MEMORANDUM OF UNDERSTANDING

BETWEEN THE

FOOD AND DRUG ADMINISTRATION

AND

DUKE UNIVERSITY

FOR THE

CARDIAC SAFETY RESEARCH CONSORTIUM
Whereas extensive cross-sector and multi-disciplinary efforts are needed to develop and to understand the clinical utility of a new generation of biomarkers and other technologies, which can be used for detection, early diagnosis, prognosis and clinical assessment tools in cardiovascular research and clinical decision-making;

Whereas such new cardiovascular assessment tools, including biomarkers, if proven effective in predicting and assessing therapeutic response in clinical trials and thereby “qualified” have the potential to be adopted as assessment tools for use in medical product development and Food And Drug Administration (FDA) regulatory evaluation and guidance;

Whereas Duke University, a nonprofit, research, education, and healthcare institution is an organization (Duke) for and on behalf of its Duke Clinical Research Institute, (DCRI) whose mission it is to develop and share knowledge that improves the care of patients around the world through innovative clinical research;

Whereas Duke started and maintains one of the nation’s first cardiovascular computerized clinical databases, said cardiovascular database being sustained for over 30 years as one of the world's largest repositories of follow-up on patients with carefully documented coronary heart disease;

Whereas Duke’s DCRI has evolved into an organization with major efforts in clinical trials, outcomes research, and health policy;

Whereas FDA, with its unique perspective on research and development activities and in-depth understanding of clinical trial design, regulatory policy, and scientific know-how in reviewing medical products, is interested in exploring biomarker technologies as assessment tools for use in FDA guidance to facilitate medical product development;

Whereas FDA, under the terms and conditions of a Cooperative Research and Development Agreement (CRADA), has collaborated with Mortara Instrument, Inc, a CRADA partner, to design and implement an ECG Warehouse to hold ECGs obtained in drug trials to assess proarrhythmic risk;

Whereas said ECG Warehouse is now operational and capable of supporting multiple research and regulatory functions;

Whereas FDA and Duke (the Parties) have agreed to each leverage their existing resources and expertise, working with multiple public and private partners to further research and the

1 Biological marker (biomarker) is a characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention. Clin Pharmacol Ther 2001;69:89-95.

2 Medical Products includes drug and biological products and medical devices
development of pre-competitive diagnostic and assessment tools in cardiovascular disease to advance public health;

Whereas the private sector, including industry, academia, non-profit organizations and others have expressed interest in working with the Parties to further scientific exploration of cardiovascular biomarkers and associated technologies to enhance diagnostics and therapeutic development of medical products;

Now, therefore, the Parties agree to collaborate under the terms and conditions of this Memorandum of Understanding (MOU), through steering committees and technical working groups, to develop strategic plans, set priorities, and leverage resources and expertise from multiple sources, including the private sector, toward the goals of identifying indicators of cardiovascular risk, predicting adverse cardiovascular events associated with therapeutic interventions, improving the clinical utility of biomarker technologies as diagnostic and assessment tools that facilitate the development of safer and more effective cardiovascular therapies, diagnostic, and assessment tools. This MOU sets forth the framework for collaboration between the Parties and for pursuing specific collaborative projects that may involve additional partners and will be implemented through separate agreements, as needed. This collaboration between the Parties shall be known as the Cardiac Safety Research Consortium (CSRC). The Parties anticipate that ideas and concepts, from multiple sources, will be developed by the steering committees and technical working groups. Such concepts and ideas may lead to partnerships that will be approved by an Executive Committee (EC) and implemented through separate agreements.

The Parties agree as follows:

RESPONSIBILITIES OF THE PARTIES

To pursue the goals described above, the Parties agree to work through the process described below.

1. **Goals of CSRC.** The Parties will form public-private steering committees, technical working groups, and an Executive Committee (EC) to develop concepts for potential pursuit as a CSRC activity. Under the framework of this MOU, these collaborative efforts will be developed under separate agreements that specify policies, terms, and responsibilities of each party. The EC, steering committees, and technical working groups shall consider approaches for the development and application of diagnostic and/or clinical assessment tools or biomarker technologies that enhance diagnostic or therapeutic strategies for various forms of cardiovascular disease. Specific areas of scientific activities will include, but will not be limited to, the following:

   a. To create an ECG library from clinical trials that could be used for identifying early predictors of cardiac risk (Cardiac Risk ECG Library)
   b. To use the Cardiac Risk ECG Library to qualify new ECG biomarkers of cardiac risk;
   c. To use the Cardiac Risk ECG Library to create a set of ECG reference standards;
d. To develop additional research and regulatory evaluation tools to facilitate clinical
decision-making and future medical product development in the interest of public
health; and

e. To develop standards, nomenclature, and tools to facilitate and accelerate the
development of standards, and the evidence base for, new diagnostics and
assessment tools, and develop educational tools to make this information more
widely available to researchers, clinicians, and patients.

2. Steering Committees and Technical Working Groups. Each steering committee and
technical working group will be responsible for developing and prioritizing concepts,
developing feasibility plans for specific projects, preparing white papers on scientific
rationale, evaluating existing knowledge gaps and available technologies, addressing
general concepts in experimental design, preparing protocols to evaluate biomarkers in
clinical trials, developing milestones and outlining approaches for assessing progress.
Moreover, the steering committees and technical working groups will consider
development of standards, nomenclature, and tools to facilitate and accelerate the
development of, and evidence base for, new diagnostics, assessment tools, and medical
products. As a result of this process, the steering committees and technical working
groups will aim to increase the scientific knowledge base for cardiovascular disease and
public health. The steering committees and technical working groups will include
representatives from each Party as well as public and private partners and will meet or
teleconference monthly. The steering committees and technical working group chairs
will report to the EC, which will make the final decisions on projects that will be
implemented. A quarterly meeting (face-to-face or teleconference) of the steering
committees and working groups will be held to discuss progress, develop consensus on
working group activities, and foster communications and directions for facilitating the
project(s).

3. Priority Projects. Priority projects that emerge from the steering committees and
technical working groups will be publicized as areas of interest of the CSRC with the
intention of involving participation and input from public and private sector partners.
Through this process, the CSRC will seek to engage the private sector in the
implementation of the research. Numerous implementation strategies are anticipated and
available. These strategies may include the following:

- The FDA may perform certain research projects directly with DCRI or through other
collaborations through separate agreements.
- The private sector may perform projects directly, or may fund the research that may
be administered, managed, and facilitated through DCRI and governed by separate
agreements. To the extent that federal agencies are involved in the implementation of
any project, each agency is bound by all applicable federal statutes, regulations, and
policies and required to act within its statutory authority.3

---

3 To the extent that federal employees are involved in the implementation of specific projects, federal employee
participation will be governed by all applicable statutes, regulations, and policies on interactions with outside
organizations and reviewed for permissibility by the appropriate authority within the employee's agency on a case-
by-case basis.
• **Special Projects.** To the extent that implementation of specific projects involves working with the non-federal sector, the Parties will, consistent with all applicable statutes, regulations, policies, and their legal authorities facilitate dialogue with the appropriate potential collaborators or other partners of interest. Such interactions, facilitated and governed by separate agreements, may include a range of stakeholders, such as private non-profit organizations, industry, industry trade organizations, academic institutions, professional organizations, and patient advocacy groups.

**GENERAL PROVISIONS**

Proprietary and/or nonpublic information will not be disclosed under this MOU, unless such disclosure is governed by appropriate confidentiality disclosure agreements, or to the extent such disclosure is permitted by law.

Any notice or other communication required or permitted under this MOU will be in writing and will be deemed given as of the date it is received and accepted by the receiving party.

**CONTACTS**

Notices or formal communications pursuant to this MOU should be sent to:

For FDA: Wendy R. Sanhai, Ph.D.
Senior Scientific Advisor
Office of the Commissioner, FDA
5600 Fishers Lane, 14B-45, HZ-1
Rockville, MD. 20857
Phone: (301) 827-7867, Fax (301) 443-9718
wendy.sanhai@fda.hhs.gov

For DCRI: Christopher H. Cabell, M.D.
Assistant Professor of Medicine
Division of Cardiology
Department of Medicine
Duke University School of Medicine
DUMC Box 2705
Durham, NC 27705
Phone: 919-668-8611, Fax: 919-668-7066
chris.cabell@duke.edu

For Duke: Office of Research Administration
Duke University Medical Center
2424 Erwin Road, Suite 1103
Durham, North Carolina 27705
Phone: 919-684-5175, Fax: 919-684-6278
TERM, TERMINATION AND MODIFICATIONS

1. This MOU constitutes the entire agreement between the Parties pertaining to the CSRC.
2. There are no representations, warranties, agreements, or understandings, express or implied, written or oral, between the Parties hereto relating to the subject matter of this MOU that are not fully expressed herein.
3. No supplements, amendments, or modifications to this MOU will be binding unless executed in writing by the Parties; such modifications are to take the form of amendments.
4. This MOU, when accepted by the Parties, will have an effective date from date of the last to sign and will remain in effect for three (3) calendar years from the effective date, unless modified or terminated. Either Party may terminate this MOU upon sixty (60) days written notice.

Signatures begin on the following page
SIGNATURES OF RESPONSIBLE PARTIES

We, the undersigned, agree to abide by the terms and conditions of this MOU.

APPROVED AND ACCEPTED FOR:

FOOD AND DRUG ADMINISTRATION

Janet Woodcock, MD
Deputy Commissioner for Operations
U.S. Food and Drug Administration

Date 8/1/06

DUKE UNIVERSITY

R. Sanders Williams, MD
Dean, School of Medicine
Duke University

Date 8/15/06