Center for Biologics Evaluation and Research, Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852–1448. Send one self-addressed adhesive label to assist that office in processing your requests. The document may also be obtained by mail or FAX by calling the Center for Biologics Evaluation and Research Voice Information System at 1–800–835–4709.

Persons with access to the INTERNET may obtain the document in several ways.

Users of ''Web Browser'' software, such as Mosaic, Netscape, or Microsoft Internet Explorer may obtain this document via the World Wide Web by using the following Uniform Resource Locators (URL's):

http://www.fda.gov/cber/cberftp.html
ftp://ftp.fda.gov/CBER/

The document may also be obtained via File Transfer Protocol (FTP). Requesters should connect to the FDA FTP Server, FTP.FDA.GOV (192.73.61.21). The Center for Biologics Evaluation and Research (CBER) documents are maintained in a subdirectory called ''CBER'' on the server. Logins with the user name of anonymous are permitted, and the user's e-mail address should be sent as the password.

The ''READ.ME'' file in that subdirectory describes the available documents which may be available as an ASCII text file (*.TXT), or a WordPerfect 5.1 or 6.x document (*.w51,wp6), or both.

The document can be obtained by ''bounce-back e-mail''. A message should be sent to:

ICH__DATA@al.cber.fda.gov

Finally, an electronic version of this draft guideline is available via the U.S. Government Printing Office's ''GPO Access.'' Internet users can access the database through the World Wide Web; the Superintendent of Documents home page address is http://www.access.gpo.gov/su__docs/

FOR FURTHER INFORMATION CONTACT:

Regarding the guideline: Richard M. Kapit, Center for Biologics Evaluation and Research (HFM–225), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301–827–3974.

Regarding the ICH: Janet J. Showalter, Office of Health Affairs (HFY–20), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–827–0864.

SUPPLEMENTARY INFORMATION: In recent years, many important initiatives have been undertaken by regulatory authorities and industry associations to promote international harmonization of regulatory requirements. FDA has participated in many meetings designed to enhance harmonization and is committed to seeking scientifically based harmonized technical procedures for pharmaceutical development. One of the goals of harmonization is to identify and then reduce differences in technical requirements for drug development among regulatory agencies.

ICH was organized to provide an opportunity for tripartite harmonization initiatives to be developed with input from both regulatory and industry representatives. FDA also seeks input from consumer representatives and others. ICH is concerned with harmonization of technical requirements for the registration of pharmaceutical products among three regions: The European Union, Japan, and the United States. The six ICH sponsors are the European Commission, the European Federation of Pharmaceutical Industries Associations, the Japanese Ministry of Health and Welfare, the Japanese Pharmaceutical Manufacturers Association, the Centers for Drug Evaluation and Research and Biologics Evaluation and Research, FDA, and the Pharmaceutical Research and Manufacturers of America. The ICH Secretariat, which coordinates the preparation of documentation, is provided by the International Federation of Pharmaceutical Manufacturers Associations (IFPMA).

The ICH Steering Committee includes representatives from each of the ICH sponsors and the IFPMA, as well as observers from the World Health Organization, the Canadian Health Protection Branch, and the European Free Trade Area.

At a meeting held on April 30, 1996, the ICH Steering Committee agreed that a draft guideline entitled ''Data Elements for Transmission of Individual Case Safety Reports'' should be made available for public comment. The draft guideline is the product of the Efficacy Expert Working Group of the ICH. Comments about this draft will be considered by FDA and the Efficacy Expert Working Group. Ultimately, FDA intends to adopt the ICH Steering Committee's guideline.

The draft guideline is intended to standardize the data elements for the electronic transmission of individual case safety reports by identifying and defining the data elements for the transmission of all types of individual case safety reports, regardless of source and destination. This includes case safety reports for both preapproval and postapproval reporting periods, and covers both adverse drug reaction and adverse event reports. The electronic format is not intended to be used for cases in the integrated safety summary of a marketing license application dossier. The draft guideline applies only to those adverse events that are subject to expedited reporting.

In the past, guidelines have generally been issued under § 10.90(b) (21 CFR 10.90(b)), which provides for the use of guidelines to state procedures or standards of general applicability that are not legal requirements but are acceptable to FDA. The agency is now in the process of revising § 10.90(b). Although this guideline does not create or confer any rights for or on any person and does not operate to bind FDA, it does represent the agency's current thinking on data elements for the electronic transmission of individual case safety reports.

Interested persons may, on or before December 30, 1996, submit written comments on the draft guideline to the Dockets Management Branch (address above). Two copies of any comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guideline and received comments may be seen in the office above between 9 a.m. and 4 p.m., Monday through Friday.

The text of the draft guideline follows:

Draft Guideline on Data Elements for Transmission of Individual Case Safety Reports

1. Introduction

1.1 Scope of this guideline

The objectives of the working group are, as defined in the concept paper, to standardize the data elements for transmission of individual case safety reports by identifying, and where necessary or advisable, by defining the data elements for the transmission of all types of individual case safety reports, regardless of source and destination. This includes case safety reports for both preapproval and postapproval periods and covers both adverse drug reaction and adverse event reports. It is not intended that this format should be used for cases in the integrated safety summary of a marketing license application dossier or that this guideline apply to every adverse event encountered in clinical trials, but only to those subjected to expedited reporting. The scope of this topic does not encompass the definition of database structures, nor the design of a paper report form, quality control/quality assurance aspects, or technical security issues.

1.2 Background

Because of national and international laws, rules, and regulations, individual case safety reports of adverse drug reactions and adverse events need to be transmitted:

- From identified reporting sources to regulatory authorities and pharmaceutical companies;
- Between regulatory authorities;
- Between pharmaceutical companies and regulatory authorities;
- Within authorities or pharmaceutical companies;
- From authorities to the World Health Organization (WHO) Collaborating Center for International Drug Monitoring.

The transmission of such individual case safety reports presently relies on paper-based formats (e.g., yellow cards, Council for International Organizations of Medical Sciences (CIOMS) forms, MEDWATCH) or electronic media (e.g., within pharmaceutical companies, or with WHO), usually by online access, tape, or file transfer.

Considering the large number of potential participants in a world-wide exchange of information, there is a need for an electronic format capable of accommodating direct database-to-database transmission using message transfers.

Successful electronic transmission of information relies on the definition of common data elements provided in this document and standard transmission procedures to be specified by the ICH M2 Expert Working Group.

1.3 Notes on format of this document

Sections 2.2.A and 2.2.B and their respective subsections (which for convenience do not carry through the 2.2 designation) contain notes that are directed toward clarifying the nature of the data that should be provided. In addition, there are notes to assist in defining the format that should be used to transmit the data.

2. Guidelines

This document has taken into account the concept paper; documents provided to date by ICH sponsors, the ENS–CARE Single Case Format, EuroSCaPE format, and the CIOMS IA proposal; and comments received following the circulation of these papers.

2.1 Definition of data elements

The format for individual case safety reports includes provisions for transmitting all the relevant data elements useful to assess an individual adverse drug reaction or adverse event report. The data elements are sufficiently comprehensive to cover complex reports from most sources, different data sets, and transmission situations or requirements; therefore, not all the data elements will be available for every transmission. In many, if not most, instances a substantial number of the data elements will not be known and therefore will not be included in the transmission. Different ways of including the same data have been provided to cope with differing information contents: e.g., age information can be sent as date of birth and date of reaction/event, age at the time of reaction/event, or patient age group according to the available information (see Section B.1.2 and the respective user guidance). In this example, age would be provided by only one set of data elements rather than including multiple elements of redundant data.

For electronic transmission between databases, the use of structured data is recommended. In certain instances, there are provisions for the transmission of some free text items, including a full text case summary narrative. The transmission of other unstructured data, such as full clinical records or images, is outside the scope of this guideline.

The minimum information for the transmission of a report should include at least one identifiable patient (Section B.1), one identifiable reporter (Section A.2), one event/suspected reaction (Section B.2), and one suspect drug (Section B.4). Because it is often difficult to obtain all the information, any one of several data elements is considered sufficient to define an identifiable patient (e.g., age, sex, initials) or an identifiable reporter (e.g., initials, address, qualification). It is also recognized that the patient and the reporter may be the same individual and still fulfill the minimum reporting criteria.

Structured data are strongly recommended in electronic transmission and provisions for including information in this way have been made. However, structuring of the data also implies the use of controlled vocabularies, which are not yet available for some data elements. It is anticipated that electronic transmission of individual case safety reports will be implemented without controlled vocabularies until they become available.

2.2 Content of the data

The data elements are divided into sections pertaining to:

- A: Administrative information and identification
- A.1 - Identification of the case safety report
- A.2 - Primary source of information
- A.3 - Information on sender and intended recipient of case safety report (receiver)
- B: Information on case:
- B.1 - Patient characteristics
- B.2 - Reaction(s)/event(s)
- B.3 - Results of tests and procedures relevant to the investigation of the patient
- B.4 - Drug(s) information
- B.5 - Narrative case summary and further information

A. Administrative and Identification Information

User Guidance:

This section contains all the relevant data to identify the report, the reporter, and the different persons or institutions involved in the processing of the report, as well as indicators of specific report management.

A.1 Identification of the case safety report
A.1.1 Identification of the country where the reaction/event was reported
A.1.2 Identification of the country where the reaction/event occurred
A.1.3 Identification of the country where the drug was obtained

User Guidance:

Generally, item A.1.1 would be the only one completed. Provisions are made to include other countries for unusual cases concerning foreign travel and sources of manufactured material (A.1.2 and A.1.3).

Note concerning transmission:

The codes to be used to complete the country data will be defined in the transmission standard.

A.1.4 Type of report

- Spontaneous report (see glossary)
- Report from study
- Other
- Not available to sender (unknown)

User Guidance:

A separate category for the designation of a literature source is covered in item A.2.2 and is not duplicated in this section, which is intended to capture the type of report. If it is unclear from the literature report whether or not the case(s) cited are spontaneous observations or arise from a study, then item A.1.4 ''Type of report'' should be ''other'' and only item A.2.2 completed.

Differentiation between types of studies, e.g., randomized controlled clinical trials or others is given in Section A.2.3.3. The ''not available to sender'' option allows for the transmission of information by a secondary reporter where the initial sender did not specify the type of report; it differs from ''other'' which indicates the sender knows the type of report but cannot fit it into the categories provided.

A.1.5 Seriousness
A.1.5.1. Serious

- Yes/no

A.1.5.2. Seriousness criteria (more than one can be chosen)

- Death
- Life-threatening
- Caused/prolonged hospitalization
- Disabling/incapacitating (as per reporter's opinion)
- Congenital anomaly/birth defect
- Other medically important condition

User Guidance:

The terms ''life-threatening'' and ''other medically important condition'' are defined in the ICH E2A guideline. These criteria apply to the case as a whole and should not be confused with the outcome(s) of individual reactions(s)/event(s) that are provided in Section B.2.i.8.

A.1.6 Date report was first received from primary source

Note concerning Transmission:

This date and the following one (A.1.7) should be full precision dates, i.e., day, month, and year.

A.1.7 Date of receipt of the most recent information for this report
A.1.8 Additional available documents held by sender
A.1.8.1 Are additional documents available?

- Yes/no

A.1.8.2 List of documents held by sender (e.g., clinical records, hospital records, autopsy reports)

User Guidance:

It is recognized that these documents may not be obtainable in many instances.

Note concerning transmission:

This is free text limited to about 100 characters.

A.1.9 Does this case fulfill the local criteria for an expedited report?

- Yes/no

User Guidance:

This item is used to provide the sender's local reporting requirements, and the definition of expedited is dependent on the local regulatory requirements. When the countries of origin and destination of the transmission differ, the receiver should be aware that the information may not be applicable to the recipient.

A.1.10 Report identification number(s)
A.1.10.1 National Regulatory Authority case report number
A.1.10.2 Company case report number
A.1.10.3 Other sender's case report number

User Guidance:

A.1.10.1 is an identifier given by a National Regulatory Authority when it is transmitting the case, and item A.1.10.2 would be provided by a pharmaceutical company when it is sending the report. Both identifiers can be transmitted if known. Companies should endeavor to have a single international report number to facilitate the identification of a report that may have been sent to many places and subject to multiple retransmissions. A.1.10.3 would be used by senders who are not representing either a pharmaceutical company or a National Regulatory Authority.

Note concerning transmission:

Alpha/numeric data.

A.1.11 Suspected duplicate

- Yes

User Guidance:

This item is used when the sender suspects the recipient may have already received the case from another sender or through other channels. Only an affirmative answer is needed, otherwise the field is left empty. If known, the suspected duplicate case report number(s) and the identification of the other sender(s) can be provided.

A.1.11.1 Source of the duplicate (e.g., name of the company, name of regulatory agency)
A.1.11.2 Case report number of the duplicate

Note concerning transmission:

Alpha/numeric data for the number and source.

A.1.12 Identification number of the report which is linked to this report

User Guidance:

This section is used in the case of a mother-child pair where both had reactions/events, or of siblings with common exposure, or several reports involving the same patient, or several similar reports from same reporter (cluster). This link does not refer to duplicates, but to links of clinical relevance (the reactions/events are shared among patients or in the same patient and appear pertinent to each other).

Note concerning transmission:

Alpha/numeric data limited to about 50 characters.

A.1.13 Case nullification

- Yes

User Guidance:

This field is used to indicate that a previously transmitted report should be considered completely void (nullified); for example, when the whole case was found to be erroneous. It is essential to use the same case report number previously submitted.

A.1.13.1 Reason for nullification

Note concerning transmission:

This is a free text field limited to about 200 characters.

A.2 Primary source of information

The primary source of the information is a person who initially reports the facts. This should be distinguished from secondary sources (senders) who are only retransmitting the information, e.g., industry to regulatory authority.

Any or all of the three subsections can be used. In the case of a published trial or published individual case, the reporter would be the investigator or author, and details on publication and trial type should also be provided.

A.2.1 Primary source(s) of this report is (are) (repeat as necessary)
A.2.1.1 Reporter identifier (name or initials)

User Guidance:

The identification of the reporter may be prohibited by certain national confidentiality recommendations, laws, or directives. The information is only provided when it is in conformance with the confidentiality requirements and this guidance applies to all the subsections of A.2.1. Notwithstanding the above, at least one subsection should be completed to fulfill the general need of having an ''identifiable'' reporter. If only the name of the reporter is known and it is prohibited to provide it because of confidentiality requirements, initials can be used.

A.2.1.2 Reporter address

Note concerning transmission:

The format for addresses will be defined in the transmission standard.

A.2.1.3 Country

Note concerning transmission:

The codes to be used to complete the country data will be defined in the transmission standard.

A.2.1.4 Qualification

- Physician
- Pharmacist
- Other health professional
- Lawyer
- Consumer or other nonhealth professional

User Guidance:

Within Europe, consumer and lawyer's reports are transmitted only when there is medical confirmation.

A.2.1.5 Was report medically confirmed if not initially from health professional?

- Yes/no

User Guidance:

This section is completed if the initial report was not provided by a health professional and it is needed because of differences in postmarketing surveillance regulations concerning lay reports.

A.2.2 Literature reference

User Guidance:

References are provided in the Vancouver Convention (known as ''Vancouver style'') as developed by the International Committee of Medical Journal Editors. The standard format as well as those for special situations can be found in the following reference:
International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. *New England Journal of Medicine*, 1991, 324:424-428.
Note on transmission:
Alpha/numeric data approximately 250 characters.
A.2.3 Study identification
A.2.3.1 Study name
A.2.3.2 Sponsor study number
User Guidance:
This section would be completed only if the sender is the study sponsor or has been informed of the study number by the sponsor.
A.2.3.3 Study type in which the event/reaction was observed
- Randomized controlled clinical trials
- Other controlled clinical trials
- Compassionate use/named patient basis
- Other studies

User Guidance:
Other studies include pharmacoepidemiology, pharmacoeconomics, intensive monitoring, PMS, etc.
A.3 Information on sender and receiver of case safety report
A.3.1 Sender
A.3.1.1 Type
- Pharmaceutical Company
- Regulatory Authority
- Health professional
- Regional Pharmacovigilance Center
- WHO Collaborating Center for International Drug Monitoring
- Other (e.g., distributor, study sponsor)

A.3.1.2 Sender identifier
User Guidance:
Identifies the sender, e.g., drug company name or regulatory authority name.
A.3.1.3 Name of person responsible for sending the report
User Guidance:
Name of person in the company or agency who is responsible for the authorization of report dissemination. This would usually be the same person who signs the covering memo for paper submissions. The inclusion of the name of this person in the transmission may be subject to national or international regulations.
A.3.1.4 Address, fax, telephone, and E-mail address
A.3.2 Receiver
User Guidance:
See all the sections concerning the sender (A.3.1).
A.3.2.1 Type
- Pharmaceutical Company
- Regulatory Authority
- Regional Pharmacovigilance Center
- WHO Collaborating Center for International Drug Monitoring
- Other (e.g., a company affiliate or a partner)

A.3.2.2 Receiver identifier
A.3.2.3 Address, fax, telephone, and E-mail address
B. Information on Case
B.1 Patient characteristics
User Guidance:
In cases where a fetus or suckling infant sustains an adverse reaction/event, information on both the parent and the child/fetus should be provided. Reports of these cases are referred to as parent-child/fetus report. Several general principles are used for filing these reports. If there has been no reaction/event affecting the child/fetus, the parent-child/fetus report does not apply. For those cases describing fetal demise or early spontaneous abortion, only a parent report is applicable. If both the parent and the child/fetus sustain adverse events, two reports are provided but they are linked by using Sections A.1.12 in each of the reports. When only the child/fetus has an adverse reaction/event (other than early spontaneous abortion/fetal demise) the information provided in this section applies to the child/fetus, and characteristics concerning the parent who was the source of exposure to the drug is provided in Section B.1.10.
Also see the user guidance on confidentiality in Section A.2.1.1, which should be applied to preserve patient confidentiality. The patient's full name and medical record number might be provided in special circumstances, and where permissible.
B.1.1 Patient initials
B.1.1.1 Patient medical record number(s) and source(s) (if allowable)
User Guidance:
Record numbers may include the general practitioner and/or specialist record(s) number(s), hospital record(s) numbers, or patient identification number in a study.
Note concerning transmission:
Alpha/numeric data. The data element should be long enough to contain more than one kind of medical record and number.
B.1.2 Age information
User Guidance:
To be used according to the most precise information available.
B.1.2.1 Date of birth
User Guidance:
If the full date of birth is not known, use Section B.1.2.2
Note concerning transmission:
Include a precise date, i.e., day, month, and year.
B.1.2.2 Age at time of onset of reaction/event
User Guidance:
If several reactions/events are in the report, use the age at the time of the first reaction/event.
Note concerning transmission:
The codes to be used will be defined in the transmission standard but should include various age units (days, months, years).
B.1.2.3 Patient age group (as per reporter)
- Neonate
- Infant
- Child
- Adolescent
- Adult
- Elderly

User Guidance:
The terms are not defined in this document and are intended to be used as they were reported by the primary source. This section should be completed only when the age is not provided more specifically in Section B.1.2.2.
B.1.3 Weight (kg)
User Guidance:
Should be the weight at the time of the event/reaction.
B.1.4 Height (cm)
B.1.5 Sex
Note concerning transmission:
The codes to be used for items B.1.3–B.1.5 will be defined in the transmission standard chosen.
B.1.6 Last menstrual period date
Note concerning transmission:
Imprecise dates are acceptable, i.e., month and year, or year only is acceptable.
B.1.7 Relevant medical history and concurrent conditions (not including reaction/event)
B.1.7.1 Structured information (repeat as necessary)

Disease/surgical procedure/etc.	Start date	Continuing Y/N/U	End date	Comments

User Guidance:
Medical judgment should be exercised in completing this section. Information pertinent to understanding the case is desired such as diseases, conditions such as pregnancy, surgical procedures, and psychological trauma. Each of the fields in the table can be repeated as necessary. If precise dates are not known and a text description aids in understanding the timing of the case, or if concise additional information is helpful in showing the relevance of the past medical history, this information can be included in the comment column.
Note concerning transmission:
Imprecise dates are acceptable for both start and end dates. The continuing block should accept values for yes, no, and unknown, and the main descriptive block

should have alpha data in concordance with the controlled vocabulary being developed. The comment should be limited to about 100 characters.

B.1.7.2 Text for relevant medical history and concurrent conditions (not including reaction/event)

User Guidance:

To be used if structured information is not available in the sender's database. Otherwise, it is preferable to send structured data in segment B.1.7.1.

Note concerning transmission:

This is a free text area of about 500 characters.

B.1.8 Relevant past drug history (repeat as necessary)

Name of drug as reported	Start date	End date	Indication	Reaction/event (if any and known)

User Guidance:

This segment concerns previously taken drugs, but not those taken concomitantly or drugs which may have potentially been involved in the current reaction(s)/event(s). Information concerning concomitant and other suspect drugs is included in Section B.4. The information provided here may also include previous experience with similar drugs. Medical judgment should be exercised in completing this section. When completing the field concerning the name of the drug, it is important to use the words provided by the primary source. Trade name, generic name or class of drug can be used, and the term ''none'' should be used when appropriate.

Note concerning transmission:

The data element for name of drug should accept alpha/numeric data and include provisions for accepting the word none. The data elements for reactions and indications will be text initially and then by a controlled vocabulary when fully developed. Both dates can be imprecise.

B.1.9. In case of death

B.1.9.1 Date of death

Note concerning transmission:

Imprecise date format.

B.1.9.2 Reported cause of death (repeat as necessary)

Note concerning transmission:

This should be a repeatable element. Controlled vocabulary should be used when fully implemented.

B.1.9.3 Was autopsy done?

Yes/No/Unknown

B.1.9.4 Autopsy-determined cause(s) of death (repeat as necessary)

Note concerning transmission:

These are repeatable text fields of approximately 100 characters. Controlled vocabulary should be used when fully implemented.

B.1.10 For a parent-child/fetus report, information concerning the parent

User Guidance:

This section is used only in the case of a parent-child/fetus report where the parent had no reaction/event. See user guidance for Section B.1. Guidance regarding confidentiality is provided above and should be considered before providing the parent identification. For the subsections B.1.10.5 through B.1.10.9, review the guidances provided for B.1.3 through B.1.5 and B.1.7 through B.1.8.

B.1.10.1 Parent identification

B.1.10.2 Parent age information

User Guidance:

Use the date of birth if the precise birthday is known, otherwise use age.

B.1.10.2.1 Date of birth

Note concerning transmission:

Date of birth should accept only a precise date.

B.1.10.2.2 Age

B.1.10.3 Gestation period at time of exposure

Note concerning transmission:

Gestation period at time of exposure is expressed by providing both a number and designation of units of days, weeks, months, or trimester.

B.1.10.4 Last menstrual period date

Note concerning transmission:

Date of last menstrual period should accept only a complete date.

B.1.10.5 Weight (kg) of parent

B.1.10.6 Height (cm) of parent

B.1.10.7 Sex of parent

B.1.10.8 Relevant medical history and concurrent conditions of parent

B.1.10.8.1 Structured information

Disease/surgical procedure/etc.	Start date	Continuing Y/N/U	End Date	Comments

B.1.10.8.2 Text for relevant medical history and concurrent conditions (not including reaction/event) of parent

B.1.10.9 Relevant past drug history

Name of drug as reported	Start date	End date	Indication	Reactions (if any and known)

B.2 Reaction(s)/Event(s)

User Guidance:

The designation of ''i.'' in this section indicates that each item is repeatable and that it carries an appropriate correspondence to the same ''i.'' in all subsections.

B.2.i.1 Reaction/event description

User Guidance:

Provided in a language agreed upon by sender and receiver. For international transmissions, English is the general accepted language. The original reporter's words and/or phrases or their translation are used to describe the reaction.

Note concerning transmission:

Alpha data-free text 250 characters.

B.2.i.2 Reaction/event term(s)

User Guidance:

The terms can be signs, symptoms, or diagnoses. Until terms from an internationally agreed terminology are available the term provided will be from an uncontrolled vocabulary at the choice of the sender, and where possible should be those of the original reporter. This also applies to the other items of structured data such as indication, and diseases in past medical history, that are expected to be controlled with an international terminology.

Note concerning transmission:

Alpha data - uncontrolled vocabulary at present.

B.2.i.3 Date of start of reaction/event

B.2.i.4 Date of end of reaction/event

B.2.i.5 Duration of reaction/event

User Guidance:

This section can usually be computed from start/end of reaction. However, sometimes, both dates and duration are useful, e.g., for reactions/events of short duration such as anaphylaxis or arrhythmia.

Note concerning transmission:

The format for the dates will allow imprecise dates and the duration will be defined by the transmission standard.

B.2.i.6 Time intervals between suspect drug administration and start of reaction/event

User Guidance:

The major uses of intervals are to cover circumstances where both the dates are known but the interval is very short (e.g., minutes, such as in anaphylaxis), and when only imprecise dates are known but more information concerning the interval is known. Dates, if available, should always be transmitted in the appropriate fields rather than intervals.

This section is to be used if there is only one suspect drug and one or more reactions/events. If there is more than one suspect drug, then the information should be captured under ''drug'' (Section B.4) and not here.

Note concerning transmission:

The codes to be used will be defined in the transmission standard.

B.2.i.6.1 Time interval between beginning of suspect drug administration and start of reaction/event

B.2.i.6.2 Time interval between last dose and start of reaction/event

B.2.i.7 Gestation period when reaction/event was observed

User Guidance:

For the parent report, when both parent and child/fetus reports are submitted as linked reports, the gestation period refers to when reaction/event occurred in the parent. For the child report, when both parent and child reports are submitted as linked reports, the gestation period refers to when reaction/event in the child/fetus was observed. The gestation period at the time of exposure is captured in Section B.1.10.3

Note concerning transmission:

Gestation period when reaction/event was observed is expressed by providing both a number and designation of days, weeks, months, or trimester.

B.2.i.8 Outcome of reaction/event at the time of last observation

- Recovered/resolved
- Recovering/resolving
- Not recovered/not resolved
- Recovered/resolved with sequelae
- Fatal
- Unknown

User Guidance:

In case of irreversible congenital anomalies the choice, not recovered/not resolved, should be used.

''Fatal'' should be used when death is possibly related to the reaction/event. Considering the difficulty of deciding between ''reaction/event caused death'' and ''reaction/event contributed significantly to death,'' both were grouped in a single category. Where the death is unrelated to the reaction/event being reported, ''death'' should not be selected here, but should be reported under Section B.1.9.

B.3 Results of tests and procedures relevant to the investigation of the patient

User Guidance:

This section captures the tests and procedures performed to diagnose or confirm the reaction/event, including those tests done to investigate (exclude) a nondrug cause, e.g., serologic tests for infectious hepatitis in suspected drug-induced hepatitis. Both positive and negative results should be reported.

B.3.1 Structured information (repeat as necessary)

Date	Test	Result	Unit	Normal ranges	More information available (Y/N)

Note concerning transmission:

Imprecise dates are acceptable. The description of the tests, results, units, and normal ranges will be in free text unless covered by a controlled vocabulary. The column entitled ''more information available'' accepts the yes/no dichotomy.

B.3.2 Description of results of test and procedures relevant to the investigation of the patient

Note concerning transmission:

Free text of about 1,000 characters.

B.4 Drug Information

User Guidance:

This section covers both suspect drugs and concomitant medications. In addition, the section can be used to identify drugs thought to have an interaction. For each drug, the status indicator clarifies the role of the medication and its status is that indicated by the primary reporter, i.e., the original source of the information. One segment is used for each drug (k) mentioned in the report and which was taken within a relevant time period before the reaction, whether suspect or not. The designation ''k'' in this and the following subsections indicates that each item is repeatable and that each subsection carries an appropriate correspondence to the ''k'' in other subsections.

Drugs used to treat the reaction/event should not be included here.

B.4.k.1 Characterization of drug role

Suspect/Concomitant/Interacting

User Guidance:

Characterization of the drug as provided by primary reporter. By convention all spontaneous reports have at least one suspect drug.

B.4.k.2 Drug identification

User Guidance:

Drug substance name and/or proprietary medicinal product name is provided as it was reported.

B.4.k.2.1 Drug substance name

User Guidance:

Provide the INN or drug substance name or drug identification code if no name exists. This information, as well as that requested in Section B.4.k.2.2, may not be known for concomitant or interacting drugs when the sender is a pharmaceutical company. In the case of blinded trials, the word ''blinded'' should precede the name of the drug. Placebos can be included as a drug.

B.4.k.2.2 Proprietary medicinal product name

User Guidance:

The name should be that used by the reporter. It is recognized that a single product may have different proprietary names in different countries, even when produced by a single manufacturer.

Note concerning transmission:

Alpha/numeric data for each of drug identification, substance name, and proprietary name.

B.4.k.3 Batch/lot number

User Guidance:

This information is particularly important for vaccines and biologicals. The section allows for multiple batch/lot numbers, each separated by a delimiter defined by the transmission standard chosen. Provide the most specific information available.

Note concerning transmission:

Alpha/numeric data, delimiter defined by the transmission standard.

B.4.k.4 Premarketing authorization or marketing identification holder and number

User Guidance:

If relevant and known, provide the name of the holder and the authorization number in the country where the drug was obtained when the case report is sent to that country. Pharmaceutical companies provide this information for their own suspect drug(s).

B.4.k.4.1 Number

Note concerning transmission:

Alpha/numeric data.

B.4.k.4.2 Country

Note concerning transmission:

Format determined by standard chosen.

B.4.k.4.3 Name of authorization holder

Note concerning transmission:

Alpha/numeric data.

B.4.k.5 Structured dosage information

e.g., 2 milligrams (mg) three times a day for 5 days

B.4.k.5.1 dose (number): 2

B.4.k.5.2 dose (unit): mg

B.4.k.5.3 number of separate dosages: 3

B.4.k.5.4 number of units in the interval: 1

B.4.k.5.5 definition of the interval: day

B.4.k.5.6 cumulative total dose number: 30

B.4.k.5.7 cumulative total dose unit: mg

User Guidance:

Please note the side-by-side illustration of how the structured dosage is provided. For the more complex example of 5 mg (in one dose) every other day for 30 days, subsections B.4.k.5.1 through B.4.k.5.7 would be 5, mg, 1, 2, day, 75, mg, respectively. In the case of a parent-child report (either a single child report, or a linked report with both parent and child affected) the dosage section applies to the parental dose. For dosage regimen that involve more than one dosage form and/or changes in dosage, the information is provided in Section B.4.k.6 as text. Categories for ''dose unit'' and for ''definition of the interval'' are described in Attachment 1.

B.4.k.6 Dosage text

User Guidance:

To be used in cases where provision of structured dosage information is not possible.

Note concerning transmission:

This is a free text field limited to about 100 characters.

B.4.k.7 Pharmaceutical form (Dosage form)

User Guidance:

E.g., tablets, capsules, vials, syrup.

Note concerning transmission:

This is a free text field until a controlled vocabulary is available.

B.4.k.8 Route of administration

User Guidance:

In the case of a parent-child report (a single report with only the child affected through indirect (parenteral) exposure, or a linked report where both parent and child are affected), this indicates the route of administration of a drug given to the child/fetus.

Note concerning transmission:

See controlled vocabulary in the route of administration list in Attachment 2.

B.4.k.9 Parent route of administration (in case of a parent child/fetus report)

User Guidance:

This section is used only in parent-child reports and indicates the route of administration to the parent.

B.4.k.10 Indication for use in the case

Note concerning transmission:

This field is about 100 characters.

Controlled vocabulary to be used when fully implemented.

B.4.k.11 Date of start of drug

Note concerning transmission:

Imprecise date formats are used in this section as well as in B.4.k.13.

B.4.k.12 Time intervals between drug treatment and start of earliest reaction/event

B.4.k.12.1 Time interval between beginning of drug administration and start of earliest reaction/event

B.4.k.12.2 Time interval between last dose of drug and start of earliest reaction/event

Note concerning transmission:

The format to be used for intervals will be defined in the transmission standard.

B.4.k.13 Date of end of drug

B.4.k.14 Duration of treatment

User Guidance:

This field is used if exact dates of drug administration are not available at the time of the report, but there is information concerning the duration of treatment. The information requested is the overall duration of drug treatment.

Note concerning transmission:

The format to be used for intervals will be defined in the transmission standard.

B.4.k.15 Action(s) taken with drug

- Drug withdrawn
- Dose reduced
- Dose increased
- Dose not changed
- Unknown
- Not applicable

User Guidance:

This data, taken together with the outcome of the reaction (B.2.i.8), provides the information concerning dechallenge. ''Not applicable'' is used in circumstances such as when the patient died or the treatment had been completed prior to reaction/event.

B.4.k.16 Effect of rechallenge (or re-exposure), for suspect drugs only

B.4.k.16.1 Did reaction recur on readministration?

- yes/no/unknown

User Guidance:

''Unknown'' indicates that a rechallenge was done but it is not known if the event recurred. This segment is not to be completed if it is unknown whether a rechallenge was done.

B.4.k.16.2 If yes to item B.4.k.16.1, which reaction(s)/event(s) recurred?

Note concerning transmission:

Controlled vocabulary to be used when fully implemented.

B.4.k.17 Relatedness of drug to reaction(s)/event(s) (repeat as necessary)

User Guidance:

This section provides the means to transmit the degree of suspected relatedness of each drug to the reaction(s)/event(s). For the purpose of reporting, there is a conventional implied suspected causality for spontaneous reports. It is recognized that information concerning the relatedness, especially for spontaneous reports, is often subjective and may not be available.

Note concerning transmission:

For subsection B.4.k.17.1, the controlled vocabulary, when fully implemented, should be used. For subsections B.4.k.17.2 through B.4.k.17.4, alpha/numeric data with uncontrolled vocabulary should be used.

B.4.k.17.1 Reaction assessed

User Guidance:

Generally the reaction assessed will be the most important or most serious reaction.

B.4.k.17.2 Source of assessment

User Guidance:

E.g., initial reporter, investigator, agency, company.

B.4.k.17.3 Method of assessment

User Guidance:

E.g., global introspection, algorithm, Bayesian calculation.

B.4.k.17.4 Result

B.4.k.18 Additional information on drug

User Guidance:

Use to specify any additional information pertinent to the case that is not covered by above sections (e.g., passed expiration date, batch and lot tested and found to be within specifications).

B.5 Narrative case summary and further information

B.5.1 Case narrative including clinical course, therapeutic measures, outcome, and additional relevant information.

User guidance:

Focused, factual, and clear description of the case.

Note concerning transmission:

10,000 characters.

B.5.2 Reporter's comments

User guidance:

Use for including the reporter's comments on the diagnosis, causality assessment, or other issues considered relevant.

B.5.3 Sender's diagnosis/syndrome and/or reclassification of reaction/event

User Guidance:

This section provides the sender with an opportunity to combine signs and symptoms that were reported into a succinct diagnosis; e.g., a reporter indicates that a patient with known heart failure developed edema, proteinuria, hypoalbuminemia, and hypercholesterolemia but is uncertain whether the diagnosis is nephrotic syndrome or heart failure. The sender, however, knows that there have been other cases of nephrotic syndrome reported with the medications. The term ''nephrotic syndrome'' could be used in this section, and the explanation would be included in Section B.5.4.

Note concerning transmission:

Uncontrolled vocabulary until the controlled vocabulary is fully implemented.

B.5.4 Sender's comments

User guidance:

This section provides information concerning the sender's assessment of the case and may be used to describe disagreement with, and/or alternatives to, the diagnoses given by the initial reporter.

Note concerning transmission:

1,000 characters.

3. Glossary

Parent-child/fetus report: Report in which the administration of medicines to a parent results in a suspected reaction/event in a child/fetus.

Receiver: The intended recipient of the transmission.

Reporter: Reporter is primary source of the information, i.e., a person who initially reports the facts. This should be distinguished from the sender of the message, though the reporter could also be a sender.

Sender: The person or entity creating the message for transmission. Although the reporter and sender may be the same person, the function of the sender should not be confused with that of the reporter.

Spontaneous adverse drug reaction report: An unsolicited communication to a company, regulatory authority, or other organization that describes an adverse medical reaction in a patient given one or more medical products and which does not derive from a study or any organized data collection scheme.

Attachment 1

Unit List

Mass

kg	kilogram(s)
g	gram(s)
mg	milligram(s)
µg	microgram(s)
ng	nanogram(s)
pg	picogram(s)
mg/kg	milligram(s)/kilogram
µg/kg	microgram(s)/kilogram
mg/m^2	milligram(s)/sq. meter
µg/m^2	microgram(s)/ sq. meter

Radioactivity

Bq	becquerel(s)
GBq	gigabecquerel(s)
MBq	megabecquerel(s)
Kbq	kilobecquerel(s)
Ci	curie(s)
mCi	millicurie(s)
µCi	microcurie(s)
nCi	nanocurie(s)

Volume

l	litre(s)
ml	millilitre(s)
µl	microlitre(s)

Other

mol	mole(s)
mmmol	millimole(s)
µmol	micromole(s)
iu	international unit(s)
kiu	iu(1000s)
Miu	iu(1,000,000s)
iu/kg	iu/kilogram
mEq	milliequivalent(s)
%	percent
gtt	drop(s)
DF	dosage form

User Guidance:

This is the list of accepted units. When having other measure units, transformation is recommended if possible. Otherwise use the free text field.

Definition of Interval List

Minutes
Hours
Days
Weeks
Months
Years
Cyclical
As necessary
Total

Attachment 2

Route of Administration List

Auricular
Buccal
Cutaneous
Dental
Endocervical
Endosinusial
Endotracheal
Epidural
Extra-amniotic
Hemodialysis
Intra corpus cavernosum
Intra-amniotic
Intra-arterial
Intra-articular
Intra-uterine
Intracardiac
Intracavernous
Intracerebral
Intracervical
Intracisternal
Intracorneal
Intracoronary
Intradermal
Intradiscal (intraspinal)
Intralesional
Intralymphatic
Intramedullar (bone marrow)
Intrameningeal
Intramuscular
Intraocular
Intrapericardial
Intraperitoneal
Intrapleural
Intrasynovial
Intrathecal
Intrathoracic
Intratracheal
Intravenous
Intravesical
Iontophoresis
Nasal
Occlusive dressing technique
Ophthalmic
Oral
Oropharyngeal
Other
Parenteral
Periarticular
Perineural
Rectal
Respiratory (inhalation)
Retrobulbar
Subconjunctival
Subcutaneous
Subdermal
Sublingual
Transdermal
Transmammary
Transplacental
Unknown
Urethral
Vaginal

Dated: September 24, 1996.

William K. Hubbard,

Associate Commissioner for Policy Coordination.

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BILLING CODE 4160–01–F

[Docket No. 96N–0322]

Mammography Facility Performance, Calendar Year 1995; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of the document entitled ''Mammography Facility Performance, Calendar Year 1995.'' This document, mandated by Congress in the Mammography Quality Standards Act of 1992 (the MQSA), is intended to inform physicians and the general public about mammography facility performance in the calendar year 1995.

ADDRESSES: Submit written requests for single copies of the document entitled ''Mammography Facility Performance, Calendar Year 1995'' to MQSA, c/o SciComm, Inc., P.O. Box 30224, Bethesda, MD 20824–9998. Requests should be identified with the docket number found in brackets in the heading of this document. Send two self-addressed adhesive labels to assist that office in processing your requests. The document is also available on the Internet (http://www.fda.gov). ''Mammography Facility Performance, Calendar Year 1995'' is available for public examination in the Dockets Management Branch (HFA–305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1–23, Rockville, MD 20857, between 9 a.m. and 4 p.m., Monday through Friday.

FOR FURTHER INFORMATION CONTACT: Carole Sierka, Office of Health and Industry Programs, Center for Devices and Radiological Health (HFZ–240), Food and Drug Administration, 1350 Piccard Dr., Rockville, MD 20850, 301–594–3534, FAX 301–594–3306.

SUPPLEMENTARY INFORMATION: The MQSA of 1992 (Pub. L. 102–539) was enacted on October 27, 1992. Under the MQSA, FDA is required annually to compile and make available to physicians and to the general public information assisting in the selection of an FDA-certified facility. The report must include a list of facilities:

(1) That have been convicted under Federal or State laws relating to fraud and abuse, false billings, or kickbacks;

(2) that have been subject to sanctions under MQSA together with a statement of the reasons for the sanctions;

(3) that have had certificates revoked or suspended, together with a statement of the reasons for the revocation or suspension;

(4) against which the Secretary of the Department of Health and Human Services has sought an injunction under MQSA, together with a statement of the reasons for the action;

(5) whose accreditation has been revoked, together with a statement of the reasons for the revocation;