# Agency Guidance on Assessment of Suicidal Ideation and Behavior in Clinical Trials

## A Progress Report

**Tiffany R Farchione, MD**
*Deputy Director, Division of Psychiatry Products*
Center for Drug Evaluation and Research
US Food and Drug Administration

# Outline

- Existing Guidance
- Process thus far
- Plans for data analysis
- Next steps

# Draft Guidance

- Prompted by findings of treatment-emergent suicidal ideation and behavior (SI/B) associated with certain drugs
- Events recognized retrospectively via meta-analysis
- Two reasons for prospective assessment:
  - Ensure timely recognition of emergent SI/B
  - Collection of more complete data

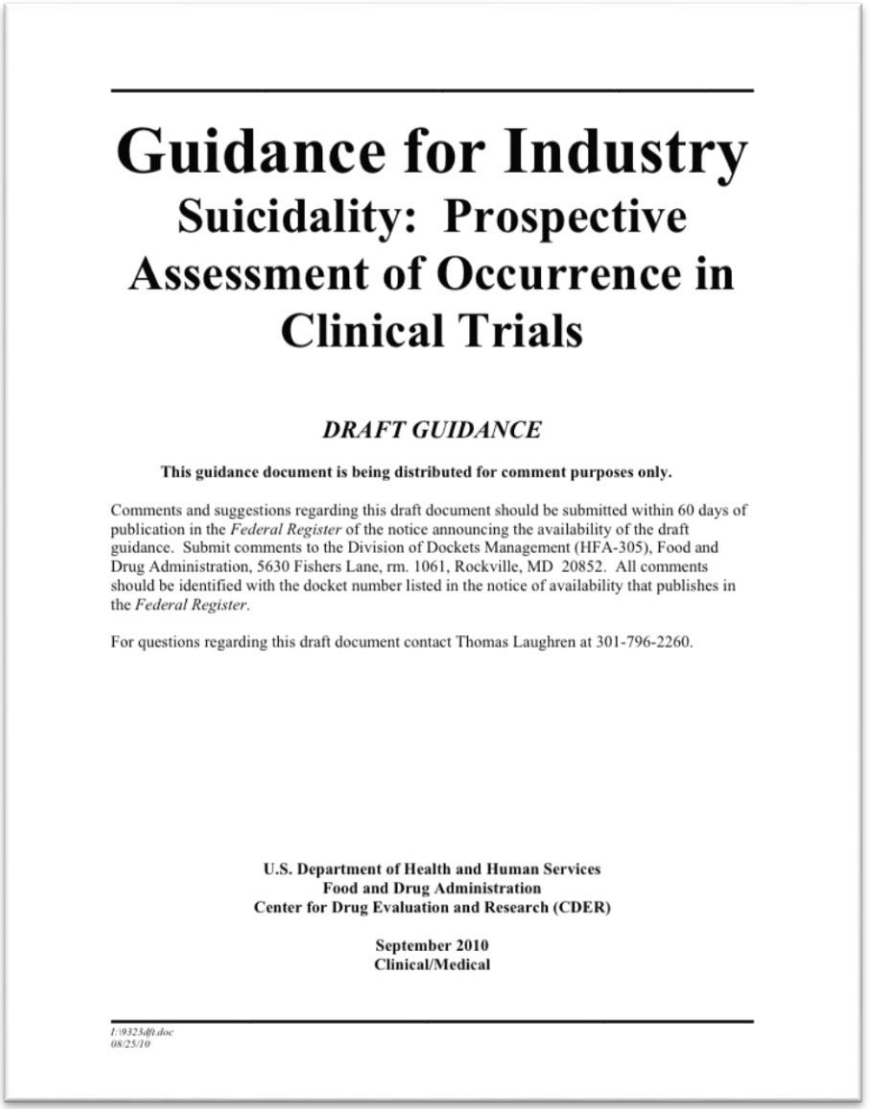
ORIGINAL ARTICLE

Suicidality in Pediatric Patients Treated With Antidepressant Drugs

*Tarek A. Hammad, MD, PhD, MSc, MS; Thomas Laughren, MD; Judith Racoosin, MD, MPH*

# Draft Guidance

- Introduced the Columbia Classification Algorithm for Suicidality Assessment (C-CASA)
- Coding developed for retrospective analysis
- Assessments should be conducted at baseline and at all planned visits



**Guidance for Industry**

**Suicidality: Prospective Assessment of Occurrence in Clinical Trials**

***DRAFT GUIDANCE***

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Comments and suggestions regarding this draft document should be submitted within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document contact Thomas Laughren at 301-796-2260.

**U.S. Department of Health and Human Services**
**Food and Drug Administration**
**Center for Drug Evaluation and Research (CDER)**

**September 2010**
**Clinical/Medical**

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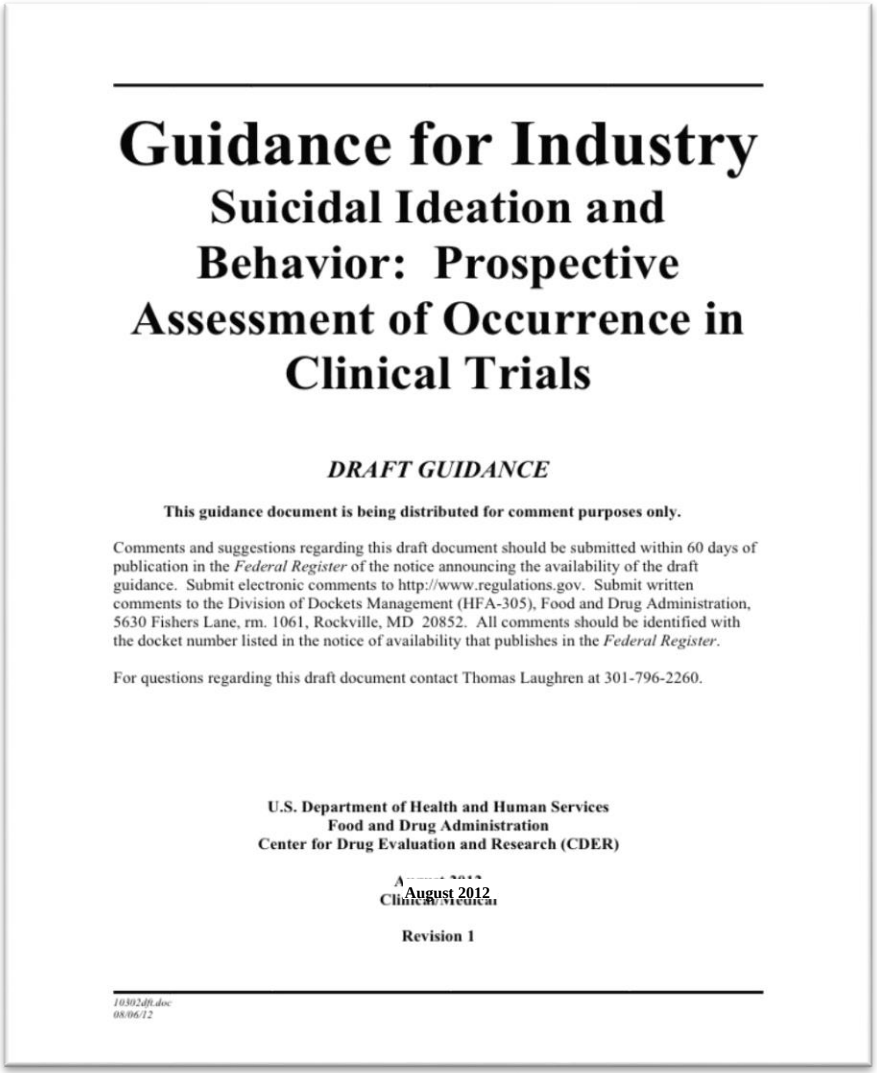
*08/25/10*

# C-CASA

- Set of preferred terms for coding
  - Completed Suicide
  - Suicide Attempt
  - Preparatory Actions Toward Imminent Suicidal Behavior
  - Suicidal Ideation
  - Self-Injurious Behavior Intent Unknown
  - Fatal Event: Not Enough Information
  - Self-Injurious Behavior Without Suicidal Intent
  - Other (Accident, Psychiatric, Medical)
  - Nonfatal Event: Not Enough Information

# Draft Guidance



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**Suicidal Ideation and Behavior: Prospective Assessment of Occurrence in Clinical Trials**

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**U.S. Department of Health and Human Services**
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**August 2012**

**Revision 1**

*10302dft.doc*
*08/06/12*

- Replaced “suicidality” with “suicidal ideation and behavior”
- Expanded classification categories
- Revised advice on types of trials in which assessment necessary

# New Categories

- Suicidal Ideation
  - Passive suicidal ideation: wish to be dead
  - Active suicidal ideation: nonspecific (no method, intent, plan)
  - Active suicidal ideation: method, but no intent or plan
  - Active suicidal ideation: method and intent, but no plan
  - Active suicidal ideation: method, intent, and plan
- Suicidal Behavior
  - Completed suicide
  - Suicide attempt
  - Interrupted suicide attempt
  - Aborted suicide attempt
  - Preparatory acts toward imminent suicidal behaviors
- Self-Injurious Behavior Without Suicidal Intent

# Since 2012

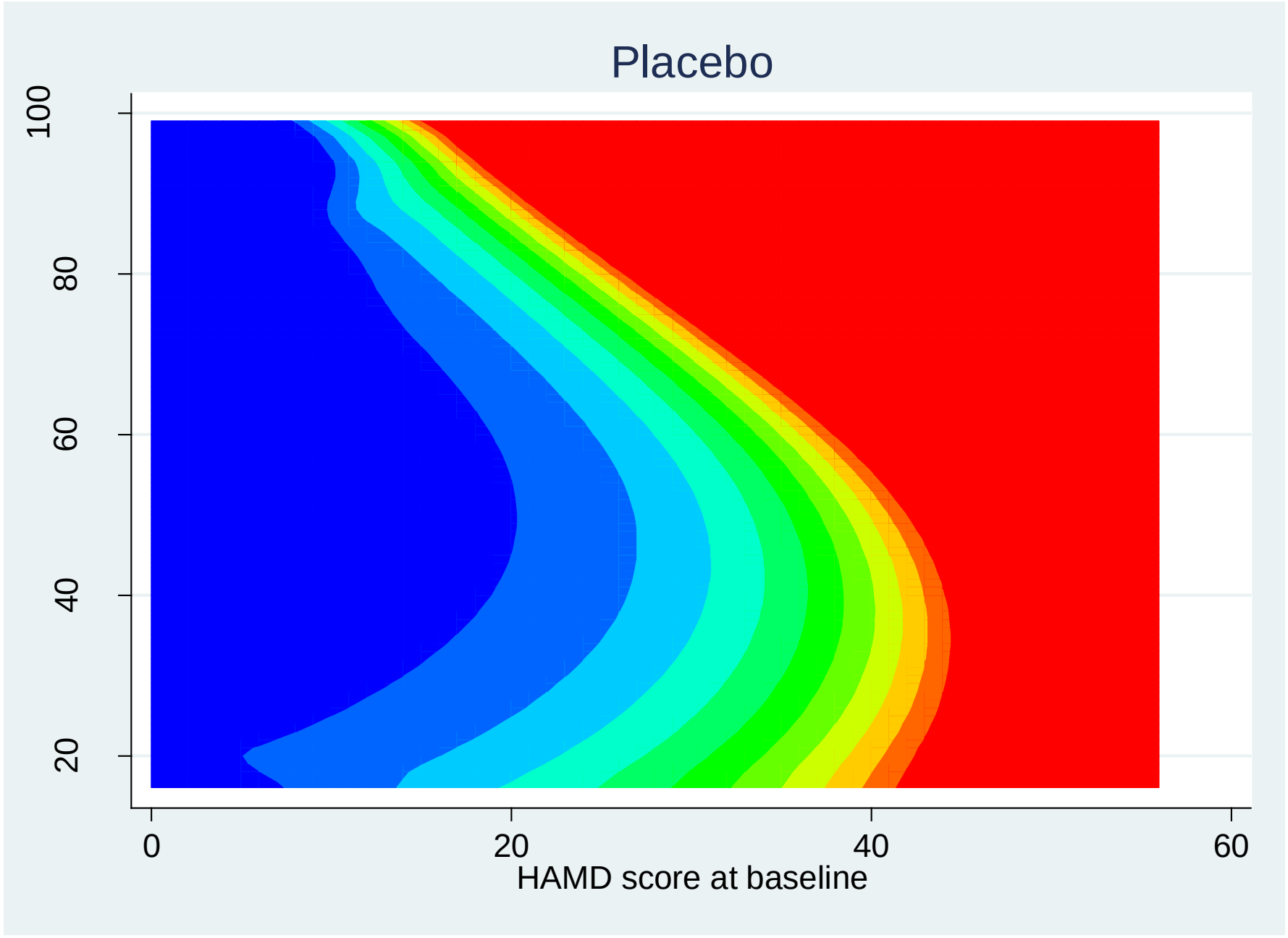
- Collection of public comments
  - Draft published in August, 2012
  - Comment period closed in October, 2012
- ISCTM consensus conference in November, 2014
  - Reviewed draft white paper
- Established workgroup within Division to draft revised Guidance

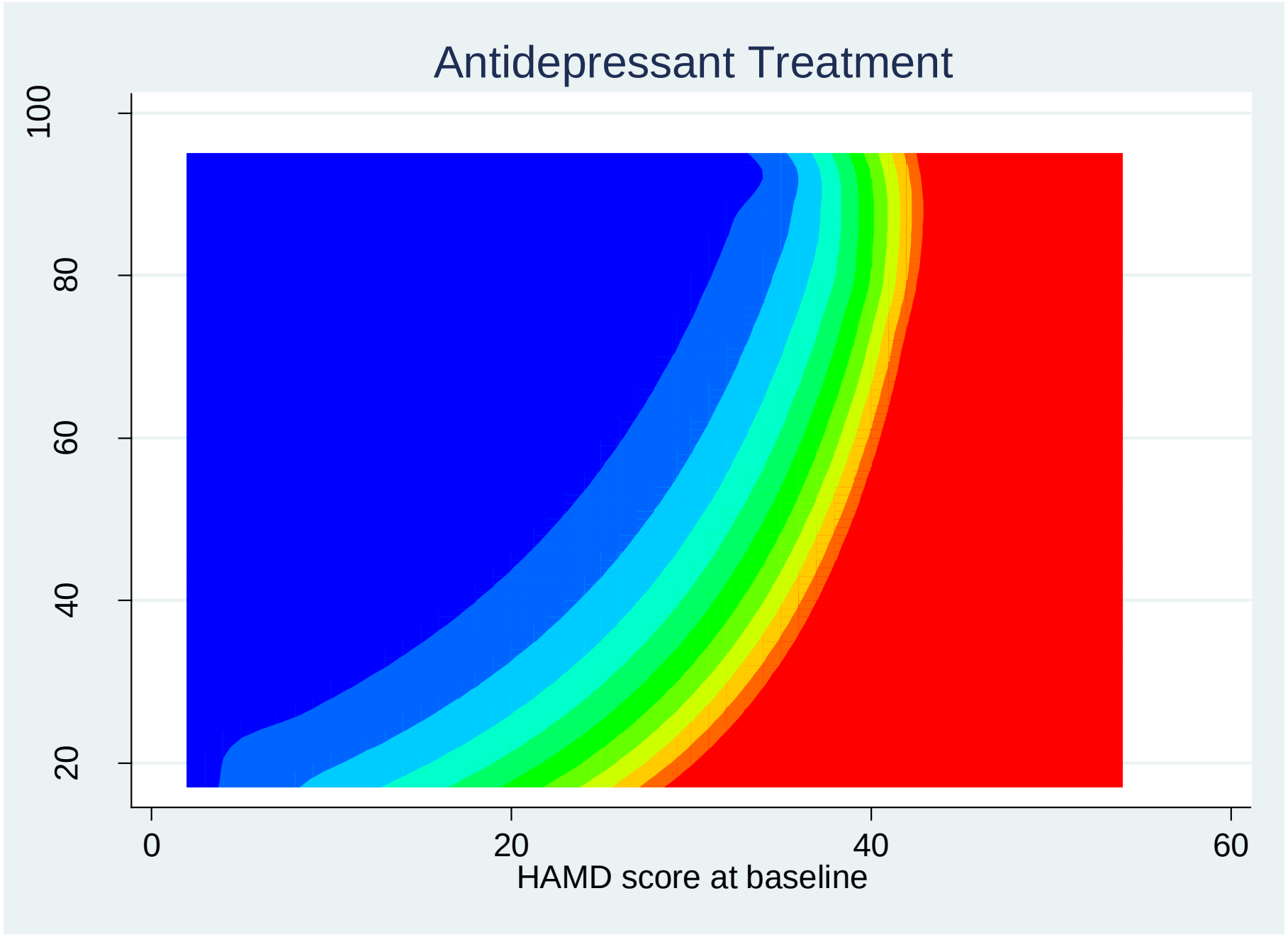
# Division Workgroup

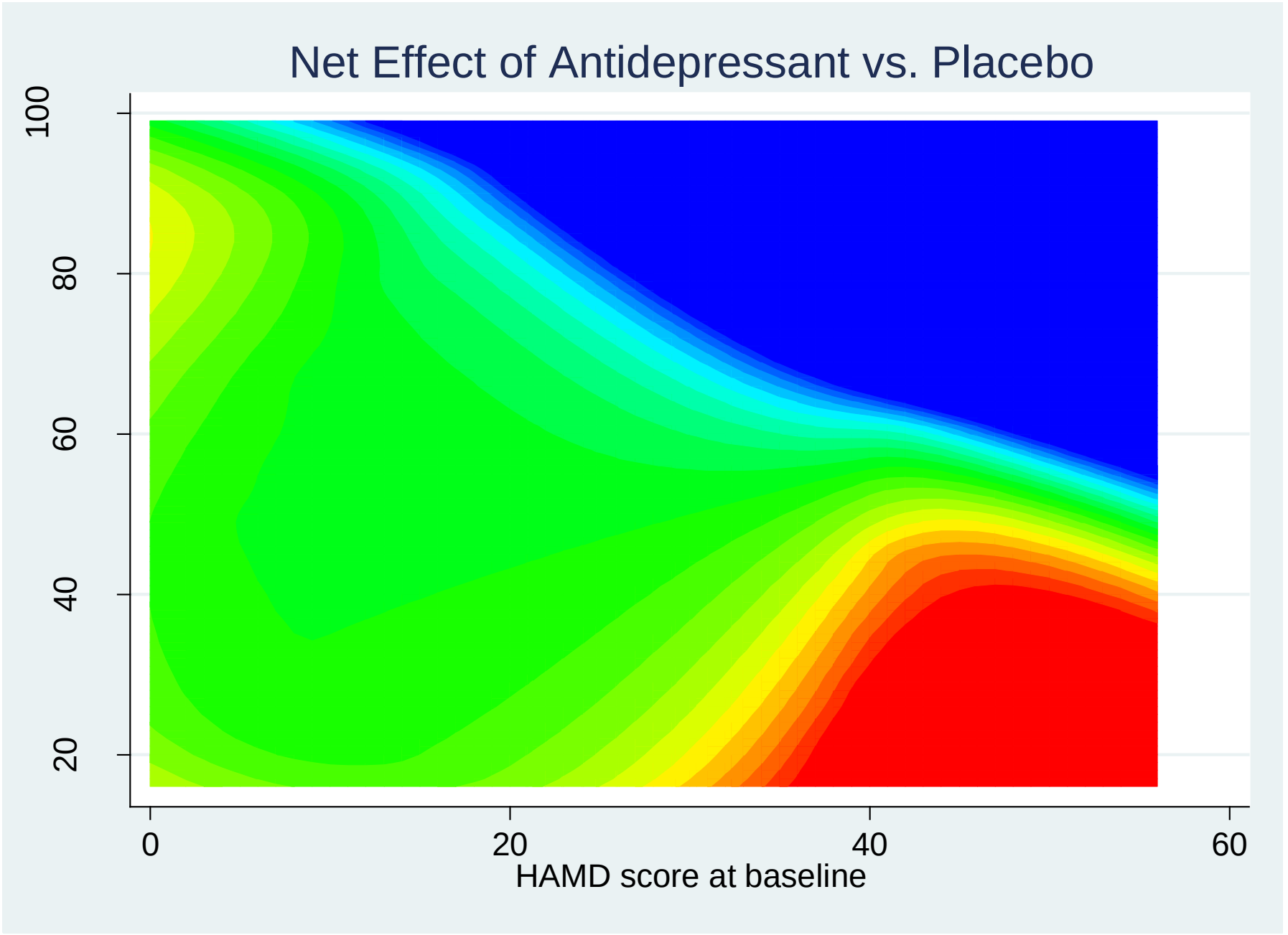
- Re-review of public comments
- Review of ISCTM document
- Scope of project
  - Revised draft Guidance vs. final Guidance?
  - Specific advice for non-CNS development programs?
  - What have we learned so far?

# A Fresh Look at Old Data

- How well do the baseline  scores on depression scales predict the incidence of suicidal behavior?
  - Used the same adult and pediatric studies that were included in FDA's original metaanalysis of clinical trial data
  - Plotted absolute risk of suicidal behavior during the trial as a function of baseline HAM-D score and age


Placebo
100
80
60
40
20
0
20
40
60
HAMD score at baseline


Antidepressant Treatment
100
80
60
40
20
0
20
40
60
HAMD score at baseline


Net Effect of Antidepressant vs. Placebo
100
80
60
40
20
0
20
40
60
HAMD score at baseline

# Additional Questions

- How much does the lifetime max suicidal ideation or behavior score change the risk of suicidal behavior during the course of a study?
- Which scale best predicted suicidal behavior during the study?
- Are there differences in analyses according to gender or patient age?
- How much sensitivity would you lose in predicting suicidal behaviors if the C-CASA categories are collapsed?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