VICTORIA – DATA SHARING CHARTER

Version 1.0 – 17-Jan-2019

Study Title:	A Randomized Parallel-Group, Placebo-Controlled, Double-Blind, Event-Driven, Multi-Center Pivotal Phase III Clinical Outcome Trial of Efficacy and Safety of the Oral sGC Stimulator Vericiguat in Subjects With Heart Failure With Reduced Ejection Fraction (HFrEF) *Ver*I*C*igua*T* gl*O*bal study in patients with heart failure and *R*educed eject*I*on fr*A*ction (VICTORIA)
Clinical Study Protocol No:	MK-1242
Date/Version of Charter:	Version 1.0 / January 17, 2019

The VICTORIA Executive Committee is fully committed to support additional scientific analyses based on the data collected in the VICTORIA Outcome Study. The roles and responsibilities of the VICTORIA Executive Committee in overseeing all scientific output(s) pursuant to the conduct of the VICTORIA trial is described in the VICTORIA Publication Committee Charter (PCC). This includes author responsibilities and the planning of primary and all subsequent manuscripts. The purpose of the Data Sharing Charter (DSC) is to describe the principles and process to provide potentially qualified external scientific researchers access to anonymized patient-level data from the VICTORIA study for conducting legitimate additional scientific research. This DSC provides the context of the ICMJE position on clinical trial data sharing. (NEJM June 8 2017 appended (Appendix 1) The data analysis process for VICTORIA will follow the following, general operating principles:

- The Study Executive Committee (EC), National Country Leaders (NLs), Study team, and investigators who have generated the clinical trial data constitute the highest priority
- The Publication Committee (PC) will develop a list of pre-specified secondary and tertiary ancillary manuscripts in advance of unblinding of the primary data set. Additional manuscripts are expected to be undertaken soon after the primary result is known. A list of such topics already planned will be similarly posted on a publicly available website. These manuscripts will be developed by the EC, NLs, and Investigators related to the VICTORIA Study.
- The Publication Committee will consider external data sharing requests for additional topics not already pursued by the EC, NLs, or investigators
- The protocol and final SAP will be available as customarily required by the Journal in which the primary manuscript is published and as required under the US FDA Amendment Act and also posted on a publicly available website.

The VICTORIA EC recognizes that data sharing principles and processes are evolving. Hence, the procedure outlined here is subject to updates as appropriate based on the PC's experience and their interpretation of the recommendations of learned external advisory groups evaluating this issue.

Eligibility

- Qualified researchers with appropriate competencies, engaged in rigorous, independent scientific research can submit a data request, for patient-level data with a research proposal to the VICTORIA PC for review. The request will require an accompanying signed data-sharing agreement prior to receiving access to clinical trial data. The research team must include a biostatistician and address potential conflicts of interest. Proposals involving predictive biomarkers should include a pre-specified hypothesis with an accompanying statistical power calculation. Studies proposing de novo biomarker discovery must include descriptions of independent training and validation sets.
- Conflict of interest will be assessed; data will not be released to individuals with significant conflict of interest or individuals requesting data access for competitive, commercial or legal interests.

- Funding requests are not supported under this procedure.

Application Process

Research proposals must be submitted through the publicly available website and must adhere to the requirements for the submission process. The following basic information will be required:

i. Detailed Research proposal which includes:
   a. Background and rationale
   b. Objectives of the research
   c. Scientific Hypothesis
   d. Statistical analysis plan
   e. Publication Plan
ii. Curricula Vitae of all researchers including the biostatistician

Scope of Data

The PC will provide access to patient-level data two years after clinical trial completion and publication of primary results manuscript.

Review Process

Completed applications will be reviewed by the PC. Researchers will receive an acknowledgement of receipt. Once the request is assessed for feasibility, the PC will assess the scientific validity of the request and the qualifications of the requesters. If the PC review determines that the request is i] scientifically valid ii] not redundant with research questions already under analysis by the EC, NLs, or investigators or other approved requests, and iii] the requesters are free of conflict of interest and have the appropriate expertise to perform the proposed analysis then the request will be approved and data will be shared.

Review Criteria

- Does the proposal contain a clearly defined research question, scientific rationale and relevance of the proposed research to medical science or patient care?
- Is there a well-documented statistical analysis plan?
- For correlative biomarker research, is there a clearly specified and biologically plausible hypothesis, and appropriate training and validation sets where de novo discovery work is anticipated?
- Is there an ability of the proposed research plan (design, methods and analysis, statistical power) to meet the scientific objectives?
- Is there an adequate publication plan for the dissemination of the research?

- Is the research applicant willing to disclose any real or potential conflicts of interest that may impact the planning, conduct or interpretation of the research?
- Does the research team have the expertise, qualifications and experience to conduct the proposed research (e.g., does it include a biostatistician as part of the research team)?
- Particular attention will be made to ensure the proposals are distinct from the pre-planned subsidiary analyses of the parent study.

Data Sharing Agreement

Prior to access to clinical trial data, the researcher must enter into a standard data sharing agreement with the PC. The data sharing agreement commits the researcher to use the data only for the stated research purposes and not to disclose the data to third parties. This is in line with data privacy legislation. In addition, researchers are expected to commit to transparency in the publication of their work.

i. The data sharing agreement also includes an expectation for the outcome of the analysis (e.g. manuscript draft, abstract) to be shared with the PC prior to submission to a journal or conference. The PC reserves the right to review any subsequent data outcomes and proposed manuscript(s) and authorship

Anonymization of Data

Protecting the privacy of patients who participate in clinical trials is an important obligation of sponsors who conduct clinical trials and therefore the PC and study sponsor will take appropriate measures, including anonymization of data, to ensure that patient privacy is safeguarded.

Signatures

The undersigned confirm they agree with the conditions described in this charter:

Study Chair on behalf of the Executive Committee

	Prof. Paul W. Armstrong, MD
Signature	
Date	January 17, 2019

Co-Principal Investigators

	Prof. Christopher O'Connor, MD
Signature	
Date	January 21, 2019
	Prof. Burkert Pieske, MD
Signature	
Date	23. January 2019

Representative of Merck (Sponsor) and Bayer

	Joerg Koglin, MD
Signature	
Date	January 18, 2019
	Lothar Roessig, MD
Signature	
Date	January 21, 2019

APPENDIX 1

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIALS

Data Sharing Statements for Clinical Trials — A Requirement of the International Committee of Medical Journal Editors

The International Committee of Medical Journal Editors (ICMJE) believes there is an ethical obligation to responsibly share data generated by interventional clinical trials because trial participants have put themselves at risk. In January 2016 we published a proposal aimed at helping to create an environment in which the sharing of deidentified individual participant data becomes the norm. In response to our request for feedback we received many comments from individuals and groups.[1] Some applauded the proposals while others expressed disappointment they did not more quickly create a commitment to data sharing. Many raised valid concerns regarding the feasibility of the proposed requirements, the necessary resources, the real or perceived risks to trial participants, and the need to protect the interests of patients and researchers.

It is encouraging that data sharing is already occurring in some settings. Over the past year, however, we have learned that the challenges are substantial and the requisite mechanisms are not in place to mandate universal data sharing at this time. Although many issues must be addressed for data sharing to become the norm, we remain committed to this goal.

Therefore, ICMJE will require the following as conditions of consideration for publication of a clinical trial report in our member journals:

1. As of July 1, 2018, manuscripts submitted to ICMJE journals that report the results of clinical trials must contain a data sharing statement as described below.

2. Clinical trials that begin enrolling participants on or after January 1, 2019, must include a data sharing plan in the trial's registration. The ICMJE's policy regarding trial registration is explained at www.icmje.org/recommendations/browse/publishing-and-editorial-issues/clinical-trial-registration.html. If the data sharing plan changes after registration this should be reflected in the statement submitted and published with the manuscript, and updated in the registry record.

Data sharing statements must indicate the following: whether individual deidentified participant data (including data dictionaries) will be shared; what data in particular will be shared; whether additional, related documents will be available (e.g., study protocol, statistical analysis plan, etc.); when the data will become available and for how long; by what access criteria data will be shared (including with whom, for what types of analyses, and by what mechanism). Illustrative examples of data sharing statements that would meet these requirements are in the Table.

These initial requirements do not yet mandate data sharing, but investigators should be aware that editors may take into consideration data sharing statements when making editorial decisions. These minimum requirements are intended to move the research enterprise closer to fulfilling our ethical obligation to participants. Some ICMJE member journals already maintain, or may choose to adopt, more stringent requirements for data sharing.

Sharing clinical trial data is one step in the process articulated by the World Health Organization (WHO) and other professional organizations as best practice for clinical trials: universal prospective registration; public disclosure of results from all clinical trials (including through journal publication); and data sharing. Although universal compliance with the requirement to

Table 1. Examples of Data Sharing Statements That Fulfill These ICMJE Requirements*

	Example 1	Example 2	Example 3	Example 4
Will individual participant data be available (including data dictionaries)?	Yes	Yes	Yes	No
What data in particular will be shared?	All of the individual participant data collected during the trial, after deidentification.	Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures, and appendices).	Individual participant data that underlie the results reported in this article, after deidentification (text, tables, figures and appendices).	Not available
What other documents will be available?	Study Protocol, Statistical Analysis Plan, Informed Consent Form, Clinical Study Report, Analytic Code	Study Protocol, Statistical Analysis Plan, Analytic Code	Study Protocol	Not available
When will data be available (start and end dates)?	Immediately following publication. No end date.	Beginning 3 months and ending 5 years following article publication.	Beginning 9 months and ending 36 months following article publication.	Not applicable
With whom?	Anyone who wishes to access the data.	Researchers who provide a methodologically sound proposal.	Investigators whose proposed use of the data has been approved by an independent review committee ("learned intermediary") identified for this purpose.	Not applicable
For what types of analyses?	Any purpose.	To achieve aims in the approved proposal.	For individual participant data meta-analysis.	Not applicable
By what mechanism will data be made available?	Data are available indefinitely at (*link to be included*).	Proposals should be directed to xxx@yyy. To gain access, data requestors will need to sign a data access agreement. Data are available for 5 years at a third party website (*link to be included*).	Proposals may be submitted up to 36 months following article publication. After 36 months the data will be available in our University's data warehouse but without investigator support other than deposited metadata. Information regarding submitting proposals and accessing data may be found at (*link to be included*).	Not applicable

* These examples are meant to illustrate a range of, but not all, data sharing options.

prospectively register clinical trials has not yet been achieved and requires continued emphasis, we must work toward fulfilling the other steps of best practice as well — including data sharing.

As we move forward into this new norm where data are shared, greater understanding and collaboration among funders, ethics committees, journals, trialists, data analysts, participants, and others will be required. We are currently working with members of the research community to facilitate practical solutions to enable data sharing. The United States Office for Human Research Protections has indicated that provided the appropriate conditions are met by those receiving them, the sharing of deidentified individual participant data from clinical trials does not require separate consent from trial participants.[2] Specific elements to enable data sharing statements that meet these requirements have been adopted at ClinicalTrials.gov (https://prsinfo.clinicaltrials.gov/definitions.html#shareData). The WHO also supports the addition of such elements at the primary registries of the International Clinical Trials Registry Platform. Unresolved issues remain, including appropriate scholarly credit to those who share data, and the resources needed for data access, the transparent processing of data requests, and data archiving. We welcome creative solutions to these problems at www.icmje.org.

We envision a global research community in which sharing deidentified data becomes the norm. Working toward this vision will help maximize the knowledge gained from the efforts and sacrifices of clinical trial participants.

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Editor-in-Chief, *BMJ (British Medical Journal)*

Frank A. Frizelle, M.B., Ch.B., F.R.A.C.S.
Editor-in-Chief, *New Zealand Medical Journal*

Fernando Florenzano, M.D.
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Jeffrey M. Drazen, M.D.
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Howard Bauchner, M.D.
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Editor's note: This editorial is being published simultaneously in *Annals of Internal Medicine*, *BMJ (British Medical Journal)*, *Bulletin of the World Health Organization*, *Deutsches Ärzteblatt (German Medical Journal)*, *Ethiopian Journal of Health Sciences*, *JAMA (Journal of the American Medical Association)*, *Journal of Korean Medical Science*, *New England Journal of Medicine*, *New Zealand Medical Journal*, *PLOS Medicine*, *The Lancet*, *Revista Médica de Chile (Medical Journal of Chile)*, and *Ugeskrift for Laeger (Danish Medical Journal)*.

Disclaimer: Dr. Sahni's affiliation as representative and past president of the World Association of Medical Editors (WAME) does not imply endorsement by WAME member journals that are not part of the ICMJE.

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2. Menikoff J. Letter from Jerry Menikoff, M.D., J.D., Director, Office for Human Research Protections, to ICMJE Secretariat. March 7, 2017 (http://www.icmje.org/).

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