NIAID Bethesda, MD USA	**POLICY**	Version No: 3.0 Date: May 4, 2009 Page 1 of 8
	Effective Date: July 2, 2009 Release Date: June 18, 2009	

Title: **NIAID POLICY ON DATA AND SAFETY MONITORING BOARD (DSMB) OPERATIONS**

APPROVAL

	Approving Entity	**Date**
Approval Mechanism:	***NIAID Executive Committee (ExCom)***	***May 28, 2009***

1.0 PURPOSE

1.1 This policy establishes requirements for the operations of Data and Safety Monitoring Boards within the NIAID.

2.0 BACKGROUND

2.1 NIH policy requires data and safety monitoring for all NIH-funded clinical trials. Since the policy issuance, Divisions within the Institute have each established policies, procedures, and guidelines to implement and comply with the general NIH policy. Although some program variances may be appropriate/necessary, a proposal for some harmonization of key issues across Divisions was put forth at the 2005 NIAID Winter Program Retreat. A Working Group representing all Divisions collected and analyzed data on Data and Safety Monitoring Board practices. This policy specifies those operational requirements for DSMBs that are mandatory across the Institute.

3.0 DEFINITIONS

3.1 Data and Safety Monitoring Board (DSMB)

"Data and safety monitoring board" refers to a committee of experts, independent of the trial investigators, pharmaceutical sponsor (if any), and funding agency, that periodically reviews the conduct and results of the trial and recommends continuation without change, continuation with change, or termination of the trial. (To avoid confusion, the name "data and safety monitoring board" should only be used for structures as described herein.)

3.2 DSMB Convening Authority

"DSMB convening authority" is the single entity with authority and responsibility to act upon the recommendations of the Data and Safety Monitoring Board.

4.0 TRIALS REQUIRING A DSMB

Clinical trials requiring DSMB oversight are randomized, multi-center trials that are large Phase II, are Phase III, or are Phase IV, plus all Division of Intramural Research (DIR)

randomized, double-blind trials regardless of size or phase of trial. The NIAID Division Directors, Clinical Director or IRB may designate other trials for DSMB oversight for specific programmatic reasons.

5.0 RESPONSIBILITIES

5.1 Policy Dissemination and Compliance

Division Directors are responsible for the dissemination of this policy to all staff and outside collaborators, if applicable, involved in DSMB oversight and operations. Division Directors must also have procedures in place within their Divisions to ensure compliance with this policy.

5.2 Policy Revisions /Update

The Division of Clinical Research (DCR), in coordination with the NIAID Clinical Research Subcommittee (NCRS), will be responsible to review and propose revisions to this policy as needed based on new/revised NIH policy or federal regulations. Section 11 of this policy establishes the frequency for mandatory review intervals. The NIAID Executive Committee must approve any revisions to this policy for them to take effect.

5.3 Policy Exceptions

The NIAID Deputy Director for Clinical Research and Special Projects must approve any exceptions to this policy, including cases where NIAID is not the DSMB convening authority.

6.0 OPERATIONS

6.1 DSMB Charter

Each DSMB must operate according to provisions of a formal charter, agreed to in advance by NIAID, the investigators, and the DSMB. Charters should address appointment of members, terms of appointment, scheduling and format of meetings, quorum requirements, distribution and disposition of meeting materials,

preparation of meeting summaries and written recommendations, management of conflict of interest, and other procedural matters.

6.2 DSMB Membership

DSMBs must consist of at least three voting members including a biostatistician experienced in statistical methods for clinical trials and a clinician with relevant expertise. Representatives of other clinical or laboratory specialties, bioethics, and the affected community are often critically important. Selection of DSMB members should include consideration of clinical trials experience, relevant expertise, prior DSMB service and absence of significant conflict of interest. When NIAID is the DSMB convening authority, NIAID staff will appoint members. DSMB membership should reflect NIAID's commitment to diversity.

6.3 Timing of Protocol Presentation to DSMB

It is best to introduce the trial to the DSMB before beginning enrollment. The DSMB should understand, before seeing interim results, how the investigators want to approach the possibility of early stopping for safety, futility, efficacy, and/or ethical reasons.

6.4 Access to Closed Safety and Efficacy Data

The hallmark of oversight by a DSMB is a strict limit on access to interim results, including results according to study arm. This applies to both safety and efficacy results. Comparative results are presented to the DSMB in closed reports and closed sessions are attended only by voting members of the DSMB and one member of the NIAID staff or contractor serving as DSMB executive secretary (apart from the statistician who prepared the reports, who may in some instances be an NIAID employee or contractor). These provisions will not limit the ability of the DSMB to invite any person to participate in any part of the meeting if it believes the person has important information or knowledge that will assist the DSMB in fulfilling its responsibilities. Exceptions to restricted access to closed report interim results, which should be rare, are addressed below.

If information from ongoing review of individual adverse event reports and summaries, or emerging information external to the trial raises concern about safety of current or future trial participants, the Division Director may authorize an

individual to receive closed safety data (in a manner that minimizes unblinding) and to attend the closed DSMB session addressing safety data. Division Directors are strongly encouraged to consult with the DSMB chair before approving a request.

6.5 DSMB Recommendations – Routing/Response

DSMB summary recommendations are reported to the DSMB convening authority who then submits them to the study chair and Program Director (or designee). The DSMB's convening authority's responsible official makes the final decision to accept them or not, after consulting with the trial leadership and relevant staff. A decision to reject a recommendation should be communicated to the DSMB with appropriate rationale.

Site investigators receive final DSMB meeting summaries and submit to their Institutional Review Boards (IRBs)/Ethics Committees (ECs).

7.0 REFERENCES/LINKS

7.1 Supersedes: Policy Version 2.0 (November 20, 2007)

7.2 The below online information is current as of the effective date of this policy.

NIH POLICY FOR DATA AND SAFETY MONITORING (June 10, 1998)
http://grants.nih.gov/grants/guide/notice-files/not98-084.html

GUIDANCE ON REPORTING ADVERSE EVENTS TO INSTITUTIONAL REVIEW BOARDS FOR NIH-SUPPORTED MULTICENTER CLINICAL TRIALS (June 11, 1999)
http://grants1.nih.gov/grants/guide/notice-files/not99-107.html

FURTHER GUIDANCE ON A DATA AND SAFETY MONITORING FOR PHASE I AND PHASE II TRIALS (June 5, 2000)
http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-038.html

Guidance for Clinical Trial Sponsors: Establishment and Operation of Clinical Trial Data Monitoring Committees
http://www.fda.gov/RegulatoryInformation/Guidances/ucm127069.htm

7.3 Other References:

DeMets, DL, Furberg, CD, Friedman, LM (editors) (2006) *Data Monitoring in Clinical Trials: A Case Studies Approach*. Springer, New York.

Ellenberg, SS, Fleming, TR, DeMets, DL (2003) *Data Monitoring Committees in Clinical Trials.* John Wiley & Sons Ltd, West Sussex, England.

Herson, Jay (2009) *Data and Safety Monitoring Committees in Clinical Trial*s, Taylor and Francis Group, Boca Raton, FL.

8.0 INQUIRIES/CONTACT INFORMATION

8.1 For questions or comments please contact NCRSexec.sec.@niaid.nih.gov

9.0 AVAILABILITY

9.1 This policy is available on the DCR website. Hard copy documents are filed in the DCR office.

10.0 ATTACHMENTS

10.1 Attachment A – List of Working Group Members

11.0 REVIEW SCHEDULE/CHANGE SUMMARY

11.1 This policy will be reviewed at least every two years. Interim revisions will be made as needed to comply with NIH or other federal regulatory changes and/or at the request of the DCR Director.

11.2 The change summary table below will be updated when the document is reviewed or revised.

Version #	Date	Replaces	Date of Review/Revision	Rationale for Revision/ Retirement
2.0	11/20/07	1.0	11/20/07	Clarification enhancements; addition of procedures for access to closed safety data and new special exceptions for data access
3.0	5/04/09	2.0	5/04/09	Overall simplification of content; Title change; deletion of specific case example; new definitions section; additional charter requirements; minimum # of members established; review interval changed to every 2 years

ATTACHMENT A

DSMB Principles Document Working Group (2008)
Member List

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