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Guidelines for Ensuring the Quality of Information Disseminated to the Public

F. Food and Drug Administration

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This guidance represents the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

This guidance provides the information quality guidelines for the Food and Drug Administration (FDA) requested under *the Guidelines for Ensuring and Maximizing the Quality, Objectivity, Utility, and Integrity of Information Disseminated by Federal Agencies* (OMB Guideline).¹ The OMB Guidelines implement section 515 of the Treasury and General Government Appropriations Act for Fiscal Year 2001 (Pub. L. 106-554; H.R. 5658). The OMB Guidelines direct agencies to issue their own information quality guidelines ensuring and maximizing the quality, objectivity, utility, and integrity of information, including statistical information, disseminated by the agency. This guidance is part of the U.S. Department of Health and Human Services (HHS) implementation plan developed to comply with the OMB

Guidelines. The principles described in the HHS plan and OMB guidance are incorporated by reference into this guidance.

This guidance describes the nature of the information disseminated by the FDA and explains FDA's standards, policies, and procedures for ensuring the quality of the information it disseminates. The guidance also explains the administrative mechanisms that are in place to enable persons to seek and obtain correction of information maintained and disseminated by the FDA that they believe does not comply with the OMB and HHS Guidelines and this guidance.

I. Agency Mission

The Agency's mission, as defined in Section 406 of the Food and Drug Administration (FDA) Modernization Act of 1997, is as follows:

The Administration shall --

1. promote the public health by promptly and efficiently reviewing clinical research and taking appropriate action on the marketing of regulated products in a timely manner;
2. with respect to such products, protect the public health by ensuring that --
 - A. foods are safe, wholesome, sanitary, and properly labeled;
 - B. human and veterinary drugs are safe and effective;
 - C. there is reasonable assurance of the safety and effectiveness of devices intended for human use;
 - D. cosmetics are safe and properly labeled; and
 - E. public health and safety are protected from electronic product radiation;
3. participate through appropriate processes with representatives of other countries to reduce the burden of regulation, harmonize regulatory requirements, and achieve appropriate reciprocal arrangements; and
4. as determined to be appropriate by the Secretary, carry out paragraphs (1) through (3) in consultation with experts in science, medicine, and public health, and in cooperation with consumers, users, manufacturers, importers, packers, distributors, and retailers of regulated products.

II. Scope and Applicability of Guidelines

FDA is a scientific regulatory agency that regulates one trillion dollars worth of consumer goods each year. This amounts to more than 20 percent of all consumer spending. FDA regulates most food that we eat, all prescription drug and over-the-counter drug products that we take, and all medical devices that we use. For foods, we ensure that products are safe, wholesome, sanitary, and properly labeled. For drugs, we ensure the products are both safe and effective for use; and for medical devices, there is a reasonable assurance of their safety and effectiveness. We also are responsible for ensuring that electronic and radiation-emitting equipment, such as x-ray machines, microwave ovens, and metal detectors, are safe for use. We certify and inspect annually all mammography facilities. We regulate animal feed and most animal drugs. We ensure that cosmetics are labeled honestly and cause no harm. Our regulatory activities include inspection and surveillance of marketed products, standard setting, bioresearch monitoring, and human subject protection. We also conduct research in support of our regulatory programs.

FDA, which employs about 10,000 people, is organized primarily by centers:

- Center for Biologics Evaluation and Research (CBER)
- Center for Devices and Radiological Health (CDRH)
- Center for Drug Evaluation and Research (CDER)
- Center for Food Safety and Applied Nutrition (CFSAN)
- Center for Veterinary Medicine (CVM)
- National Center for Toxicological Research (NCTR)
- Office of the Commissioner (OC)
- Office of Regulatory Affairs (ORA)

Our Office of the Ombudsman, which is responsible for monitoring complaints regarding information dissemination and our response to those complaints, resides in the Office of the Commissioner.

As described in detail in the paragraphs that follow, we disseminate many different types of information to a wide variety of audiences, including the regulated

industry, health care professionals and organizations, consumers, patients, other governmental agencies, and international organizations and agencies. Information dissemination is an important part of our mission to promote and protect the public health. FDA recognizes that public access to high quality information is critical to achieving this mission and public input, in turn, improves the quality of the information we disseminate.

Because of the nature of this information, our goal has been and remains to ensure that all the information we disseminate meets the high standards of quality (including objectivity, utility, and integrity) described in the OMB and HHS Guidelines. As discussed in detail in [Section V](#), we have established several policies, standards, and processes to ensure the quality of the information we make available to the public. FDA also will ensure that information collected under the Paperwork Reduction Act of 1995, 44 U.S.C. chapter 35, will be collected, maintained, and used in a manner consistent with the OMB and HHS Guidelines and this guidance document. With the following specific exceptions, the OMB Guidelines apply to most categories of FDA-disseminated information (see discussion in following sections):

- A. Documents relating to internal FDA procedures
- B. Internal government correspondence
- C. Correspondence with individuals that is not normally made public
- D. Press releases (unless they contain new substantive information not covered by previous information dissemination)
- E. Archival records
- F. Distributions intended to be limited to subpoenas or adjudicative documents including findings and determinations made in the course of an administrative proceeding pursuant to 21 CFR Parts 10, 12, 13, 14, 15, 16, 17 and 19.
- G. Scientific publications that only contain the views of the authors and are not used to support an official agency position
- H. Responses to requests for information under the Freedom of Information Act (FOIA), the Privacy Act, the Federal Advisory Committee Act, or other similar laws.

In the pages that follow, we describe the types of information we disseminate ([Section III](#)), the methods we use to disseminate this information ([Section IV](#)), and the quality assurance policies, standards, and processes that have been put in place to ensure the quality of the information we distribute ([Section V](#)). Some of the information described below may include information that falls under one of the types of information specifically excluded above. To the extent that information in one of the categories listed below includes information listed in one of the exceptions, the OMB Guidelines do not apply. In [Section VI](#), we discuss the procedures to be used by persons who want to request that information we have disseminated be corrected. [Section VII](#) discusses the types of information we have identified to be influential according to the OMB Guidelines and the principles we apply to information that will be disseminated regarding risks to human health, safety, and the environment. The principles that are used have been adapted from the quality principles applied by Congress to risk information pursuant to the Safe Drinking Water Act Amendments of 1996 (42 U.S.C. 300g-1(b)(3)(A) and (B)). [Section VIII](#) describes some special circumstances that may apply to certain information dissemination activities.

The pre-dissemination review described in the HHS guidelines only applies to information disseminated on or after October 1, 2002. The administrative mechanism for correction applies to information that the agency disseminates on or after October 1, 2002, regardless of when the agency first disseminated the information.

III. Types of Information Disseminated

We make a large number of documents and information available to a variety of audiences. The major types, with examples of each, are provided here.

A. Public Communications About Risk

As part of our mission to protect the public health and safety, we provide the public with a wide variety of information on risk, including information on food safety and the risks involved with using medical products. Some examples of our communications are listed here.

- Consumer advice and fact sheets (for example, News Release No. 0020.01, January 2001 provides advice to consumers to reduce the risk of illness from foodborne *Listeria monocytogenes*)
- "Dear Health Care Professional" letters (for example, Agency August 2001 letter to health care professionals warning about rhabdomyolysis, a serious, potentially fatal adverse effect of all statin drugs)
- Public health and safety alerts (for example, "FDA Announces New Alcohol Warnings for Pain Relievers and Fever Reducers," October 1998; "Seniors and Food Safety -- Preventing Foodborne Illness," May 1999; "Learning About Lasik Eye Surgery," on the Internet; "FDA Patient Safety News," a video targeting hospitals; "Tips and Warnings for Consumers About Buying Medicines and Medical Products Online," on the Internet; "An Important Message for Pregnant Women and Women of Childbearing Age About the Risk of Mercury in Fish," March 2001; "FDA Public Health Notification: Reducing Radiation

Risk from Computed Tomography for Pediatric and Small Adult Patients," November 2001)

- FDA Talk Papers (for example, FDA Announces Availability of *Vibrioparahaemolyticus* Risk Assessment, January 18, 2001)
- Various subject matter brochures intended for consumers. Some are produced as low-literacy brochures aimed at consumers with no more than a fifth-grade reading level. Some are also produced in other languages, particularly in Spanish. Some are mailed directly to specific audiences; some are disseminated at large professional meetings (for example, "Reprocessing of Single-Use Medical Devices by Hospitals" (November 2000), "Buying Contact Lenses on the Internet, by Phone, or by Mail" (August 2001)).
- Posters are distributed to health clinics and schools with consumer information on FDA-related health issues.

B. Rulemaking Documents

Like many Federal agencies, we engage in rulemaking. This process includes publishing a proposed rule and explanatory material in the *Federal Register*, obtaining public comment, and publishing a final rule and response to the comments. Some examples include:

- Additional Criteria for Classifying Over the Counter Drugs as Generally Recognized as Safe and Effective and Not Misbranded, a final rule that published on January 23, 2002
- Medical Devices; Device Tracking, a final rule that published on February 8, 2002
- State Certification of Mammography Facilities, a final rule that published on February 6, 2002
- Implantation or Injectable Dosage Form New Animal Drugs: Trenbolone and Estradiol; a final rule that published on February 7, 2002
- Foreign Establishment Registration and Listing, a final rule that published on November 27, 2001
- Substances Affirmed as Generally Recognized as Safe: Menhaden Oil; a proposed rule that published on February 26, 2002
- Hazard Analysis and Critical Control Point (HACCP): Procedures for the Safe and Sanitary Processing and Importing of Juice; a final rule that published on January 19, 2001

As part of the rulemaking process, we may also publish advanced notice of proposed rulemaking documents (ANPRs) and direct final rules.

C. Product Approvals

1. Medical Products

When we evaluate applications for approval to market medical products, we produce reviews of the data collected, analyzed, and submitted by applicants. On approval of drugs², we compile our reviews into an approval package that provides the basis for the Agency clearance of a decision to approve a product. To provide as much information as possible to health care practitioners and consumers so they can make informed decisions about treatment, we make the medical product approval packages, including generic drug approvals, available on the Internet. An approval package can range from 100 to more than 1,000 pages, redacted to remove confidential and trade secret information. Contents usually include individual discipline reviews; correspondence between the company and FDA; administrative documents; and labeling. For example, the package for Clarinex [desloratadine], an antihistamine to treat seasonal allergic rhinitis, was approved on December 21, 2001. We posted the 500-page package on the Internet on February 12, 2002.

We also post on the Internet, for animal drug products, an FOI summary of the approval and for device premarket approvals, a detailed summary of safety and effectiveness, the approval order, and the draft labeling.

2. Food and Color Additives

When we evaluate applications for premarket approval of food additives and color additives, we produce reviews of the data and analyses submitted by the applicant. For direct food additives and color additives, we publish a final rule in the *Federal Register* explaining the basis for Agency approval of the product and issuance of a regulation in the U.S. Code of Federal Regulations. For other food additives, we announce their approval via Internet listings that are updated at least monthly. In all cases, the published listings include specifications and use limitations necessary to ensure the safe use of the product. In addition, the documents and information that form the basis for Agency approvals are available under the Freedom of Information Act.

D. Guidance and Regulatory Assistance

We develop guidance and other policy documents usually with input from the public, to assist industry, consumers, hospitals, reviewers, and other health care related organizations and individuals interested in our statutes and regulations. In addition, we provide procedural guidance to our field offices. In compliance with our policy involving good guidance practices, under 21 CFR 10.115, we publish notices announcing the availability of guidances in the *Federal Register*, and make the guidances available in the public docket and on the Internet. Some examples of guidances are provided here:

- *Guidance to Hospitals, Nursing Homes, and Other Health Care Organizations -- FDA Public Advisory on the risks of death and injury related to medical gas mix-ups* (April 2001)
- *Small Business Compliance Guides* -- guidances to help small businesses; required by the Regulatory Flexibility Act (5 U.S.C. 602) for all rulemakings that will have a significant impact on small entities (for example, *Sterility Requirement for Aqueous-Based Drug Products for Oral Inhalation -- Small Entity Compliance Guide*, November 2001)
- *Formal Dispute Resolution: Appeals Above the Division Level* (March 2001)
- Food Security Guidance (January 2002)
- Food Code; 2001 Revision (December 2001)
- Guidance for Industry: Studies to Evaluate the Safety of Residues of Veterinary Drugs in Human Food: Genotoxicity Testing, VICH GL23
- *Guidance on Enforcement Priorities for Single-Use Devices Reprocessed by Third Parties and Hospitals* (August 2000)
- The Policy Guidance Help System (January 2000; revised November 2001) -- a computerized system containing all Mammography Quality Standards Act regulations and final guidance (Internet and as a stand-alone downloadable program)
- CDRH develops "Plain Talk" guidance on how to comply with our regulations and provides a unique interactive Website called "Device Advice" to answer specific device related questions.
- Compliance Policy Guides are issued to the field offices to ensure that our regulations and policies are followed consistently. These Compliance Policy Guides are made public and treated as guidances.
- Regulatory Procedures Manual provides FDA procedural guidance and instruction for use by FDA and the public. The manual is publicly available and is treated as guidance.

E. Reports

We also develop reports on a variety of topics. Some examples include:

- *Managing the Risks From Medical Product Use -- Report to the FDA Commissioner from the Task Force on Risk Management* (May 1999)
- *Prescription Drug Marketing Act of 1987 -- Report to Congress* (June 2001)
- *FDA Fiscal Year 2002 Congressional Budget Request* (annual report)

- *Import Detentions Reports (IDRs)* -- IDRs provide information on the products detained by the Agency (that is, products for which our District Offices have issued a "Notice of Detention and Hearing"). The IDR is generated from data collected by FDA's Operational and Administrative System for Import Support (OASIS) and is updated monthly and is posted on the FDA website for a period of time (on the average of 12 months). Archived data are not available on the Internet but is available under the Freedom of Information Act.
- *FDA Enforcement Report* -- Published weekly, this online publication contains information on recalls and other actions taken in connection with Agency regulatory activities.
- *Mammography Facility Adverse Event Report* -- an annual report of adverse actions taken against mammography facilities issued to help health professionals and consumers in evaluating the performance of their mammography facilities

F. Citizen Petitions and Responses

When citizens petition the FDA to address an issue, we write a response to the petitioner explaining our position. Although these responses are letters addressed to individuals or organizations, the petitions and our responses are made available through the public docket and often on the Internet. In recent years, we have responded to an average of 250 citizen petitions per year. For example, on February 15, 2002, we issued a response to a petitioner asking us to refrain from approving a generic version of an antibiotic (Ceftin) if the generic drug product's active ingredient were wholly or partially in crystalline form.

G. Press Items and Publications

The Agency releases much information through the press and related media. Some examples include:

- News releases (for example, HHS and USDA Release *Listeria monocytogenes* Risk Assessment and *Listeria monocytogenes* Action Plan, Release No. 0020.01, January 18, 2001; Cape May Foods Recalls Chopped Clams Because of Possible Health Risk, January 15, 2002)
- *FDA Consumer Magazine* (bimonthly magazine targeting consumers) and reprints of selected feature articles from *FDA Consumer*.
- *FDA Veterinarian* (bimonthly newsletter targeting veterinarians and the food animal industry)
- Frequently Asked Questions: What Can I Do to Protect Myself from Food Poisoning? (Internet only)

IV. Types of Dissemination Methods

Transparency is one of the Agency's key goals. It is critical that our audience understand what we do, how we do what we do, and why we do something. Because our audience is so diverse, we use a variety of media to disseminate public health and safety information. Some examples are provided here:

- **Oral Presentations** in public forums sponsored by FDA or outside parties, such as professional societies or trade associations (for example, the FDA Science Forum)
- **Internet** (medical product approval packages; device summaries of safety and effectiveness; safety alerts; guidance documents; special issue papers, such as those on "Online Medicine Sales" and the "Agency's Bioterrorism Activities")
- **Federal Register** (proposed and final rules; notices announcing the availability of guidances; meeting notices; other notices)
- **The public docket** (citizen petitions and responses; transcripts of certain meetings; information about advisory committee meetings; public comments on guidances, regulations, and any other documents that publish in the *Federal Register*)
- **Videos** (on the Internet and for dissemination to outside organizations and use in meetings and conferences. For example, "Science and our Food Supply: Investigating Food Safety from Farm to Table")
- **CD ROM** (for example, *Listeria monocytogenes* draft risk assessment documents and models)
- **FDA's E-mail lists** (see topics at www.fda.gov/emaillist.html)

V. Agency Quality Assurance Policies, Standards, and Processes

As described in the HHS Implementation Plan, as one of the HHS operating divisions, we have established a number of quality assurance policies, standards, and processes for ensuring the quality of the information we disseminate to the public. Our documents undergo a rigorous review and clearance evaluation according to pre-established procedures, documented in our regulations and guidances.

Generally, Agency documents are cleared as follows:

- Document is developed by an individual or team
- Document is circulated to working group members, and often an editor, and comments are incorporated
- Document is circulated and cleared by center managers
- We publish many documents (for example, guidances, proposed rules) for comment by members of the public, and some documents are reviewed by outside advisory committees comprising experts in the subject matter of the document
- If required by regulation or policy, documents are circulated to and cleared by the Office of the Chief Counsel, Office of Policy, Planning, and Legislation, the Department (HHS), and the Office of Management and Budget (OMB).

In addition to these clearance procedures, we use a number of mechanisms to ensure the quality of the information we disseminate. FDA reviews the quality (including the objectivity, utility, and integrity) of information before it is disseminated and treats information quality as integral to every step of the development of information, including its creation, collection, maintenance, and dissemination. Quality, as defined in the OMB Guidelines, encompasses (1) utility, the usefulness of the information to its intended users, including the public; (2) objectivity, whether information is being presented in an accurate, clear, complete, and unbiased manner; and (3) integrity, the information is protected from unauthorized access or revision.

A. Utility

We only disseminate information that we believe will be useful to the public or a segment of the public. In fact, often we disseminate information because members of the public or the regulated industry have requested it. We develop many guidances as a result of public questions about a specific topic. We also have processes (21 CFR 10.30) by which members of the public can petition us to take certain actions, such as initiating rulemaking or taking specific administrative or enforcement actions. Requests for dissemination of information also can be submitted through petitions.

We developed our good guidance practice (GGP) policy as a result of public request. Congress later enacted the policy into law, and we codified our GGP policy in our regulations at 21 CFR 10.115. The GGPs describe our procedures for developing, issuing, and using guidance documents and include detailed procedures on how members of the public can suggest areas for guidance development, submit drafts of proposed guidance documents, and request the revision or withdrawal of an existing guidance document. We also maintain a guidance Agenda, which is a list of guidances we are planning to develop in the coming year. We post the list on the Internet and publish it annually in the *Federal Register*. We publish the Agenda to keep the public up-to-date on guidance development plans and solicit input from the public on what guidances are needed.

In addition, we are subject to the Freedom of Information Act and the Electronic Freedom of Information Act Amendments (5 U.S.C. 552), which provide for the dissemination of information to members of the public and posting on the Internet certain information that is, or is likely to be, responsive to multiple information requests.

In accordance with the Regulatory Flexibility Act (5 U.S.C. 602), the General Services Administration publishes a semiannual regulatory agenda describing the regulatory actions being developed. The Secretary welcomes comments on this agenda and suggestions for improvements and initiatives.

B. Objectivity

As already mentioned, we have many different systems in place to ensure that the information we disseminate is presented in an accurate, clear, and unbiased manner. We have a strong commitment to writing all our new documents in plain English. We have provided plain English training to many of the employees who write our documents. We also continue to solicit feedback from stakeholders on our efforts

to present written information clearly.

We also take steps to ensure that our regulatory decisions are based on objective information. If we rely on information submitted to us by third parties in support of an application for product approval or in a rulemaking proceeding, we make sure that this information meets the appropriate standards for quality and objectivity. We have a number of regulations and guidances that set standards for the generation of information in support of regulatory decisions. For example, the supporting data may be generated in new research using good laboratory practices (GLPs)³, in clinical studies subject to Good Clinical Practices (GCPs)⁴, in reviews of existing information obtained primarily from peer-reviewed scientific literature, or obtained from surveys based on widely accepted scientific survey techniques. Interpretations of quantitative results of Agency studies are commonly subjected to statistical analyses. Even though we may be unable to fully disclose the information on which our actions are based because it has been submitted by a third party with a proprietary interest in maintaining its confidentiality, we make special efforts to ensure that the information submitted meets these standards for objectivity and is of high quality.

The methods by which we ensure the objectivity of the information for some of our major regulatory activities are described here.

1. Product Review Activities

One key FDA responsibility is the evaluation of data submitted to the Agency in medical and veterinary medical product applications and in food and color additive petitions or notifications. In general, firms that want to market certain products (for example, drugs and medical devices) submit applications to FDA. These applications contain data or information on which the firm relies to claim that its product is safe and effective for its intended uses. We base our decisions about safety and effectiveness primarily on our analyses of the integrity of the submitted data. When we approve a product and post a drug review package on the Internet, we are ensuring that our analyses of the data submitted to us are available for public scrutiny.

We develop regulations and guidance documents to help ensure that the data submitted to us result from the best available studies, that the studies are conducted in accordance with sound and objective scientific practices, and that the data are collected using scientifically accepted methods. For example, FDA regulations specify the format and content of the clinical studies that are submitted in support of an application to market a new drug product. They specify how the data are to be collected and the types of analyses that are to be performed. In the case of biological products, we have developed guidance on the format and content of reports on clinical studies that are submitted to the Agency. Other FDA guidances provide detailed descriptions of appropriate methodologies, analyses, and procedures.

Since the early 1990s, we have been involved in an intensive international effort to harmonize technical requirements for the conduct of studies in support of marketing applications and the content and format of applications with the goal of allowing the submission of a common application for marketing around the world. The International Conference on Harmonisation for Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) brings together scientific experts from different countries to develop a consensus on the appropriate requirements. We also are engaged in international activities in the device, food, and animal drug areas. For example, International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Products (VICH) is the veterinary counterpart to ICH. The Global Harmonization Task Force (GHTF) is working to harmonize device regulations and guidance. The Codex Alimentarius committees are working to harmonize international food regulations. Many agreements reached are then embodied in regulations issued through notice-and-comment rulemaking and in guidance documents that describe in more detail appropriate ways to comply with the regulations. As a result of these efforts, most of our actions on product

approval applications are consistent with international standards for data collection and quality of analysis.

We also are in the process of developing good review practices (GRPs) for drug reviews with the goal of making our drug product review process consistent across all divisions in the Center for Drug Evaluation and Research. A major emphasis of the GRP project is to ensure that the reviews we make available to the public are consistently formatted and clearly written so interested individuals can access important health and safety information.

We frequently consult with scientific experts on product approval applications and broader issues. We have 31 standing Advisory Committees⁵, whom we routinely consult on whether the data in particular applications are sufficient to support an approval decision. As noted above, we incorporate our approval decisions into drug approval packages and device summaries of safety and effectiveness that contain our analyses of the submitted data. These packages and summaries do not include confidential commercial, trade secret, and other information exempt from disclosure when we place them on the Internet.

2. Food Safety Activities

One of FDA's major areas of responsibility is ensuring the safety of the food we eat. Food safety activities include research, risk assessment, inspections, surveillance, compliance, education, and system coordination activities. We must make sure that the information we provide on food safety is presented in an accurate, clear, complete and unbiased manner. This means that the data on which we base our decisions must be collected in an objective manner using sound scientific principles for data collection.

We collect information to support our food safety activities through many sources, including research, risk assessment, inspection and surveillance, peer-reviewed literature, and advisory committee opinions. We conduct in-house research on a variety of food safety topics and also fund a substantial amount of extramural research every year. The Center for Food Safety and Applied Nutrition (CFSAN) participates in collaborative research on processing and packaging through the National Center for Food Safety and Technology, which is a consortium of government, industry, and academia, and we coordinate food safety research activities through a cooperative program with the University of Maryland. Topics of both internal and external research interest are determined by CFSAN's 3-year research plan. This plan is developed in conjunction with other federal agencies to prioritize our research to inform our most critical food safety efforts and to avoid duplication of effort.

We also gather information for certain food safety activities through risk assessment. Risk assessments are a very useful tool for evaluating the benefits of pursuing various rulemaking strategies. To date, we have conducted or been involved in four risk assessments related to food safety. We conducted a joint risk assessment with USDA on *Salmonella* Enteritidis in shell eggs that was published in 1998. More recently, we published risk assessments on the **Public Health Impact of *Vibrio parahaemolyticus* in Raw Molluscan Shellfish and the Relative Risk to Public Health from Foodborne *Listeria monocytogenes* Among Selected Ready-to-Eat Foods**. We also intend to use the risk assessment model developed for USDA by Harvard University on bovine spongiform encephalopathy to determine the risk reduction outcomes of various rulemaking efforts we are considering.

We gather data for FDA food safety activities through use of surveys designed for specific purposes and advisory committee opinions. The surveys include the Health and Diet Survey and the Total Diet Study, both of which are used in our development of safety and exposure assessments for various compounds. When information is not available through research or

literature, we have several advisory committees that are able to render expert opinions on particular matters. These committees include the National Advisory Committee on Microbiological Criteria for Foods, which considers a variety of food safety issues for FDA and USDA, and FDA's Transmissible Spongiform Encephalopathy Advisory Committee (TSEAC), which specifically considers issues related to TSE diseases. Finally, our food safety activities are informed through the participation of FDA scientists in a variety of professional organizations such as Codex Alimentarius, International Commission on Microbiological Specifications for Foods, Institute of Food Technologists, American Society for Microbiology, the International Association for Food Protection, Society for Toxicology, American Chemical Society, the National Academy of Sciences, International Life Sciences Institute, and editorial review boards of several publications including *Journal of Food Protection* and *Journal of Food Science*.

3. Adverse Events Analysis for Medical Products

Once products are marketed, we continue to monitor their safety after approval and disseminate information about their risks to health care providers, patients, and consumers. We undertake a number of data collection activities to ensure the objectivity of the information we disseminate on medical products.

a. Human Drug and Biological Products

The Adverse Event Reporting System (AERS) is an Oracle-based computerized information system designed to support the Agency's postmarketing safety surveillance program for all approved drug and therapeutic biologic products. The structure of the database complies with the international safety reporting guidance (*E2B Guidance on Data Elements for Transmission of Individual Case Safety Reports*, January 1998⁶), including content and format for electronic submission of the reports from the manufacturers. The ultimate goal of AERS is to help reduce the risks associated with medical product use by providing the best available tools for storing and analyzing safety reports. Information from this system is used to support decisions to disseminate information of product safety. By systematizing the submission of data to the Agency, we have greatly improved the quality (and objectivity) of related decisions and information dissemination efforts.

A separate system is used to monitor the safety of vaccines after approval. The Vaccine Adverse Events Reporting System (VAERS) is a cooperative program for vaccine safety of the FDA and the Centers for Disease Control and Prevention (CDC). VAERS is a postmarketing safety surveillance program, collecting information about adverse events that occur after the administration of U.S. licensed vaccines. Other systems are in place to monitor the quality of manufacturing of drugs and biological products and blood related products.

b. Medical Devices

We use a variety of tools to identify problems and safety issues related to medical devices that are approved and being used by health care practitioners and consumers. Tools include both voluntary and mandatory reporting of adverse events; monitoring of product performance through other data sources, such as registries and various research efforts; and the use of both mandatory and voluntary postmarket studies aimed at examining specific safety issues.

Adverse events related to either product problems or issues associated with the use of the device are reported by both manufacturers and device users. Although both

the manufacturing and user communities have mandatory reporting requirements for device-related problems, this surveillance system is virtually a passive system that depends on the reporter to recognize an event and follow through in reporting. This passive surveillance system is augmented by a more active reporting network composed of hospitals and other health care facilities, where reporting is encouraged and supported through educational activities and feedback. Adverse event reports are immediately triaged to quickly identify problems that require urgent attention; all reports are then reviewed by clinical analysts and others with appropriate expertise to decide if further follow-up is needed.

c. Animal Drugs

An Adverse Drug Event (ADE) report for veterinary medicinal products consists of either an undesired side effect or the lack of a desired effect associated with drugs administered to animals. Reports may also involve product defects and potential harm posed to persons administering or using animal drugs. For example, in the year 2000, FDA's Center for Veterinary Medicine reviewed 14,497 ADE reports consisting of: 13,757 undesired side effects and lack of desired effect; and 740 product defects.

Adverse event reports related to animal drugs are maintained in a separate database, the Center for Veterinary Medicine's adverse drug event reporting system (ADERS). This database is used to identify adverse effects not detected during pre-market testing of FDA-approved animal drugs and to monitor the performance of drugs not approved for use in animals. The ADERS depends upon the detection of an adverse clinical event by veterinarians and animal owners, the attribution of the clinical event to the use of a particular drug ("suspect" drug), and the reporting of the ADE either to the manufacturer of the suspected drug or directly to FDA. Data from these ADE reports are reviewed, coded and entered into the computerized ADERS.

The ADE for veterinary drugs generates current information on the safety and efficacy of veterinary drugs. These data expand the knowledge base used in animal drug approvals and ultimately contribute to reducing the risks associated with veterinary medical products. Summary information from this system is available to support decisions about disseminating information on product safety.

d. Foods, Including Dietary Supplements, and Cosmetics

We use several reporting systems to identify problems associated with foods, including dietary supplements, and cosmetics.

- The Adverse Reaction Monitoring System (ARMS) collects spontaneous reports from consumers and health professionals regarding alleged adverse effects from food products.
- The **Special Nutritional Adverse Event Monitoring System (SN/AEMS)** collects spontaneous reports from consumers and health professionals regarding adverse effects from special nutritional.
- The **Cosmetic Adverse Reaction Monitoring System (CARMS)** collects spontaneous reports from consumers and health professionals regarding alleged adverse effects from cosmetic products.
- CFSAN receives adverse event reports linked to the products it regulates through FDA's MedWatch program.

4. Research to Support the Regulatory Functions of FDA

FDA conducts peer-reviewed research that supports the regulatory functions of the Agency. To accomplish this mission, the FDA seeks feedback from its stakeholders and partners, including its center scientists, other government agencies, industry, and academia. In addition, the FDA Science Board (SB) provides guidance on specific complex and technical issues as well as emerging issues within the scientific community, in industry, and academia. The SB conducts ongoing reviews of the research programs themselves and how these programs are keeping pace with technical and scientific evolutions in the fields of regulatory science. Their review includes advice on developing an appropriate research agenda and on upgrading FDA's scientific and research facilities to keep pace with these changes. The SB is composed of non-governmental scientists from industry, academia, and consumer organizations. This board is further supplemented with subject matter experts and scientists representing all FDA centers. Research programs can be via collaborations through partnerships with other scientific organizations. Scientific and monetary collaborations include interagency agreements with other government agencies, Cooperative Research and Development Agreements and technology transfer with industry, and grants or informal agreements with academic institutions.

Each FDA Center and Office also uses several strategies to ensure the quality (including objectivity) of its extramural research and the accuracy of data collected in association with these studies. For example, study protocols may be developed collaboratively by principal investigators and program officials. A project advisory group (PAG) consisting of experts who oversee extramural research projects in a particular field may be appointed.

To ensure the data are accurate and timely, FDA monitors research progress at the project level on a recurring basis. FDA quality assurance staff assess experiments that fall within the scope of FDA's Good Laboratory practice guidelines for compliance. Additionally, agency scientists publish research manuscripts, book chapters, and abstracts in recognized, peer-reviewed scientific journals. FDA's research findings are also presented at national and international scientific meetings, many of which are sponsored or co-sponsored by FDA. Many FDA scientists also serve on international scientific advisory boards.

C. Integrity

We strive to maintain the integrity of the information we collect and use, and protect it against disclosure, alteration, loss, or destruction. We require all of our operating divisions to adhere to a series of Agency guidelines to ensure our data integrity operations. Guidelines include:

- FDA Staff Manual Guide 3250.17 Data Security\Data Integrity
- Computer Security Act of 1987
- Computer Fraud and Abuse Act of 1986
- Clinger-Cohen Act of 1996
- Federal Managers Financial Integrity Act
- Government Information Security Reform Act (GISRA)
- Office of Management and Budget (OMB) Circular A-130, Appendix III, Management of Federal Information Resources, Revised 2/96
- HHS Automated Information Systems Security Program Handbook (Release 2.0), 5/94
- NIST Special Publication 800-14, Generally Accepted Principles and Practices for Securing Information Technology Systems (September 1996)

All data submitted for inclusion in our systems must be accompanied by information about origin, sensitivity, reliability, and the date of most recent revision. We have systems in place to ensure that data modifications

are accomplished in a managed and controlled manner and that all information is protected from unauthorized access, revision, corruption, or falsification.

Transactions affecting sensitive or valuable information can only be processed if the originating individual or system has been validated as authorized to submit such transactions. Additionally, transactions must be initiated only through source documents or computerized messages in which the originating individual or system is clearly identified. All transactions intended for input into a multi-user production computer system must first be subjected to reasonableness checks, edit checks, and/or validation checks.

Transactions that fail such checks must either be:

- Rejected with a notification of the rejection sent to the submitter
- Corrected and resubmitted or
- Suspended pending further investigation

Management has established and maintains preventive and detective security measures that ensure that our information is protected from undetected alteration. All rejected input transactions are placed in a suspense file and listed in exception reports until they are successfully resubmitted for processing. Resubmission and corrections are subject to the same validation procedures that original input transactions receive. Management reviews the reasonableness and accuracy of all changes to internal records. If a client or customer brings record errors to our attention, an investigation of the errors is initiated promptly.

The Office of Public Affairs provides guidance to the Agency on best communications principles and practices to help assure that public messages are accurate, understandable and consistent with current Agency policies. The quality, objectivity, utility and integrity of information posted on the FDA Internet is assured by the internal clearance process used to clear printed documents.

VI. Agency Administrative Complaint Procedures

A. Format for Submitting Complaints

As described below, we intend to use existing complaint mechanisms to address complaints from the public concerning our information dissemination activities. You may use any of the mechanisms outlined below to request correction of information disseminated by FDA that you believe does not meet the applicable OMB or HHS Information Quality Guidelines, or this Guidance.

If you request a correction of any information disseminated by us, we would appreciate it if you clearly designate the request as a request for correction of information under this guidance and the OMB and HHS Guidelines. You should use the following format for your request:

1. Your name, mailing address, fax number or e-mail address, telephone number, and organizational affiliation, if any, of the requestor,
2. A detailed description of the specific material that needs to be corrected including where the material is located, i.e., the publication title, date, and publication number, if any, or the website and web page address (Uniform Resource Locator or url),
3. The specific reasons for believing the information does not meet applicable OMB, HHS, or FDA guidelines and is in error, and supporting documentation,
4. The specific recommendations for correcting the information,
5. A description of how the person submitting the complaint is affected by the information error.

B. Procedures for Submitting Complaints

We have clear procedures in place to address complaints from the public. Requests should be submitted to

the Agency in accordance with the procedures described below for dispute resolution (i.e., beginning with the employee or division that disseminated the information, or by contacting the center, the Agency, or an ombudsman). To help us track and monitor complaints, regardless of which procedures you use, we ask that you also send a copy of your request for correction to:

Office of the Ombudsman
Food and Drug Administration
5600 Fishers Lane
Room 14B03, HF-7
Rockville, MD 20857

FDA regulations at 21 CFR 10.75 provide a mechanism for any interested person (a person who submits a petition, comment, or objection, or otherwise asks to participate in an informal or formal administrative proceeding or court action) to obtain formal review of any Agency decision or action by raising the matter with the supervisor of the employee who made the decision. These procedures can be used to submit an initial complaint about an FDA information dissemination. If the issue is not resolved at the primary supervisory level, the interested person may request that the matter be reviewed at the next higher supervisory level. This process may continue throughout the Agency's chain of command, through the centers to the Commissioner of the FDA.

Regulations for dispute resolution during the application review process (21 CFR 312.48; 314.103; and 814.42 (d), 814.46(c), 814.112(b), and 808.25 (e)) specify procedures similar to those outlined above. CDRH also established a Medical Devices Dispute Resolution Panel to hear scientific disputes. Regulations for CDER and CBER also provide that a sponsor may request that we seek the advice of outside experts. In addition, we may refer major issues to an appropriate advisory committee for its recommendations (§§ 312.48(c)(3) and 314.103(c)(3)).

Several guidances explaining the dispute resolution process also are available:

- *Formal Dispute Resolution: Appeals Above the Division Level* (for drug and biological products, February 2000),
- *Resolving Scientific Disputes Concerning the Regulation of Medical Devices, a Guide to Use of the Medical Devices Dispute Resolution Panel* (July 2001)
- *Medical Device Appeals and Complaints: Guidance on Dispute Resolution* (February 1998)
- *A Suggested Approach to Resolving Least Burdensome Issues* (September 2000)

Finally, 21 CFR 5.200 provides for the establishment of an Agency ombudsman. We have established an Ombudsman Office within the Office of the Commissioner, and each center has identified or is identifying an ombudsman. Information about when and how to contact an Agency or center ombudsman can be found on our Internet site⁷. We encourage interested parties who may be reluctant to contact a program person in a specific program, division, office or center to feel free to contact a center or Agency ombudsman.

Existing public comment procedures for rule-makings and other formal agency actions already provide well established procedural safeguards that allow affected persons to raise information quality issues on a timely basis. Accordingly, FDA will use these existing procedures to respond to information quality complaints that arise in this process.

In cases where the agency disseminates a study, analysis, or other information prior to the final agency action or information product, requests for correction will be considered prior to the final agency action or information product in those cases where in the agency's judgment issuing an earlier response would not unduly delay issuance of the agency action or information product and the complainant has shown a reasonable likelihood of suffering actual harm from the agency's dissemination if the agency does not resolve the complaint prior to the final agency action or information product.

You should be aware that you bear the "burden of proof" with respect to your request for correction.

C. FDA's Response to Complaints

Based on a review of the information you provide in your complaint, we will determine whether a correction is warranted and, if so, what action, if any, we will take. We will respond to you in a manner appropriate to the nature and extent of your complaint (for example, by letter, e-mail, fax, press release, mass mailing) and will indicate whether, and if so how, we intend to correct the information. We will respond in accordance with the time frame specified in the complaint mechanism you use. Where a procedure does not specify a time frame for a response, we will respond within 60 days, in accordance with the OMB and HHS Guidelines. We will respond by either issuing a decision or by informing you that more time is required, explaining why, and providing you with an estimated decision date. In deciding how to respond, we will consider all of our legal obligations and policies.

D. Requests for Reconsideration

If you do not agree with FDA's decision about your complaint (including any corrective action), you may send a request for reconsideration within 30 days of receipt of our decision. You may use any of the **Procedures for Submitting Complaints** described above. A request for reconsideration should state the reasons why you believe the response is inadequate, should be designated as an "Information Quality Appeal," and should include a copy of your original request and the agency's decision. The agency will respond to all requests for appeals within the time frame specified in the procedure you use. Where a procedure does not specify a time frame for a response to your appeal, we will respond in a timely manner, in accordance with the OMB and HHS Guidelines.

VII. Influential Scientific, Financial, and Statistical Information

As illustrated by the number and types of information we disseminate and the variety of methods we use to disseminate them, it is clear that we strive for a high degree of transparency with regard to all of our information dissemination activities. The OMB Guidelines, however, apply special quality standards to the dissemination of information that is considered influential. Such information must meet high standards of transparency of the data and methods used to facilitate the reproducibility of such information by third parties. As defined below, influential scientific, financial and statistical information that FDA disseminates will meet the high standards in the OMB Guidelines for such information.

A. Definition of the Term *Influential*

The term *influential information*, when used in the OMB Guideline in the phrase "influential scientific, financial, or statistical information," applies when the agency can "reasonably determine that dissemination of the information will have or does have a *clear and substantial impact* on important public policies or important private sector decisions" (67 FR 8452; February 22, 2002). However, because each agency is different, and there are vast differences in the types of information they disseminate, each agency has been asked to elaborate on the definition of influential in the context of their missions and duties, "with due consideration of the nature of the information they disseminate." As stated in the OMB Guideline (V.9), "[e]ach agency is authorized to define 'influential' in ways appropriate for it given the nature and multiplicity of issues for which the agency is responsible."

For purposes of this guidance, *influential information* is defined as disseminated information that results from or is used in support of agency actions that are expected to have an annual effect on the economy of \$100 million or more or will adversely affect in a material way the economy, a sector of the economy, productivity, competition, jobs, the environment, public health or safety, or State, local or tribal governments or communities. It should be noted that the definition applies to "information" itself, not to decisions that the information may support. Even if a decision or action by FDA is itself very important, a particular piece of information supporting it may or may not be "influential."

Two examples of what FDA considers to be influential information follow.

- Quality Mammography Standards

On October 28, 1997, we issued a final rule (62 FR 55852) amending our regulations governing mammography to provide increased assurance of adequate and consistent evaluation of mammography facilities on a nationwide level and compliance of the facilities with quality standards. Costs of the regulation include replacing below standard mammography units and film processors, providing written results of tests to patients, providing telephone results of tests to referring physicians, and conducting required weekly image quality tests. Because this rulemaking was expected to have an annual effect on the economy of more than \$100 million, the information FDA disseminated in support of this rulemaking would be considered influential information.

- Hazard Analysis and Critical Control Point (HACCP); Procedures for the Safe and Sanitary Processing and Importing of Juice

On January 19, 2001, we adopted a final rule (66 FR 6138) to ensure the safe and sanitary processing of fruit and vegetable juices. The regulations mandate the application of HACCP principles to the processing of these foods. HACCP is a preventive system of hazards control. FDA adopted this rule in response to a number of food hazards associated with juice products and because preventive control measures are the most effective and efficient way to ensure that these products are safe. The final regulation involves costs to the manufacturers and processors of juice products for implementing procedures consistent with the regulation that exceeded \$100 million. Therefore, the information disseminated in connection with this rulemaking would be considered influential information.

B. Transparency

If information that meets the criteria for influential information is disseminated, the OMB Guidelines provide that it must meet certain higher standards of transparency and methods to facilitate the reproducibility of information by qualified third parties. When we disseminate information, but particularly in those cases involving influential information, we strive to ensure that the information is accurate and unbiased, as well as substantially reproducible and replicable. This goal is accomplished by using reliable data sources and sound analytical techniques, and by employing a high degree of transparency about the data, methods, measures, assumptions and limitations used to develop the information to facilitate reproducibility by third parties. Our goal is to provide a clear explanation of the assumptions and data upon which we base our conclusions, the criteria used to determine the suitability of the data for use, the methods used in our analysis, and the conclusions we have drawn.

Because of legal obligations to maintain the confidentiality of data supplied by third parties, there may be instances when original or supporting data may not be available to the public. In such cases, we will disclose the specific data sources used and the specific quantitative methods and assumptions employed. We will also conduct especially rigorous robustness checks of any models used in the analysis and the analytic results so that there will be a high degree of confidence in the results.

Biases, if any, will be revealed. All assumptions used in the analysis, the scientific rationale, and data used to estimate the impact of the various factors influencing the analysis should be clearly stated. This ensures that biases will be eliminated or minimized and that any introduced biases will be clearly identified.

Clarity includes ensuring the information disseminated is clear and understandable. When detailed technical information is needed to provide sufficient information so that a qualified third party could reproduce the analysis, the resulting document may be lengthy and difficult the public to understand. One approach that can provide additional transparency in such cases is to develop an interpretative summary document as a companion to the technical analysis. The summary document can provide a non-technical explanation of the data, process, results, and conclusions in a manner that the public can understand. As discussed under "Objectivity," we have a strong commitment to writing all our new documents in plain English. As we revise

and update existing documents, we will ensure that they are written in plain English. Our goal is to make our written communications more understandable.

A *participatory process* should be used. The process for generating information defined as influential should be transparent. One approach is to invite public comment on the information to be disseminated and encourage stakeholders to submit scientific data and information that can be used in preparing the information. As appropriate, we will solicit advice and opinions of advisory committees as well as peer review from experts within and outside of the agency. To the extent practicable under confidentiality laws, we will strive to make supporting data and analyses available to the public for technical review and comment. This can be accomplished by posting the information on our web pages and providing printed copies as requested.

C. Risk Assessment

Some of the influential information that we disseminate is based on an analysis of the risks to the public of certain actions or exposures to hazardous substances. For purposes of this guidance, we are defining risk as the likelihood that injury or damage is or can be caused by a substance, technology, or activity. We use risk analysis (the integration of risk assessment with risk management and risk communication) as a tool to enhance the scientific basis for all of our regulatory decisions.

The OMB Guidelines provide that in addition to the ordinary standards for utility, objectivity, and integrity that apply to dissemination of information, special considerations must be taken into account in certain risk assessments, i.e., those that provide the basis for the dissemination of influential information. The Guidelines state that "With regard to analysis of risks to human health, safety, and the environment maintained or disseminated by the agencies, agencies shall either adopt or adapt the quality principles applied by Congress to risk information used and disseminated pursuant to the Safe Drinking Water Act Amendments of 1996 (SDWA) (42 U.S.C. 300g-1(b)(3)(A) and (B)).

The SDWA risk assessment principles are as follows:

1. To the degree that the agency action is based on science, the agency shall use
 - a. the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices
 - b. data collected by accepted methods (if reliability of the method and the nature of the decision justify use of the data)
2. In the dissemination of public information about risks, the agency shall ensure that the presentation of information about risk effects is comprehensive, informative, and understandable.
3. In a document made available to the public in support of a regulation, the agency shall specify, to the extent practicable
 - a. Each population addressed by any estimate of applicable risk effects
 - b. The expected risk or central estimate of risk for the specific populations affected
 - c. Each appropriate upper-bound or lower-bound estimate of risk
 - d. Each significant uncertainty identified in the process of the assessment of risk effects and the studies that would assist in resolving the uncertainty and
 - e. Peer-reviewed studies known to the agency that support, are directly relevant to, or fail to support any estimate of risk effects and the methodology used to reconcile the inconsistencies in the scientific data

Many of our actions are based on scientific experts' judgments using available data, are essentially qualitative, and are generally carried out for non-cancer-causing hazards. Such assessments provide useful answers in most instances that are sufficient for regulatory purposes, and much more elaborate, quantitative estimates extrapolating beyond the data are unnecessary. For example, we may issue regulations on submission requirements for product approval applications, electronic submission of product labeling, or periodic reporting by manufacturers of adverse events from drugs; devices; and biologics, including blood, vaccines, and tissues. Regulations like these do not always lend themselves to the types of quantitative risk assessments contemplated by the Safe Drinking Water Act principles.

Other actions are based on research and supporting data that are generated outside FDA. For example, most product approval actions are based on scientific studies conducted by sponsors seeking marketing approval in accordance with our regulations and guidance documents. Our regulations and guidance documents describe sound scientific practices for conducting human and animal studies of medical products and analyzing the resulting data. Most information in these studies is considered confidential commercial information and is closely held by the sponsors. As a result, formal peer-review of the data is rare. However, for certain drug approval applications, the safety and/or effectiveness information is presented to scientific advisory committees for recommendations. Evaluations of food safety and nutritional data are also presented to scientific advisory committees.

As a result, we have adapted the general principles for risk assessments from the SDWA to fit these situations. The principles we intend to apply to risk assessments involving the dissemination of influential information affecting product approval actions or regulations that do not lend themselves to quantitative risk assessment are as follows:

1. The Agency will use
 - a. the best available science and supporting studies conducted in accordance with sound and objective scientific practices, including peer reviewed science and supporting studies when available
 - b. data collected by accepted methods (if reliability of the method and the nature of the decision justify use of the data)
2. In the dissemination of public information about risks, the Agency will ensure that the presentation of information about risk effects is comprehensive, informative, and understandable.

In situations requiring a quantitative risk assessment, we generally follow basic risk assessment principles in the NAS paradigm of 1983. Our needs for quantitative risk assessments range over a wide variety of hazards including physical hazards encountered during use of a medical device, food chemical residues, and antimicrobial resistance genes in bacteria. Thus, we also ascribe to the statement from NAS when it revisited the risk assessment process in 1994 (*Science and Judgment in Risk Assessment*, NAS 1994): "Risk assessment is not a single process, but a systematic approach to organizing and analyzing scientific knowledge and information. "In each of the areas we regulate, we apply risk assessment practices to the specific task that are widely accepted among relevant domestic and international public health agencies.

For quantitative risk assessments in support of the dissemination of influential information, FDA intends to apply the following principles:

1. The agency will use-
 - a. the best available science and supporting studies conducted in accordance with sound and objective scientific practices, including peer reviewed science and supporting studies when available;
 - b. data collected by accepted methods (if reliability of the method and the nature of the decision

justifies use of the data)

2. In the dissemination of public information about health risks, the agency shall ensure that the presentation of information is comprehensive, informative, and understandable, within the context of its intended purpose.
3. In a risk assessment document made available to the public, the agency shall specify, to the extent practicable-
 - a. Each population addressed by any estimate of applicable effects;
 - b. The expected or central estimate of risk for the specific populations affected;
 - c. Each appropriate upper-bound and/or lower-bound risk estimate and the methodology used to reconcile the inconsistencies in the scientific data;
 - d. Data gaps and other significant uncertainties identified in the process of the risk assessment and the studies that would assist in characterizing the uncertainties; and
 - e. Additional studies not used to produce the risk estimate that support or fail to support the findings of the assessment, and the rationale of why they were not used.

VIII. Special Considerations for Agency Dissemination

Under certain circumstances, we may need to disseminate information without fully applying the principles for ensuring the quality, objectivity, utility and integrity of the information outlined above. Even in these cases, however, FDA intends to use its internal review process to evaluate the data received and the information it plans to disseminate to ensure to the degree practicable the accuracy, objectivity, and transparency of the relevant information, and will entertain requests for correction after the exigent circumstances have passed. The specific situations where this may occur are as follows:

- **Public Health Emergencies:** In the case of a public health emergency, there may not be time for the Agency to submit relevant information to all levels of review or review by an Advisory Committee prior to dissemination of the information.
- **Statutory or Other Legal Requirement:** If a statutory requirement, Executive Order, or court order requires immediate implementation of a policy, we may have insufficient time to apply the OMB requirements prior to disseminating information relevant to that policy.
- **Other Circumstances:** There may be unforeseen circumstances in carrying out our mission that could prevent the Agency from applying all of the OMB guidelines when disseminating information to the public.

As mentioned above, in all such special circumstances, the Agency will be particularly careful to use its internal review processes to the extent practicable when considering the dissemination of relevant information to the public.

IX. References

Clinger-Cohen Act of 1996.
 Code of Federal Regulations (CFR), Title 21, Parts 5, 10, 50, 56, 58, 312, and 314.
 Computer Fraud and Abuse Act of 1986.
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 HHS Automated Information Systems Security Program Handbook (Release 2.0), May 1994.
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 FDA Staff Manual Guide 3250.17, Data Security/Data Integrity.
 Federal Food, Drug, and Cosmetic Act (21 U.S.C. 301 et seq.).
 Federal Managers Financial Integrity Act.
 Food and Drug Administration Modernization Act of 1995 (Public Law 105-115).
 Freedom of Information Act and Electronic Freedom of Information Act Amendments (5 U.S.C. 552).
 Government Information Security Reform Act (GISRA).
 ICH guidance, *E2B Guidance on Data Elements for Transmission of Individual Case Safety Reports*, January 1998.
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 Office of Management and Budget (OMB) Circular A-130, Appendix III, Management of Federal Information Resources, rev. February 1996.
 Public Health Service Act (42 U.S.C. 201 et seq.).
 Regulatory Flexibility Act (5 U.S.C. 601-612).

Safe Drinking Water Act Amendments (Public Law 104-182).
Treasury and General Government Appropriations Act, 2001.

Endnotes

1. These guidelines published in the Federal Register on January 3, 2002 (67 FR 369) and were republished with corrections on February 22, 2002 (57 FR 8452).
2. All product reviews undergo extensive review through a hierarchical process (see [Section V](#)).
3. Good laboratory practices (GLPs) for nonclinical laboratory studies are discussed in 21 CFR 58.
4. Regulations at 21 CFR 312, guidances developed as part of the Agency's international harmonization efforts (for example, E6 and E8), and guidances developed by FDA that address clinical development of drugs to treat specific indications provide requirements and recommendations on good clinical practice (GCP). In addition 21 CFR parts 50 and 56 address issues related to informed consent and investigational review boards (IRBs), respectively.
5. FDA also administers an HHS Advisory Committee that has 18 panels.
6. This guidance is being updated and should be available soon.
7. Information on the FDA Ombudsman Program can be found at www.fda.gov/oc/ombudsman/homepage.htm.