Supporting Statement B for

Interactive Informed Consent for Pediatric Clinical Trials

Submitted By:

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B.1 Respondent Universe and Sampling Methods

284 subjects (136 children aged 11-17 years of age and 148 parents) attending the pre-anesthesia or outpatient clinics at the University of Michigan's Mott Children's Hospital will be included. Children must have permission of a parent to participate. Children will be otherwise healthy and those who are seriously ill will be excluded. Consecutive parents and children attending the pre-anesthesia or outpatient clinics will be randomized to receive information about a hypothetical clinical asthma trial using either standard written consent information or the parent or child versions of the ArchieMD Pediatric Informed Consent Program for Clinical Trials. Previous studies from our group have shown that this sampling and recruitment strategy provides a diverse sample of research participants by gender and minority status that is reflective of the local and regional demographics.

A planned target enrollment is shown in the table.

	American Indian Alaskan Native	Asian/ Pacific Islander	Black, Non-Hispanic Origin	Hispanic	White, Non-Hispanic Origin	Other/ Unknown.	Total
Female	1	4	25	15	97	0	142
Male	1	4	25	15	97	0	142
Totals	2	8	50	30	194	0	284

The sample size was based on previous studies that have examined parents' and children's understanding of consent information presented using either video or standard written information. These numbers provide 80%power ($\alpha = 0.05$, two-tailed) to detect clinically significant differences in parents' and children's understanding of the asthma trial information between the ArchieMD computer-based program or standard written information groups.

In the Phase I trial, 9 subjects (5 parents and 4 children) were recruited, which represented a 100% response rate.[1] However, based on our experience with these types of studies, we anticipate that in a larger population there will be approximately 15% of subjects who will

decline participation. We do, however, anticipate that of those who do consent to participate, 94-100% will complete all aspects of the study.

B.2 Procedures for the Collection of Information

***Sampling*:**

Consecutive participants presenting at our pre-anesthesia or outpatient clinics will be randomized using computer-generated randomization schedules to receive information about a hypothetical clinical asthma trial using either standard written consent information or the parent/child versions of the ArchieMD computer-based interactive consent program. Previous experience with this sampling approach has provided randomized groups that have similar socio-demographics (i.e., age, gender, race/ethnicity, and education) and that are representative of the local and regional populations.

Procedures:

Consecutive parents and children (11-17 yrs) attending the pre-anesthesia or outpatient clinics will be recruited and asked to provide parental permission and child assent to participate. Baseline demographic characteristics will be obtained for all subjects and will include age, gender, education, and race/ethnicity. No protected health information (PHI) will be collected and the data will carry no identifiers.

Parent and child participants will be interviewed by trained research nurses and assistants. Our group has approximately 15 year experience with these types of interviews involving both parents and children. Participants (parents and children) will initially be given a short pre-test to elicit their baseline understanding of clinical trial concepts e.g., randomization, blinding, etc.).

Participants will then be randomized to receive information about the clinical asthma trial using either standard written information or the parent or child versions of the ArchieMD Pediatric Informed Consent Program for Clinical Trials. Per our normal practice, participants will be allowed sufficient time to assimilate the information and ask questions. A trained research assistant will be available to help participants navigate the ArchieMD consent program.

Once the participants have read either the standard written information or the ArchieMD program (per randomization), they will be interviewed to determine their understanding of the elements of the clinical asthma trial (e.g., risks, benefits, protocol, purpose, etc.). Parents' and children's understanding of the information will be evaluated using a semi-structured, face-to-face interview. Items for these interviews will be based on a modification of the Deaconess Informed Consent Comprehension Test (DICCT).[2] Responses will be written down verbatim by trained interviewers and scored independently by two assessors using the DICCT scoring system. Assessors will be blinded to whether the participant received the standard information or the interactive ArchieMD consent program. Scores of 0, 1, and 2 will be assigned based on the subject having no understanding, partial understanding, and complete understanding respectively. In the event of discrepancies in the interpretation of responses, the two reviewers will meet to discuss differences and attempt to reach a consensus. If these differences cannot be reconciled, a third reviewer will score the responses independently such that a decision can be reached.

Participants will also be tested a second time to test their "new" understanding of the key clinical trial concepts provided in the baseline pre-test (i.e., randomization, blinding, etc).

A subjective self-assessment of satisfaction and attitudes toward the informed consent process will also be conducted. We will ask the subjects to provide their perceptions of the clarity, amount of information, perceived effectiveness of the message, and their overall satisfaction with the consent information (i.e., ArchieMD vs standard informed consent documents) using 0-10 visual analog scales where 10 = high. At the end, the subjects will be shown both the standard and ArchieMD material and asked which they prefer. We have used these questions successfully in our previous studies.

Parents' and children's literacy will be measured using the Slosson Oral Reading Test Revised (SORT-R3).[3] Numeracy i.e. ability to understand and work with numbers and percentages will be assessed using the validated 8-item Subjective Numeracy Scale (SNS)

developed by Fagerlin and Zikmund-Fisher. These assessments are self-completed by the parents and children. Parents and children's demographics e.g., age, gender, race/ethnicity, education, previous research participation, and previous hospitalization will also be recorded.

For parents and children randomized to the interactive computer-based consent program we will also evaluate their satisfaction with the message delivery and their perceptions of the effectiveness and quality of the interactive format.

The study protocol as described above, including the pre and post-test interviews, the administration of the SNS, and SORT-R3, and the survey of participants' perceptions of the information delivery will be conducted ONCE per participant. Based on our experience with this type of research, we anticipate that participation in this study will take approximately 30-40 minutes/participant to complete. Subjects will be provided with a $10 gift card for participation in this study.

Statistics:

Data will be analyzed using PASW statistical software (PASW, Chicago, IL). Data will be extracted from the data collection forms and entered into an anonymous database (no identifiers). Data will be checked and double-checked for accuracy and completeness prior to analysis. Data will be presented as frequency distributions. Comparison of parametric data between groups will utilize t tests. Non-parametric data will be calculated using Mann-Whitney U tests, Wilcoxon signed rank tests and Chi square analysis as appropriate. Inter-rater reliability and levels of agreement between the two assessors will be determined by Spearman's correlation coefficient (r) and kappa (κ) statistics, respectively. Previous studies using the same semi-structured interviews revealed excellent inter-rater reliability ($r = >0.8$) between these two assessors. A P value of < 0.05 will be accepted as statistically significant.

B.3 Methods to Maximize Response Rates and Deal with Non-response

Our experience with these types of studies provides us with confidence that the non-response rate will be minimal. In the Phase I contract for this study which involved 9 subjects, we obtained 100% response rates.[1] Similarly, in a study involving interviewing adult patients regarding their understanding of cardiac catheterization procedures using standard written versus computer-based information, 128 patients out of 135 who consented to participate completed the study i.e., a response rate of 94.8%.[8] As such, we anticipate similar response rates for this study and thus do not believe that non-response bias will be an issue. We will have ongoing quality assurance of the data. All data are checked and double-checked for accuracy and completeness. If for any reason, we find that a particular survey question is systematically being missed or is misinterpreted, we will rewrite or rephrase the question to insure that it is no longer ambiguous or misleading. None of the questions in the interviews are sensitive or potentially harmful.
Previous work using similar populations and methodology have yielded samples that are very representative of the target population (universe). We have no reason to believe that the results from this proposed study will not be generalizable to the greater population.

B.4 Test of Procedures or Methods to be Undertaken

All interviews and assessment tools have been carefully selected to balance scientific validity with a desire to reduce the burden to the participants. All the interview items and assessment tools have been used by our group in similar populations without difficulty or undue burden. All assessments are valid and appropriate for both parents and this age-group of children. Participants will complete the procedures, as described, ONCE only. All procedures can be accomplished in one visit i.e., subjects will NOT be re-contacted for subsequent testing. We anticipate that the entire assessment process will take 30-40 minutes to complete.

Survey procedures: See Appendices A and B

Appendix A: Interviews

1. Pre-test:

Parents and children will complete a 4-item interview to determine their baseline understanding of clinical trial concepts i.e., “Clinical trial,” “Randomization,” “Placebo,” and “Blinded study.”

2. Post-test:

Following randomization to either the standard written information or the ArchieMD Pediatric Informed Consent Program for Clinical Trials, parents and children will be re-interviewed to determine their “new” understanding of the terms: “Clinical trial,” “Randomization,” “Placebo,” and “Blinded study.” In addition, parents and children will be interviewed to determine their understanding of the elements of the clinical asthma trial (risks, benefits, etc.).

Appendix B: Questionnaire

Parents and children will complete a short 9-item questionnaire to determine their perceptions of the message delivery and their satisfaction with the way in which the information about the clinical asthma trial was presented.

Assessment procedures

Literacy:

Parents and children will complete the validated shortened Slosson Oral Reading Test (SORT-R3) to measure their grade literacy levels.[3] This well-established shortened version of the SORT test requires the subject to read aloud from a list of words arranged in ascending order of difficulty. It is appropriate for adults and the age groups of children involved in this study.

Numeracy:

Parents and children will complete the validated 8 –item subjective numeracy test (SNS). This simple test requires subjects to describe their facility with using numbers and percentages.

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

All sample size and statistical aspects of the design were initiated by and will be analyzed by:

Alan R. Tait, PhD

University of Michigan Medical School

Professor of Anesthesiology

734-763-8128

Data will be analyzed by Dr. Tait who has over 20 years of experience analyzing these types of datasets. He is currently the Endowed Professor of Anesthesiology at the University of Michigan where he serves as the Director of Clinical Research. He is also a former long-standing member of the University of Michigan's Institutional Review Board and serves as the Chair of the Research Committee for the Society of Pediatric Anesthesia. He is trained in classical epidemiology and biostatistics and has over 30 years of experience in clinical outcomes research, psychometrics, qualitative research, and in the management and analysis of large datasets. In addition, Dr. Tait has access to the University of Michigan's Center for Statistics and Consultation and Research (CSCAR) which provides free independent review and consultation of research data. Dr. Tait is very familiar with the qualitative and quantitative analyses required in this research. In analyzing the data, Dr. Tait will be blinded with respect to the subjects' assignment to either the standard written information or the ArchieMD Pediatric Informed Consent Program.

Data collection oversight, analyses checking and analysis write up will be performed by:

Terri Voepel-Lewis M.S.N., R.N. Research Area Specialist Lead
University of Michigan Medical School
Department of Anesthesiology
734-936-0747

Ms. Voepel-Lewis has many years of experience with these types of analyses. Her research has focused on two areas related to improving the perioperative experience of children: 1) to improve the manner in which research and treatment information is provided to parents and children, and 2) to improve pain assessment for both cognitively intact and cognitively impaired children. She has been a co-investigator with Dr. Tait on his previous NIH-funded studies related to informed consent and assent and has co-authored numerous articles with him. As part of her interest in sedation and pain management, she has developed and validated two important scales (The FLACC pain scale and UMSS sedation scale) designed to improve the assessment of these important areas of clinical practice. The FLACC scale,

in particular, is currently in use throughout the world for pain assessment in both children and adults. She also has experience in administering various psychosocial tests, psychometric testing, and the statistical analyses proposed for this study. She has experience with all quantitative and qualitative measures used in this application.

Data will be collected and entered into an anonymous database (no-identifiers) by trained research nurses and research assistants from the University of Michigan's Department of Anesthesiology. Data entry will be checked and double-checked by different research nurses and assistants.

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