

**Official Charter of the
Independent Study Monitoring and Oversight
Committee (iSMOC) for the
National Children's Study (NCS)**

11 August 2009

Version 2.00



Committee Chairperson Name

Committee Chairperson Signature

Date

The *Eunice Kennedy Shriver* National Institute of Child Health and Human
Development (NICHD)
National Institute of Health (NIH)

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Independent Study Monitoring and Oversight Committee (iSMOC) Charter for the National Children’s Study (NCS)

I. Introduction

This Charter is for the independent Study Monitoring and Oversight Committee (iSMOC) for the National Children’s Study.

This charter is a living document and will be reviewed at least annually by the iSMOC to determine whether changes in procedure are needed throughout the duration of the study. All finalized and approved versions to this document are tracked in Table 1 (below) and will be numbered as whole numbers (e.g. 2.0, 3.0, etc.).

Table 1: Independent Study Monitoring and Oversight Committee (iSMOC) Charter version updates

Version Number	Date Need for Change Was Identified	Details of Change	Date Change was Finalized
2.0	8 June 2009	<p style="text-align: center;">Section II:</p> <ol style="list-style-type: none"> 1. Add a responsibility to Table 2 that stipulates: Review of controversial/sensitive analyses referred by Publications subcommittee or NCS Director in terms of the interpretation of data prior to presentation/publication. 2. Addition of the word communities to the phrase: “unanticipated problems involving risks to subjects or others” <p style="text-align: center;">Section III:</p> <ol style="list-style-type: none"> 3. Change 4) from “the absence of any conflict of interest” to “the absence of any undisclosed conflict of interest” <p style="text-align: center;">Section IV:</p> <ol style="list-style-type: none"> 4. Change terms of service (Table 4) to reflect initial terms of service as either 3, 4, or 5 years. During the first three years of the committee, three years of service will be the minimum term, with the possibility of extension. <p style="text-align: center;">Section V:</p> <ol style="list-style-type: none"> 5. Change section to clarify that NIH members serving on iSMOC are not compensated. <p style="text-align: center;">Section VI:</p> <ol style="list-style-type: none"> 6. Change section to reflect discussed changes in meeting frequency for first year. Section will be altered to reflect a minimum of 2 in-person and 2 teleconference meetings of all iSMOC members for this year. The next in- 	

		<p>person meeting will be held in November, 2009.</p> <p>7. Move language detailing initial meeting responsibilities, tasks, and details into a memo on that subject leaving only ongoing responsibilities outlined in charter.</p> <p style="text-align: center;">Appendix C:</p> <p>8. Change statement “I will retain any confidential documentation until the conclusion of my term of service on the iSMOC” to I may retain access to any confidential documentation until the conclusion of my term of service on the iSMOC”</p>	
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Each member of the iSMOC must agree to the terms outlined in this charter. Each member will sign the *Acceptance of iSMOC Terms and Conditions*, *Conflict of Interest Statement* and the *Confidentiality Agreement* to demonstrate this agreement. Once this charter is finalized, it is to be reviewed at an iSMOC meeting, signed by all members, and the signed copies will be provided to the NICHD Executive Secretary, for the study.

II. Purpose and Responsibilities of the iSMOC

The members of the iSMOC identified in this Charter for the National Children’s Study are responsible to:

- a) monitor human subject safety through review and evaluation of accumulated study data,
- b) review study conduct and progress, and
- c) make recommendations concerning continuation or modification of the National Children’s Study.

This Committee will serve as an independent advisory group to the Director of NICHD, and is required to provide recommendations about starting, continuing, and stopping the National Children’s Study.

Confidentiality shall be maintained during all phases of iSMOC review and deliberations.

The iSMOC of the National Children’s Study will review the study protocol and identify any major concerns prior to implementation or as soon thereafter as possible. During the study, the iSMOC will review:

- data regarding procedure-related adverse events,
- unanticipated problems involving risks to subjects, communities, or others,
- adherence to the protocol,
- factors that might affect study outcome or compromise study data (e.g., protocol violations, losses to follow-up, breach of subject confidentiality), and,

- barriers to study progress or completion (e.g., slow enrollment, new data or findings, other milestones, change in resources, rate of endpoint accumulation).

The iSMOC will determine appropriateness of notification and referral of individual participants for significant abnormal findings on testing of stored samples.

The Committee will be responsible for identifying mechanisms to complete various tasks that will impact the safety and efficacy of all study procedures, and overall conduct. Table 2 identifies the key areas where oversight is necessary and the ways in which the Committee for the National Children’s Study will complete those tasks.

Table 2: Basic responsibilities of the NCS iSMOC

Basic Responsibility of iSMOC	Method the National Children’s Study iSMOC will use to complete task
Familiarize themselves with the study protocol	CC will provide members with protocol as developed/modified
Monitor adverse events	CC will provide reports to the Committee quarterly or as needed for unscheduled review.
Monitor data quality	CC will provide reports to the Committee quarterly or as needed for unscheduled review.
Oversee participant recruitment and enrollment	CC will provide reports to the Committee quarterly or as needed for unscheduled review.
Develop an understanding of the Study’s risks and benefits	CC will provide reports to the Committee quarterly or as needed for unscheduled review.
Monitor that the proper reporting occurs (e.g., OHRP, IRBs, etc.)	CC will provide reports to the Committee quarterly or as needed for unscheduled review.
Review of controversial/sensitive analyses in terms of the interpretation of data prior to presentation/publication	Publications Subcommittee or NCS Director will refer material as needed for unscheduled review.

III. iSMOC Members, Organizational Chart, & Communications

Members

The iSMOC for the National Children's Study is comprised of a chair and 12 members from the areas listed in Table 3. In addition, their roles and responsibilities are identified in the table.

Requirements for membership include; 1) relevant expertise, 2) experience conducting clinical observational, epidemiological or environmental studies and statistical knowledge, 3) independence from any direct management of the study, and 4) the absence of any undisclosed conflict of interest.

Only voting members, invited guests and NICHD program members of this iSMOC may attend closed sessions of this Committee.

In addition, this iSMOC will include an Executive Secretary (ES) to provide an unbiased staff interface for the iSMOC, especially during executive sessions. The ES is responsible for assuring the accuracy and timely transmission of the final recommendations and iSMOC minutes.

The Executive Secretary will be a Non-voting Member

Until such time that an ES can be appointed by the NICHD Director, John Moye, M.D., will serve as the interim ES.

Executive Subcommittee

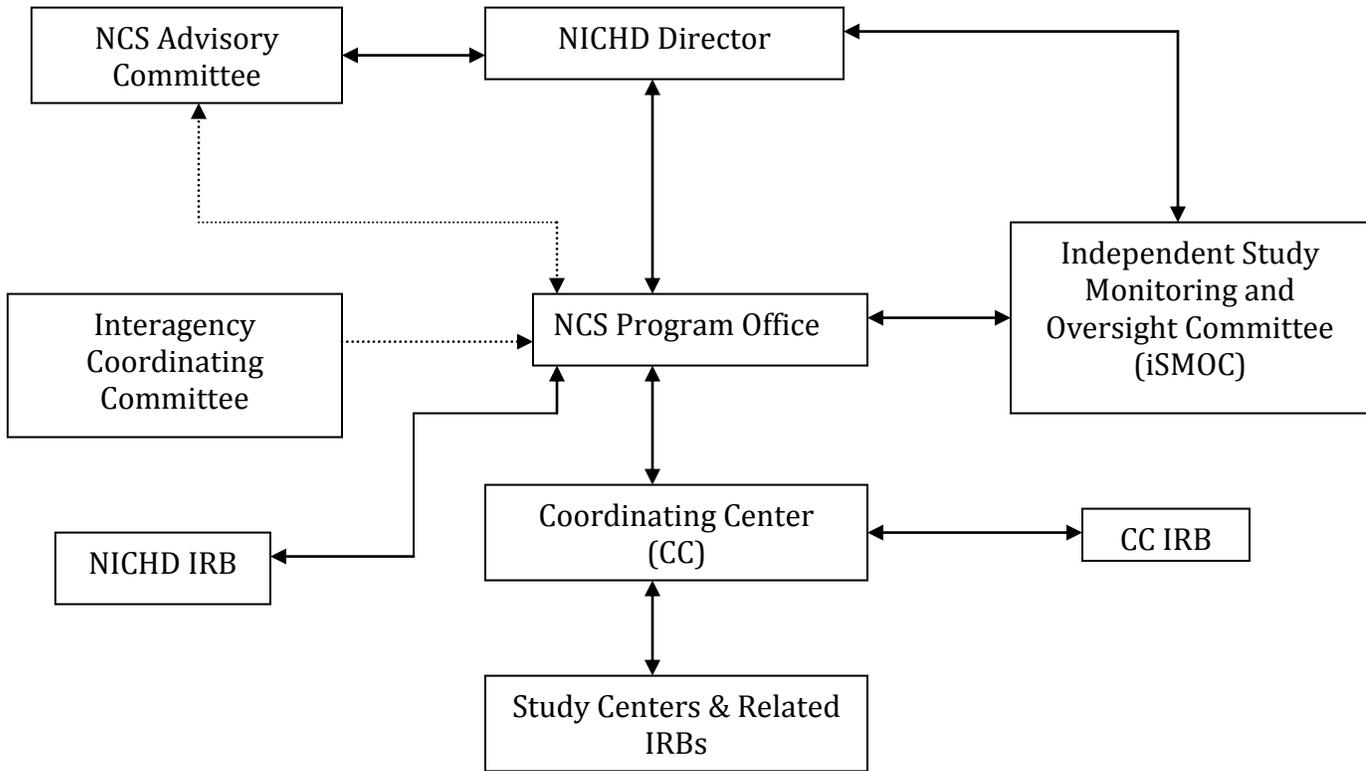
The Executive Subcommittee will consist of the iSMOC Chair, the ES, representatives from the NICHD Program Office and the Coordinating Center. The Executive Subcommittee will meet and communicate on a regular basis between iSMOC meetings to discuss business relevant to the National Children's Study.

Table 3: Members comprising iSMOC and their roles and responsibilities

Name of Member	Role on iSMOC	Responsibilities
Chair	Lead iSMOC meetings	Lead iSMOC meetings Provide direction for the committee and agenda Determine meeting type Review and approve summary and formal minutes before distribution
Ethicist	Voting member	Represent area of expertise
Study participant representative	Voting member	Represent area of expertise
Community representative	Voting member	Represent area of expertise
Environment/Toxicology	Voting member	Represent area of expertise
Epidemiology/Prevention	Voting member	Represent area of expertise
Geneticist	Voting member	Represent area of expertise
Obstetrician	Voting member	Represent area of expertise
Pediatrician	Voting member	Represent area of expertise
Social Health	Voting member	Represent area of expertise
Statistician	Voting member	Represent area of expertise
Developmental Psychology	Voting member	Represent area of expertise
Maternal/Child Health	Voting member	Represent area of expertise
Executive Secretary	Non-voting member	Assures accuracy and timely transmission of final recommendations; writes, prepares and disseminates meeting minutes; distributes meeting agenda and teleconference information.
Coordinating Center	Non-voting member	Presents information for the data to be reviewed and other study information as necessary.

Organizational Chart

The following diagram illustrates the relationship between the iSMOC and other entities in the National Children’s Study.



Communication

Communication to members of this iSMOC will be primarily through the NCS web-portal. Investigators from the National Children’s Study will not communicate directly with the iSMOC members about the study, except when making presentations or responding to questions at iSMOC meetings or during scheduled conference calls.

IV. Term of Service

Service on the NCS iSMOC will consist of four – year terms with staggered expiration dates. Because the iSMOC is just beginning, the terms of service for each member are itemized in Table 4. Members of the iSMOC are appointed by and serve at the discretion of the NICHD Director.

iSMOC members will serve terms of four years each; the terms are staggered so that approximately one-third of the seats will be renewed at any given time. This was achieved by dividing the iSMOC members into three groups, where the terms of each group expires after the first three years, and so on (see Appendix D). Should an iSMOC member resign their duties, the replacement will fulfill the remaining term of

the seat and then upon renewal, commit to a four year term. Upon conclusion of a member’s term of service, re-appointment is at the discretion of the NICHD Director.

Table 4: Term of service for each member

iSMOC Member Seats	Group	Initial term of service	First year for new member
Chair	III	5 years	2014
Ethicist	II	4 years	2013
Study participant representative	I	3 years	2012
Community representative	III	3 years	2012
Environment/Toxicology	II	5 years	2014
Maternal/Child Health	I	4 years	2013
Epidemiology/Prevention	III	3 years	2012
Geneticist	II	3 years	2012
Obstetrician	I	5 years	2014
Pediatrician	III	4 years	2013
Social Health	II	3 years	2012
Statistician	I	3 years	2012
Developmental Psychology	III	5 years	2014

V. Conflict of Interest (COI) and Compensation

It is extremely important that all members of the iSMOC state any real or apparent conflicts of interests at the onset of the study. Members of the iSMOC shall read the NICHD Clinical Research Guidance Document regarding Conflicts of Interest and provide their signed summary of any COI to the Executive Secretary, for the study, at the onset of their membership to the iSMOC. A table summarizing any COI within the iSMOC is provided in Table 5.

Table 5: Conflict of interest information

iSMOC Member Name	Date Submitted Signed COI Policy	Was a potential COI identified?	Will the Member Remain part of the Committee?

Prior to each meeting, all members of the National Children’s Study iSMOC will have an opportunity to state whether they have developed any new conflicts of interest since the previous meeting. As a new COI is identified it must be documented in the above table and a new, signed summary of the COI should be provided to the Executive Secretary for the Study.

If a new conflict is reported, the NICHD will determine if the conflict limits the ability of the iSMOC member to participate in discussions.

All iSMOC members (excluding Federal Government members) will be compensated for their role in supporting the committee. Compensation will include the standard NIH reimbursement for service on such committee's and for review of materials pertinent to the committee. Currently (June 2009) the rate of reimbursement is approximately \$200 per day. If travel is required to attend an in-person meeting, NIH will coordinate travel and pay the iSMOC member the per diem rate at the time of travel for the travel dates.

Members of the iSMOC will be required to sign the *Acceptance of iSMOC Terms and Conditions, Conflict of Interest and Confidentiality Agreement* annually.

VI. Scheduling, Quorum, & Organization of Meetings

Once all members had been recruited and agreed to participate as NCS iSMOC members, the committee held its first in-person meeting on June 8, 2009.

During the first meeting, the iSMOC determined the following logistics for meetings (both in person and teleconferences). During its initial year, the full iSMOC will meet for a minimum of two in-person meetings and two teleconference meetings. The next in-person meeting will be held in November, 2009. The schedule of the proposed meetings and whether these meetings will be in person or via teleconference will be documented and distributed to the iSMOC members, the NICHD Program office, and the CC.

It is expected that all iSMOC members that are identified in Table 3 will make every attempt to attend each meeting. However, it is recognized that this may not always be possible. Therefore, the iSMOC for the National Children's Study has established the following quorum for voting. A quorum of this iSMOC for the National Children's Study is considered to be seven of the voting members. Quorum must be reached in order for an item to be voted on.

VII. Materials and Protocol for iSMOC Meetings

In consultation with NICHD and CC staff, the Executive Secretary will draft and distribute the iSMOC meeting agenda and call information. The iSMOC Chair will review the finalized agenda prior to distribution to the members.

The agenda and meeting materials will be distributed to the iSMOC by the CC one week before each meeting or call, to allow members adequate time to prepare for the meeting. Meeting materials will include the following reports and data:

- General Overview & Update

- Enrollment data
- Quality and completeness of study data
- Adverse event data
- Other safety data
- Reporting results

The iSMOC members will review the above information prior to each meeting and discuss necessary information to ensure proper conduct of the Study.

Meeting Protocol

iSMOC meetings and calls for the National Children’s Study will be organized into open, closed and executive sessions. Definitions for each type of session are included below. The sessions will be classified into one of three types in accordance with the listing below by the ES in consultation with NICHD and the CC prior to providing the iSMOC Chair with the meeting agenda.

- **Open sessions:** Information will be presented to the iSMOC by the CC, study investigators and NICHD staff as appropriate, with time for discussion.
- **Closed sessions:** the iSMOC, CC, and NICHD staff will discuss confidential data from the study, including information on efficacy and safety.
 - a. If the closed session occurs on a conference call, steps will be taken to ensure that only the appropriate participants are on the call, and to invite others to re-join the call only at the conclusion of the closed session.
- **Executive sessions:** Only the iSMOC members and NICHD Executive Secretary (ES) are present to discuss study issues independently.
 - a. If the executive session occurs on a conference call, steps will be taken to ensure that only the appropriate participants are on the call, and to invite others to re-join the call at the conclusion of the executive session.

At the conclusion of the closed and executive sessions, all participants will re-convene so that the iSMOC Chair can provide a summary of the iSMOC’s recommendations. This provides an opportunity for study investigators, the CC, and NICHD to ask questions to clarify the recommendations. If there is no further discussion, the meeting will then be adjourned.

VIII. Reporting Requirements for the National Children’s Study iSMOC

Records will be generated from each of the iSMOC meetings to ensure there is documentation of any and all decisions and recommendations. The documentation that will be gathered for iSMOC meetings for the National Children Study includes the following:

- **Initial summary:** The NICHD ES is responsible for assuring the accuracy and transmission of a brief summary of the iSMOC's discussion and recommendations. The discussion and recommendations will be reviewed within 48 hours of the meeting or call by the NCS iSMOC Chair before being forwarded to the NICHD Director. The Director, or designee, will review this summary and approve or disapprove the recommendation(s), or request additional information. The recommendations will then be sent to the CC, and the clinical investigators.
- **Formal minutes:** The NICHD ES is responsible for the accuracy and transmission of the formal iSMOC minutes for the Director and NICHD, within 30 days of the meeting or call. These minutes are subject to FOIA requests and are prepared accordingly to summarize the key points of the discussion and debate, requests for additional information, response of the investigators to previous recommendations, and the rationale for recommendations from the current meeting. These minutes will be reviewed by the iSMOC members, NICHD staff, key study personnel and the CC before being forwarded to the iSMOC Chair for final review and approval. The iSMOC Chair may sign the minutes or indicate approval electronically via e-mail. Then, the minutes are sent back to the CC and the relevant investigators, and included in the materials for the subsequent iSMOC meeting to be approved by voice vote at that meeting. Once they have been voted on and approved by the Committee, they will be considered Final.
- **Action plan:** If the iSMOC's recommendations require significant changes or follow-up, NICHD staff and the CC will collaborate to prepare an action plan outlining the steps required to implement the recommendations. The action plan will be reviewed by the Committee and by NICHD staff and will then be distributed to key study personnel, before being forwarded to the iSMOC Chair for final review and approval.

IX. Reports of iSMOC Proceedings for IRBs

This Committee is required to submit reports to IRBs at each of the participating sites.

If the iSMOC does not identify any safety or other protocol-related concerns, within 30 days after an iSMOC meeting, the ES in consultation with the NICHD Program Office will prepare a Summary Report that will state that:

- A review of outcome data, adverse events, and information relating to study performance (for example, data timelines, completeness, and quality) across all centers took place on [INSERT DATE OF MEETING]; the observed frequency of adverse events did not exceed what was expected and indicated in the informed consent;
- A review of recent literature relevant to the research took place and;
- The iSMOC recommended that the study continue without modification of the protocol or informed consent.

If concerns are identified, the report to the clinical centers will outline the concerns, the iSMOC discussion of the concerns, and the basis for any recommendations that the iSMOC has made in response to the concerns.

The report will be distributed by the CC to each clinical center involved in this Study. It is the responsibility of each Study Center to forward this information to the local IRB.

Appendix A

Acceptance of iSMOC Terms and Conditions

I, _____, a member of the Independent Study Monitoring and Oversight Committee (iSMOC) for the National Children's Study, attest that I have read and understand the terms of membership outlined in the iSMOC Charter for the National Children's Study version 1.0. If the charter is changed at any time, all iSMOC members will review the changes and must agree to the new charter.

Signature

Printed Name

Date

iSMOC Chair Signature

Printed Name

Date

Appendix B

NCS iSMOC Conflict of Interest Statement

I, _____, assuming the role of
[Name, Title]

_____ for the National Children's Study do agree to the following statements:

I agree to:

- Protect the interests and safety of study participants;
- Uphold the integrity of the research process including data collection and analysis to be as free from bias and preconception as I am able;
- Adhere to the highest scientific and ethical standards, to comply with all relevant regulations and to eliminate or disclose, during my involvement with the proposed clinical research project, any real or apparent conflicts of interest.

In addition:

I affirm that I and my spouse/domestic partner and dependent children have no financial interest in the National Children's Study, where financial interest is defined by the DHHS, as anything of monetary value, including but not limited to, salary or other payments for services (for example, consulting fees or honoraria); equity interests (for example, stocks, stock options or other ownership interests); and intellectual property rights (for example, patents, copyrights and royalties from such rights).

The financial interest term does not include various items which can be found in The Federal regulation, PHS DHHS Part 50 – Policies of General Applicability; Subpart F – *Responsibility of Applicants for Promoting Objectivity in Research for Which PHS Funding Is Sought*.

For Federal Employees, financial interests that are allowable and require disclosure are:

Financial Interest Disclosure: Financial interest that require disclosure of stock holdings in pharmaceutical firms, medical device manufacturers, and biotechnology companies.

Allowable Financial Interests: In a company that produces a product that is being evaluated by a study, participants may hold up to \$15,000 of stock; and up to an aggregate of \$25,000 of stock of that company and its competitors who produce that (or a similar) product. As an alternative to individual stock holdings, participants may hold up to an aggregate of \$50,000 in sector mutual funds-including pharmaceutical/health care sectors.

Appendix C

iSMOC Confidentiality Agreement

I understand that I will be provided with information from the Coordinating Center or Study sites or similar organizations for the National Children's Study, including proprietary and confidential information.

I understand that I will have access to these records in order to participate in the Independent Study Monitoring and Oversight Committee (iSMOC) for the National Children's Study.

In my role as the _____, I, _____ hereby
[Role/ Position] *[Name, Title]*
agree that I shall not release, publish, or reproduce these records. I further agree that I shall not make any use of these records except for the limited purpose of participation in the Independent Study Monitoring and Oversight Committee for the National Children's Study.

I will take reasonable precautions to prevent access by any other persons to these confidential records or to work products that result from review of those records. I may retain access to any confidential documentation until the conclusion of my term of service on the iSMOC. Upon the conclusion of my term of service, I will destroy the documents and all related materials.

I understand that members of the iSMOC are not expected to be spokespersons for the Committee or the National Children's Study. As such, I will inform the Chair and the Executive Secretary of the iSMOC promptly of any media contacts related to the iSMOC or the National Children's Study.

I have read the terms of this agreement and agree to abide by these terms.

Signed: _____ Date: _____
[Name, Title]

Appendix D

Members	Year																					
	2009	2010	2011	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030
Statistician	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Obstetrician	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Maternal/Child Health	0	1	1	1	1	1	1	1	1	1	1	1	2	2	2	2	2	2	2	2	2	2
Participant Representative	9	0	1	2	3	4	5	6	7	8	9	0	1	2	3	4	5	6	7	8	9	0
Ethicist																						
Environment/Toxicology																						
Geneticist																						
Social Health																						
Chair																						
Community Representative																						
Epidemiology/Prevention																						
Pediatrician																						
Developmental Psychology																						

Initial Term starts in 2009

First group renewed in 2012 (initial term is 3 years)

Second group renewed in 2013 (initial term is 4 years)

Third group renewed 2014 (initial term is 5 years)

= Term of Service