ISCTM SIB Consensus Statements for the Analysis of Suicidal Ideation and Behavior (SIB) Data Working Group

Description/Overview: *This group focused their efforts on the development of future clinical trials for SIB and how to most accurately evaluate and summarize suicidal ideation and behavior.*

W*ith respect to the analyses to address SIB, the following items were surveyed:*

- *should suicidal ideation be assumed when behavior is reported, and if a consensus is needed around relevant analyses and statistical approaches to mediational analyses*
- *if a SIB-specific meta-analysis guide is needed,*
- *defining appropriate time windows to collect recent SIB history for use in inclusion/exclusion criteria and/or treatment emergence assessments,*
- *the role of Suicide/self-injury MedDRA standardized MedDRA query when a prospective assessment has/has not been included,*
- *what data should be explored to identify potential treatment mediator variables of SIB outcomes, what potential mediator variables should be explored first, and the identification of relevant data elements to be further studied,*
- *steps for harmonization of selected data fields to SIB mediators across different types of databases,*
- *identifying top predictors of imminent suicidal behavior and protective factors that may mitigate risk of imminent suicidal behavior,*
- *how to assess the relationship of drug exposure to suicide behavior.*

In addition, members were also surveyed on how to advance collaboration across research centers to understand more proximal mediators of SIB, and what information is needed to describe critical periods for suicidal behavior as it relates to dose titration.

Objective of WG: The goal of this working group was to achieve a consensus on items relating to the analysis of suicidal ideation and behavior with respect to data analysis.

Statements Voted on at F2F Meeting on Nov 18

Statement	% Strongly Agree	% Agree	% Disagree	% Strongly Disagree	% Not Knowledgeable To Answer
1. AD1. Recognizing that data collection of potential clinical moderators and mediators for SIB is	58.75	37.5	1.25	0	2.5

exploratory, analyses of such data across studies may advance our understanding of risk assessment. In clinical trials in which SIB is a primary or key secondary objective, potential clinical moderators or mediators should be collected using common data elements.	96.25% Agree or Strongly Agree				
2. AD2. Recognizing that data collection of biomarkers for SIB is exploratory, analyses of such data across studies may advance our understanding of the biological basis of risk assessment. In clinical trials in which SIB is a primary or key secondary objective, potential moderators or mediators should be collected using common data elements.	39.47	47.37	6.58	1.32	5.26
	86.84% Agree or Strongly Agree				
3. AD3. Recognizing that data collection of potential protective factors for SIB is exploratory, analyses of such data across studies may advance our understanding of risk assessment. In clinical trials in which SIB is a primary or key secondary objective, potential protective factors should be collected using common data elements.	47.44	39.74	8.97	0	3.85
	87.51% Agree or Strongly Agree				
4. AD4. Prospective scale data should contain all suicide related events, and is the primary source for summaries or analysis of SIB.	49.38	37.04	4.94	2.47	6.17
	86.42% Agree or Strongly Agree				

Statements Not Voted On—

Please include below any other statements that your group reached consensus on that were not voted on at the meeting. Statements may be grouped by topic or as most helpful to a naïve reader; use the format that best suits your needs. The strength of agreement may be indicated if desired, or feel free to include any other information deemed useful. You may also wish to indicate in some way the statements that are most important or highest priority (eg, bolded text or by order).

With respect to the development of clinical trials to address SIB, the survey results of the Working Group's responses are as follows:

Additional statements to be considered as consequential for field that could be considered are:

- Completed suicide is exceptionally rare in context of randomized control trials and the relation of short term predictors for suicidal ideation and attempts to completed suicide is not well understood
- Need for more information about relation of drug exposure to suicide behavior in context of randomized control trials
- A meta-analytic guidance that is specific to SIB would be beneficial
- Prospective scale should be reconciled with other existing study data so that analyses of the prospective scale can be trusted as containing all cases of suicidal ideation and behavior occurring during the study
- FDA Guidance on Prospective data should be updated to provide additional clarity on some key topics
- FDA Guidance on Retrospective data should be updated to incorporate suggestions on completeness and efficiency

General questions regarding clinical trial development for SIB:

- 82% of respondents agreed that there should be a consensus around the most relevant analyses and statistical approaches to mediational analysis.
- 61% of respondents felt that suicidal ideation should NOT always be assumed when behavior is reported.
- Although respondents felt that it depended upon the purpose, design, and length of the study, the majority wanted a time window of at least year to collect history of 'recent' suicidal behavior. However, there was no clear consensus of the time window (1 month/3 months/ 1year) for ideation. In general, it appeared that a longer collection time was needed to collect the history of suicidal behavior vs. ideation.
- 57% of respondents felt that a summary table of Suicide/self-injury MedDRA SMQ should be created for all studies in which Suicide/self-injury is of interest regardless of whether a prospective SIB instrument is included.

Questions relating to predictors of Suicidal Behavior:

- When ranking the top 3 predictors of imminent suicidal behavior, the 3 most important predictors were 'aggression and impulsivity' (55 responses), 'agitation' (38 responses), and 'social distress' (33 responses).
- 'Social support' was clearly identified as the most important protective factor which may mitigate risk of imminent suicidal behavior, followed by 'early response to treatment' and 'absence of comorbid personality disorders'.
- 46/128 respondents answered 'what information is needed to fully describe critical periods for suicidal behavior as it relates to dose titration'; the most common responses (i.e., >10%) were: Dosing frequency and duration, adherence to dosing, dose level, PK characteristics (Tmax, half-life, etc.), frequent/daily assessments of SIB, drug withdrawal.
- Of the 50/128 respondents who addressed 'what information is needed to assess the relationship of drug exposure to suicide behavior in the context of randomized trials', the most common responses were: length of drug exposure, pharmacokinetics, drug blood levels, dosing time relative to onset of SIB, accurate assessments of drug adherence, SIB history, data from validated measures of suicidal behavior.

Questions regarding Mediator variables:

- When developing clinical trials to address SIB, 89% of respondents thought that the potential mediator variable of 'change in clinical scales' should be explored first; less than 10% of respondents were interested in. 'Potential biomarkers' and 'Other' mediator variables. No one indicated interest in 'lab values'.
- Of the 48/128 respondents who named 'up to 3 relevant data elements to SIB mediators that should be further studied', the most common responses (i.e., >10%) were: history of suicide/suicidal ideation, hopelessness, anxiety, depression, substance abuse, impulsivity, and precipitating events.