

MEMORANDUM OF UNDERSTANDING BETWEEN
THE FOOD AND DRUG ADMINISTRATION
AND
NATIONAL INSTITUTES OF HEALTH

I. PARTIES

This Agreement is between the U.S. Department of Health and Human Services, U.S. Food and Drug Administration (FDA) and the U.S. Department of Health and Human Services, National Institutes of Health (NIH), collectively, "the Parties."

II. OVERVIEW

A. Introduction

The FDA and the NIH both recognize the need for a unified federal approach to adverse event (AE) reporting. Such a harmonized approach will facilitate and streamline submission of both pre- and post-market AE reports while improving data quality and analysis, as well as improving human subject protections. The FDA and NIH began discussions to determine the feasibility of combining efforts to develop web-based portals for AE reporting in order to leverage these efforts and develop a single product that could be used by both Agencies to improve report quality, lower costs, and reduce delivery time. This Agreement memorializes the joint efforts that will be undertaken to effectuate this goal.

B. Background

The FDA, as part of its ongoing work in improving the nation's safety surveillance system, has commenced work on a project, titled MedWatch[™], to create an Agency-wide portal through which adverse event, consumer complaint, and product problem reports are received and processed to make the information available to adverse event analysis systems. The FDA has invested resources over a period of three years to achieve American National Standards Institute (ANSI) approval of a technical standard for exchanging adverse event data, called the "HL7 - Individual Case Safety Report (ICSR)." The use of the HL7 ICSR standard as part of the MedWatch[™] project enables FDA to implement the standard for all FDA-regulated products (e.g., animal and human food/feed (medicated and unmedicated), cosmetics, dietary supplements, animal and human drugs, biologics, devices, combination products, pet treats, vaccines, etc.). Currently, FDA's adverse event (AE) data collection needs in MedWatch[™] are for adverse events associated with the use of marketed products. FDA expects to receive electronic submission of AE's in clinical trials in the future.

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The NIH, through extensive consultation with more than 300 nationally recognized leaders in academia, industry, government, and the public, identified harmonization of clinical research requirements as the highest priority concern of investigators, IRBs, and others involved in clinical research. Furthermore, these stakeholders urged that the NIH assume as its first priority streamlining the highly diverse Federal requirements for the reporting of adverse events that occur during clinical trials. These requirements are imposed by the FDA, NIH, and other agencies of the Federal government.

At present, in reporting a given adverse event, an investigator typically has to submit separate reports to multiple agencies, using different forms, vocabularies, severity criteria, and reporting timeframes. Oversight bodies and agencies receiving this information are often faced with tremendous volumes of data reported in idiosyncratic ways, which often frustrates efforts to conduct meaningful aggregations and analyses of data, or to cull from reports information key to important safety concerns.

To address this problem, the NIH Director, along with the Director of the HHS Office of Human Research Protections (OHRP), established the Federal Adverse Event Task Force (FAET) as a collaborative effort among the FDA, the NIH, the OHRP, the Centers for Disease Control and Prevention, the Department of Veterans Affairs, the Department of Defense, and the Agency for Healthcare Research and Quality, collectively, the "FAET Agencies." Chaired and staffed by the NIH's CRpac Program, the FAET is charged with proposing specific means for promoting harmonized requirements and processes for reporting adverse events in clinical research to the relevant federal agencies.

To fulfill the adverse event reporting requirements and needs of the FAET Agencies, the FAET proposed a consensus standard, for data elements of a Basal Adverse Event Report (BAER). The value of this accomplishment can only be realized if it is translated into reporting tools for investigators and agencies alike.

To this end, NIH plans to develop a Web-based portal whereby investigators would prepare a single report using a standard format (the BAER). Investigators, sponsors, clinicians, and consumers will be able to convey instantaneously one report – utilizing, to the extent possible, a universally accepted vocabulary and format – to all agencies with oversight for that particular study.

C. Purpose

FDA and NIH are agreeing to collaborate on a project of mutual interest, specifically the development of a "Rational Questionnaire" and a prototype to test the feasibility of a central web-based portal for AE reporting (together, the "Project").

Put broadly, NIH and FDA aim to develop a Project that will result in a web-based method for consumers, health professionals, investigators, sponsors, and other parties to electronically submit AE reports. The Project is expected to create tools that will allow any user to submit adverse event information that corresponds to a wide range of forms already in use by many agencies (e.g. FDA 3500 and 3500A forms, and NIH and other

MedWatch^{Plus} Rational Questionnaire

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agency specific forms). The Project includes the development of at least two products: (1) a "Rational Questionnaire" – an interactive help system that will assist reporters of information in determining what specific data need to be submitted and to whom, and (2) a prototype to test the feasibility of a central, Federal web-based portal to provide direct, seamless, online submission of adverse event reports to appropriate agencies. The Rational Questionnaire is a reporting method component dependent on a web-based portal technical infrastructure. The central, Federal web-based portal prototype will provide an opportunity for NIH and FDA to better understand the technology infrastructure that may be needed to support a broader group of federal agencies.

This Agreement describes the terms of collaboration between FDA and NIH on the Project. Information will be shared and transparent, as permitted by law, so that the Parties can maximize efficient use of government resources to reach the Project goals.

D. Priorities and Funding

The Project is critical to the missions of both MedWatch^{Plus} and the Federal Adverse Event Task Force. Successful completion of the project on schedule is vital. The FDA has a need to implement an electronic AE reporting system as soon as possible to satisfy several important mandates, including the requirement to receive mandatory AE reports for dietary supplements and to accommodate those reporters that prefer to submit electronically. FDA and NIH program needs will be prioritized as the Project and schedule for completion are developed.

The NIH has begun some work on the Project, including establishing contacts with technical experts and contractors to develop the two products described. The NIH will continue to serve as the primary point of contact for these contractors. The FDA will provide needed technical assistance but no funds will be transferred to NIH for these activities.

III. RESPONSIBILITIES OF THE PARTIES

A. General

The Parties agree as follows:

1. They will jointly participate in the Project (to develop the Rational Questionnaire and portal prototype), including all phases of project management.
2. Project results will be available to both Parties to implement as they individually see fit, consistent with law.

3. The NIH, or its contractor(s) will provide explicit training to FDA personnel in the technical architecture and implementation of the prototype and application developed in the Project. The issue of ongoing maintenance will be resolved during the Project's development.
4. The Project will follow the HHS Enterprise Performance Lifecycle (EPLC) standard, as applicable, including for the production of all required documents.
5. The scope of the Project will be further, and mutually, defined and documented early in the Project.
6. A unified Requirements Matrix will be prepared, and appropriate FDA and NIH technical representatives will approve it.
7. Any software developed in the course of the Project will be available for both FDA and NIH to continue to use, develop and extend as they individually see fit, without limitation but subject to applicable law.
8. The Project documents will be maintained using agreed upon tools, with access granted to FDA and NIH staff as needed.
 - a. FDA will be responsible for providing resources to maintain and manage the Project documents for the marketed products portion of the project
 - b. NIH will be responsible for providing resources to maintain and manage the Project documents for the clinical trials portion of the project
9. The technology stack chosen to implement the Project will be approved in advance by the designated technical representatives from FDA and NIH.
10. The prototype Rational Questionnaire will be jointly developed and deliverable at a mutually agreed-upon date. The system will be developed in an iterative or

multi-phase fashion to enable FDA and NIH end-users to evaluate and refine the system during the course of development. The common components of the Questionnaire will be developed first and the marketed products and clinical trials components will be developed next in parallel, with different timelines, and with appropriate contributions to each.

11. The prototype portal in which the Rational Questionnaire will reside and by which the Parties can test the feasibility of generating adverse event reports through the Questionnaire for submission to Federal agencies will be jointly developed.
12. Before conclusion of this agreement, the Parties will discuss and decide if an Independent Validation and Verification test plan is needed in order to ensure that the Project meets all relevant specifications.
13. User Acceptance Testing (UAT) will be performed to ensure that the project meets requirements.

B. FDA

The FDA agrees to perform the following activities and provide the following resources in support of the project:

1. Collaborate and provide non-monetary resources for the project management of the common components of the Questionnaire and the marketed products components as well as the development of the portal prototype.
2. Provide useful, actionable requirements for the Project to satisfy FDA needs.
3. Participate in all Project management meetings as scheduled.
4. Collaborate in the design of the Project.
5. Provide FDA resources as needed to learn the technical architecture.
6. Provide FDA resources for implementation of the Project.

C. NIH

The NIH agrees to perform the following activities and provide the following resources in support of the project:

1. Collaborate and provide resources for the project management of the common components of the Questionnaire, and the clinical trial components as well as the development of the portal prototype.
2. Provide useful, actionable requirements for NIH needs.

3. Participate in all Project management meetings as scheduled.
4. Collaborate in the design of the Project.
5. Direct the contractor(s) in performance of their duties with input and agreement from FDA.
6. Provide NIH resources for implementation of this project.

IV. PROJECT DURATION

The Project shall be considered finished when the key deliverables, the Rational Questionnaire and portal prototype are delivered and operational, but no later than three (3) months after the agreed-upon and scheduled completion date, which will be determined after work has begun.

V. ISSUE RESOLUTION

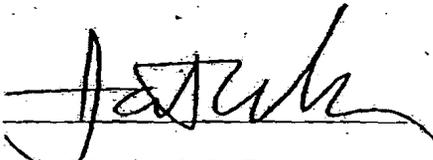
The FDA and NIH program staff working on the Project are committed to productive and collaborative activities to achieve the important public health goals of the Project. Consistent with Federal law and agency practice, staff will work together to resolve any programmatic disputes and communicate within agency chain-of-command any differences or other concerns as necessary. It is expected that the first line of communication above the project staff will be FDA's Executive Sponsor of MedWatch^{Plus} and NIH's Director for Science Policy, Office of the Director.

VI. INFORMATION SHARING

As sister public health agencies within the Department of Health and Human Services, there are no legal prohibitions that preclude FDA or NIH from sharing with each other most agency records in the possession of either agency. Both agencies recognize and acknowledge, however, that it is essential that any confidential information that is shared between FDA and NIH must be protected from unauthorized use or disclosure. See, e.g., 21 USC. sec. 331(j); 18 U.S.C. section 1905; 21 C.F.R. Parts 20 and 21; 42 C.F.R. Parts 5 and 5b. Safeguards will be followed to protect the interests of, among others, owners and submitters of trade secrets and confidential commercial information; patient identities and other personal privacy information; privileged and/or predecisional agency records; and information protected for national security reasons.

VII. PERIOD OF AGREEMENT AND MODIFICATION/TERMINATION

This Agreement will become effective when signed by all Parties. The Agreement will continue for not more than five years thereafter, unless amended by mutual agreement of the Parties, until the Project is completed. It is expected that the Project will take not more than two years to complete. Either party may terminate this Agreement by providing one hundred twenty (120) days written notice to the other party. Consistent with the expectation that no funds will be transferred between the Parties, each party shall be solely responsible for the payment of any expenses it has incurred in the event this Agreement is terminated before completion. This Agreement is subject to the availability of funds.

 9/26/07  9/29/07

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