U.S. Food & Drug Administration

Obtaining Information for Evaluating Nominated Bulk Drug Substances for Use in Compounding Drug Products Under Section 503B of the Federal Food, Drug, and Cosmetic Act.

OMB Control No. 0910-NEW

SUPPORTING STATEMENT—**Part B: Statistical Methods**

1. Respondent Universe and Sampling Methods

Research will generally rely on qualitative methods and is not intended to yield results that are projectable to the national population. As described below, research will target individuals with specific types of clinical expertise to provide their expert opinions, as well as a pre-identified group of parents of children with Autism Spectrum Disorder.

UMD-CERSI Expert Interviews and Focus Groups

Researchers will conduct in-depth interviews and focus groups with an estimated 150 experts/specialists annually to obtain their opinions on the use of compounded drugs containing specific bulk drug substances in patient care. Experts will be identified through various means, including contacts at the University of Maryland School of Medicine as well as referrals obtained through contacts at applicable national medical professional organizations.

UMD-CERSI Expert Questionnaire

After completion of the interviews and focus groups, a tailored questionnaire will be utilized to obtain a more detailed understanding of how compounded drugs containing specific bulk-drug substances are used in patient care. Researchers will engage applicable national medical professional organizations for each medical specialty to facilitate questionnaire distribution and participation. Researchers will seek to obtain participation of at least 50 experts from each specialty group (a total of 750 clinicians) annually.

JHU-CERSI Parent Questionnaire

Researchers will use a questionnaire to obtain information from parents of children with autism spectrum disorder (ASD) on the use of compounded drugs containing any of six bulk drug substances in these patients. Recruitment will be conducted through SPARK (Simons Foundation Powering Autism Research for Knowledge) and their online autism research registry, which has

20,000 individuals with ASD and their families. Researchers will seek to recruit approximately 1,000 families from SPARK (consisting of parents and caregivers of children with ASD). SPARK registry participants have previously consented to be in SPARK and have agreed to sharing of de-identified data with outside researchers. Since JHU faculty or staff will not have access to the registry or private information, SPARK staff will query their registry to find parents and caregivers with at least one child with ASD. Once identified, eligible families will be emailed an invitation to complete the online ASD Treatment Questionnaire.

2. Procedures for the Collection of Information

UMD-CERSI Expert Interviews and Focus Groups

Potential participants will be contacted via email to schedule the interview or focus group. Each interview and focus group will last one or two hours, respectively, and will include questions regarding the participants' knowledge and experience using a bulk substance. Interviews will be conducted in-person if the participant is local, but researchers will also conduct interviews by telephone to support a more geographically diverse group of participants. The interviews and focus groups will be conducted using a semi-structured approach which will allow the participant to expand on his or her previous experience, as needed.

UMD-CERSI Expert Questionnaire

The questionnaire will be administered using a web-based platform and will be distributed via email. The questionnaire will include a combination of free-text and prompted responses and will include questions regarding his or her knowledge, experience, frequency, and indications of use for each substance. We estimate the questionnaire will take respondents approximately 30 minutes to complete.

JHU-CERSI Questionnaire

Information on the six bulk drug substances that are the subject of JHU-CERSI's research will be collected as part of a broader questionnaire on medical and behavioral treatments used to treat ASD, including both conventional therapies and complementary and alternative medicine (CAM). Participants will be asked to identify and answer questions about specific interventions they have used to treat their children with ASD. These outcome measures will be used to identify the treatments used most often and the characteristics of individuals who use them.

The questionnaire includes a short series of basic demographic questions, followed by questions about the child's co-occurring medical conditions. The following sections present extensive lists

of medical and behavioral therapies used to treat ASD and prompt the respondent to select all that they have tried on his or her child. The lists include the six bulk drug substances of interest. For each treatment selected, the respondent will be asked to answer an additional series of questions detailing the use and experience with the treatment. Estimated average completion time for the questionnaire is 30 minutes, though will vary by child and will depend on the number of treatments a child has used.

Researchers will examine the response rates of participation by comparing the number of SPARK participants invited to complete the questionnaire to the number who agreed to participate. We will also examine if any one item on the questionnaire has limited response rates, and work to identify factors associated with response/ non-response.

Conventional statistical techniques for response data, such as descriptive statistics, t-tests, chi-square tests, and regression models will be used to analyze the data. Researchers will examine use of the six compounds of interest and will examine phenotypic and demographic indicators of endorsement of use.

3. Methods to Maximize Response Rates and Deal with Nonresponse

As noted, research methods are primarily qualitative, and respondent groups for questionnaires consist of samples of convenience and individuals within specialty organizations with specific expertise. Efforts will be made to maximize response rates, but results will not be nationally representative.

UMD-CERSI Expert Interviews and Focus Groups

Researchers will conduct outreach through local and national networks until approximately 10 specialists from each of 15 medical specialties are identified and participate. Thematic analysis of each interview and focus group will be completed utilizing NVivo to identify common indications, dosing, and experience using each substance.

UMD-CERSI Expert Questionnaire

Bi-weekly reminder emails will be sent to obtain a target participation of approximately 50 experts from each specialty group (a total of 750 experts). Quantitative and qualitative analyses will be conducted to evaluate both response frequency as well as common response themes.

JHU-CERSI Questionnaire

Up to three reminders will be sent over a 4-week period until recipients respond. Recipients who have not responded after 6 weeks will be considered to have refused participation. The 6-week time frame for the project has been validated by SPARK in prior online research invitations.

4. Test of Procedures or Methods to be Undertaken

Small adjustments may be made to questionnaires based on information obtained through interviews and focus groups with experts.

5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

UMD-CERSI

Statistical analysis beyond simple response rate frequency is not anticipated. The following individuals participated in research design and will participate in results analysis:

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JHU-CERSI

Simple statistical analysis will be conducted of JHU-CERSI's parent questionnaire results. The following individuals participated in research design and will participate in results analysis:

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