PROTOCOL TYPE

Which IRB

(•) Medical ( ) NonMedical

Protocol Process Type

( ) Exemption
( ) Expedited (Must be risk level 1)
(•) Full

PROJECT INFORMATION

Title of Project: (If applicable, use the exact title listed in the grant/contract application).

A Causative Role for Amylin in Diabetic Peripheral Neuropathy

Short Title Description

Note: "Short Title" should consist of a couple key words to easily identify your study - these key words (rather than the whole title) will be displayed on the Dashboard in the listing for your study.

DMII Amylin Study

Anticipated Ending Date of Research Project: 6/30/2019

Number of human subjects: 40

Study is/will be open to new subject enrollment (or data/specimen collection): (•) Yes ( ) No

PI CONTACT INFORMATION

The Principal Investigator's (PI) contact information is filled in automatically based on who was logged in when the application was created (with LinkBlue ID). If research is being submitted to or supported by an extramural funding agency such as NIH, a private foundation or a pharmaceutical/manufacturing company, the PI listed on the grant application or the drug protocol must be the same person listed below.

If you are not the Principal Investigator, do NOT add yourself as study personnel. You may change the PI contact information on an application that is in Researcher edit mode by:

- clicking the "Change Principal Investigator" link below;
- searching for the PI's name using the search feature;
- clicking "Select" by the name of the Principal Investigator, then "Save Contact Information".

You will automatically be added as study personnel with edit authorization so you can continue editing the application.

Please fill in any blank fields with the appropriate contact information (gray shaded fields are not editable). Required fields left blank will be highlighted in pink after you click "Save".

To change home and work addresses, go to myUK and update using the Employee Self Service (ESS) portal. If name has changed, the individual with the name change will need to submit a 'Name Change Form' to the Human Resources Benefits Office for entering into SAP. The new name will need to be associated with the individual's Link Blue ID in SAP before the change is reflected in E-IRB. Contact the HR Benefits Office for additional information.

Note: Principal Investigator (PI) role for E-IRB access
The PI is the individual holding primary responsibility on the research project with the following permissions on the E-IRB application:

1. Read;
2. write/edit;
3. receive communications; and
4. submit to the IRB (IR, CR, MR, Other Review*).

Change Principal Investigator:

First Name:	John	Room# & Bldg:	KY Clinic, 740 S. Limestone, Wing D, J401
Last Name:	Slevin	Speed Sort#:	40536
Department:	Neurology	Degree:	MD
PI's Employee/Student ID#:	00005357	Rank:	Professor
PI's Telephone #:	859-323-0028	Dept Code:	7H852
PI's e-mail address:	jslevin@email.uky.edu	PI's FAX Number:	859-323-2623
PI is R.N.	○ Yes ◉ No	Trained:	Yes
		Date Trained	10/13/2017

Do you, the PI, have a significant financial interest related to your responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2)?

○ Yes ◉ No

RISK LEVEL

Indicate which of the categories listed below accurately describes this protocol

- ○ (Risk Level 1) Not greater than minimal risk
- ○ (Risk Level 2) Greater than minimal risk, but presenting the prospect of direct benefit to individuals subjects
- ◉ (Risk Level 3) Greater then minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
- ○ (Risk Level 4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects.

*"Minimal risk" means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves from those ordinarily encountered in daily life or during the performance of routine physical or psychological examination or tests [45 CFR 46.102(i)]

Download UK's guidance document on assessing the research risk for additional information on risk [PDF]

SUBJECT DEMOGRAPHICS

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 18 to 99

Indicate the targeted/planned enrollment of the following members of minority groups and their subpopulations
(Please note: The IRB will expect this information to be reported at Continuation Review time):

Enter Numbers Only!

Ethnic Origin	#Male	#Female
American Indian/Alaskan Native:		
Asian:		
Black African American:		
Hispanic/Latino:		
Native Hawaiian/Pacific Islander:		
White/Caucasian:		
Other or Unknown:		

If unknown, please explain why: Unable to estimate at this time

Indicate the categories of subjects and controls to be included in the study. Depending on the subject category applicable to your research you may be required to complete additional forms. [Note, if the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check mark populations which the research does not specifically target. For instance, a large record review of a diverse population may incidentally include a prisoner or an international citizen, but, if the focus or intent of the study has nothing to do with that status, you do not need to check those category(ies).]

Check All That Apply (at least one item must be selected)

- ☐ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults

ADDITIONAL INFORMATION:

- Children
- Emancipated Minors
- Impaired Consent Capacity Adults: Instructions; Link to required Form
- Students as Subjects - Guidances: - University of Kentucky Students [PDF] - College of Medicine Students [requirement of OME] - K-12 [PDF]

☐ Pregnant Women/Neonates/Fetal Material	• UKMC Residents or House Officers [see requirement of GME]
☐ Prisoners	• Non-English Speaking [see instructions for recruitment and E-IRB Research Description section on same topic]
☐ Non-English Speaking	
☐ International Citizens	
☐ Normal Volunteers	
☐ Military Personnel and/or DoD Civilian Employees	• Prisoners
☑ Patients	• International Citizens [HTML] (DoD SOP may apply [PDF])
☐ Appalachian Population	• Military Personnel and/or DoD Civilian Employees (DoD SOP may apply [PDF])

The next questions involve assessment of the study relative to potential recruitment of subjects with impaired consent capacity (or likelihood).

☐ Check this box if your study does not involve direct intervention or direct interaction with subjects (e.g., record-review research, secondary data analysis). (you will not need to answer the impaired consent capacity questions)

Does this study focus on adult subjects with any of the clinical conditions listed below that present a high *likelihood* of impaired consent capacity or *fluctuations* in consent capacity? (see examples below)

○ Yes ◉ No

If Yes, go to the following link and complete and attach the indicated form unless you are filing for an exemption certification: http://www.research.uky.edu/ori/ORIForms/FormT/Scale.asp

Examples of such conditions include:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia or other mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

Attachments

INFORMED CONSENT/ASSENT PROCESS/WAIVER

You must check the box for at least one of the consent items and/or check mark one of the waivers, then if applicable attach the corresponding document(s) **as a PDF** (if open to enrollment).

After making your selection(s) be sure to scroll to the bottom of this section and SAVE your work!

- ☐ Informed Consent Form (and/or Parental Permission Form)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script (and/or Assent Script)
- ☑ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol

Consent/Assent Tips:

For your informed consent attachment(s), please download the most up-to-date version listed in "All Templates" under the APPLICATION LINKS menu on the left, and revise to be in accord with your research project.

- **It is very important that only the documents you wish to have approved by the IRB are attached; DELETE OUTDATED FILES -- previously approved versions will still be available in Protocol History.**
- **If you have multiple consent documents, be sure to upload each individually (not all in a combined file).**
- **Changes to consent documents (e.g., informed consent form, assent form, cover letter, etc...) should be reflected in a 'tracked changes' version and uploaded separately with the Document Type "Highlighted Changes".**

With the exception of the "Highlighted Changes" version, attachments listed here at the time IRB approval is issued will be considered the version(s) to be used for enrolling subjects and will be stamped accordingly.

Additional Resources:

- Issues and Sample Consent Language for Specimen Banking Studies [PDF]
- Sample Research Repository Consent [WORD]
- Instructions for Proposed Informed Consent Document [HTML]
- Instructions for Proposed Assent Form [HTML]

Attachments

Attach Type	File Name
CoverLetter	IRB Memo Amylin Study.pdf
CoverLetter	IRB Memo Amylin Study Modification #2.pdf
CoverLetter	IRB Memo Amylin Study Modification #3 SP Add Alcala.pdf
Informed ConsentHIPAA Combined Form	Clean_DMII_Amylin-Form_C_Med_and_HIPAA_1.5.2018.....pdf
InformedConsent_HighlightedChanges	Tracked_DMII_Amylin-Form_C_Med_and_HIPAA_1.5.2018.pdf

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval for waiver of the requirement for the informed consent process, or alteration of some or all of the elements of informed consent (i.e. medical record review, deception research, or collection of biological specimens), complete Section 1 and Section 2 below.

Note: The IRB does not approve waiver or alteration of the consent process for greater than minimal risk research, except for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1.

Check the appropriate item:

☐ I am requesting waiver of the requirement for the informed consent process.

☐ I am requesting alteration of the informed consent process.

If you checked the box for this item, describe which elements of consent will be altered, and/or omitted, and justify the alteration.

SECTION 2.

The IRB may consider your request provided that **all** of the following conditions apply to your research and are appropriately justified. Explain in the space provided for each condition how it applies to your research.

a) The research involves no more than minimal risk to the subject.

b) The rights and welfare of subjects will not be adversely affected.

c) The research could not practicably be carried out without the requested waiver or alteration.

d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertinent information after they have participated in the study.

☐ Request for Waiver of Documentation of Informed Consent Process

If you are requesting IRB approval for waiver of the requirement for documentation of informed consent (i.e. telephone survey or mailed survey, internet research, or certain international research), your research activities must fit into one of two regulatory options:

1) The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves participants who use illegal drugs).

2) The research presents no more than minimal risk to the participant and involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script).

Select the option below that best fits your study, and explain in the space provided how your study meets the criteria for the selected regulatory option.

Note: The IRB cannot waive the requirement for documentation or alter the consent form for FDA-regulated research unless it meets Option #2 below. FDA does not accept Option #1.

Note: Even if a waiver of the requirement for documentation is approved by the IRB, participants must still be provided oral or written (e.g., cover letter) information including all required and appropriate elements of consent so they have the knowledge and opportunity to consider whether or not to participate. To help ensure required elements are included in your consent document, please use the **Cover Letter Template** as a guide: *English*- [WORD] [RTF], Spanish- [WORD] [RTF] The cover letter template was developed specifically for survey/questionnaire research; however, it may be useful as a guide for developing a consent document for other types of research as well.

○ **Option 1**

a) The only record linking the participant and the research would be the consent document:

b) The principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves subjects who use illegal drugs).

Under this option, each participant must be asked whether (s)he wants to sign a consent form; if the participant agrees to sign a consent form, only an IRB approved version should be used.

○ **Option 2**

a) The research presents no more than minimal risk to the participant:

b) Involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script):

STUDY PERSONNEL

Do you have study personnel who will be assisting with the research?
After selecting 'Yes' or 'No' you must save by hitting the 'Save Study Personnel Information' button.

(•) Yes ( ) No

Manage Study Personnel

Identify other study personnel assisting in research project:

- The individual listed as PI in the 'PI Contact Information' section should NOT be added to this section.
- If the research is being completed to meet the requirements of a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed as such below.

To add an individual via the below feature, search for applicable personnel first, then click "select" by the listing for the person you want to add as study personnel to your protocol. For each individual selected, be sure to specify responsibility in the project, whether authorized by the principal investigator to obtain informed consent, AND denote who should regularly receive E-IRB notifications.

NOTE: Study personnel are required to receive human research protection (HSP) training before implementing any research procedures (e.g., CITI). For information about mandatory training requirements for study personnel, visit UK's FAQ's on Mandatory Training web page, or contact ORI at 859-257-9428. If you have documentation of current HSP training other than that acquired through UK CITI, you may submit it to ORI (Jen.Hill@uky.edu) for credit.

Study personnel assisting in research project:

Add Personnel

My Study Personnel	Last Name	First Name	Responsibility In Project	Role	A C	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	Removed?	Last Updated	Recorded Training	SFI
Details	Alcala	Ramona	Study Coordinator	SP	Y	N		P	Y	10/10/2017	N	01/24/2018	00009290	N
Details	Babalonis	Shanna	Sub-Investigator	SP	N	N	PhD		Y	03/01/2017	N	10/18/2017	10001351	N
Details	Barnes	Benjamin	Sub-Investigator	SP	Y	N	MD		Y	04/11/2017	N	09/20/2017	10218674	N
Details	Despa	Florin	Sub-Investigator	SP	N	N	PhD		Y	06/14/2017	N	09/20/2017	10993611	N
Details	Goldstein	Larry	Sub-Investigator	SP	N	N	MD		Y	06/08/2017	N	09/20/2017	12100460	N
Details	Kuhl	Judi	Consultant/Advisor	DP	N	Y			Y	09/06/2017	N	09/20/2017	00005724	N
Details	Moliterno	Nathaniel	Study Coordinator	SP	Y	Y			Y	11/01/2017	N	11/30/2017	10886333	N
Details	Morris	Stephanie	Project Assistance/Support	DP	N	Y			Y	09/11/2017	N	11/30/2017	10659474	N
Details	Nsoesie	Michael	Study Coordinator	DP	Y	Y	MS		Y	08/26/2016	N	10/25/2017	12223473	N
Details	Ryan	Stephen	Sub-Investigator	SP	N	N	MD		Y	05/05/2016	N	09/20/2017	00010938	N
Details	Taylor	Deborah	Project Assistance/Support	DP	N	Y	MS		Y	03/22/2016	N	10/24/2017	00002533	N
Details	Wagner	Renee	Study Coordinator	DP	Y	Y	RN		Y	01/23/2018	N	09/20/2017	00009487	N

RESEARCH DESCRIPTION

****!!!PLEASE READ!!!** Known Issue: The below text boxes do not allow symbols, web addresses, or special characters (characters on a standard keyboard should be ok). If something is entered that the text boxes don't allow, user will lose unsaved information.**

Workaround(s):

- **Save your work often to avoid losing data.**
- **Use one of the attachment buttons in this section, or under the Additional Information section to include the information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background: Provide an introduction and background information. Describe past experimental and/or clinical findings leading to the formulation of your study. For research involving investigational drugs, describe the previously conducted animal and human studies. You may reference grant application/sponsor's relevant protocol pages and attach as an appendix in the E-IRB "Additional Information" section. For research that involves FDA approved drugs or devices, describe the FDA approved uses of this drug/device in relation to your protocol. Attach a copy of the approved labeling as a product package insert or from the Physician's Desk Reference in the applicable E-IRB "Study Drug" or "Study Device" section.

Impaired blood flow through microvessels (arterioles and capillaries) leads to irreversible damage to cells within the affected watershed. In addition to hypertension and age, Type-2 diabetes (DMII) independently contributes to microvascular disease (1,2). Distinct from other diabetic complications, the impact of diabetes on neurovascular function has not clearly been shown to correlate with measures of hyperglycemia or peripheral glucose regulation (3,4). The pathophysiology underlying the association between type-2 diabetes, vascular injury and neural damage, including CNS parenchymal loss and PNS neuropathy, remains uncertain. Normally amylin, a byproduct of the synthesis of insulin by pancreatic ß-cells, crosses the blood brain barrier (5) and binds to neurons in feeding centers (6-8) where it is believed to induce anorexic effects (9). Amylin aggregates are found in microvessels of pancreas, brain, hearts and kidneys of individuals with DMII or obesity (10-13). We have demonstrated amylin aggregates in microvessels of peripheral nerves in rats overexpressing human amylin (unpublished). It is unknown whether amylin deposits are a consequence or a trigger of vascular injury, but they are clearly associated and may present a potential target for reducing diabetes-associated microvascular disease. Furthermore, their accumulation in peripheral nerve microvasculature and red blood cells (RBCs) offers possible foci for a peripheral biomarker of diabetes-induced CNS microvascular disease.

Objectives: List your research objectives. You may reference grant application/sponsor's relevant protocol pages and attach as an appendix in the E-IRB "Additional Information" section.

Hypothesis: Patients with DMII have significant amylin deposition in the peripheral vasa nervorum and on RBCs that correlates with severity of clinical peripheral polyneuropathy and reduction of peripheral nerve conduction velocities (NCVs); these amylin measures thereby become surrogates of microvascular disease and may serve as metrics of disease severity. Aim: Obtain serum HbA1c, skin punch biopsy, RBCs, NCVs and clinical sensory examination from forty consenting adults previously diagnosed with DMII. Skin biopsy from volar forearm and red blood cell samples will be processed for amylin deposition. This pilot study will provide preliminary data to fuel a larger, potentially multi-center, clinical trial investigating the utility of peripheral amylin or RBC amylin as a quantitative biomarker of microvascular disease that would include monitoring the effect of potential therapies. Measuring serum HbA1c will allow for possible correlation to chronic extracellular glucose concentration. Based on our preliminary data from a rat model of type-2 diabetes that expresses human amylin in the pancreas, we anticipate an increased amylin deposition in the skin blood vessels with the progression of type-2 diabetes as measured by sensory examination and NCVs.The ability to easily identify and target a potential driver of microvascular disease may help prevent the devastating effects of the vascular complications of DMII, including cardiovascular disease, retinopathy, nephropathy and dementia.

Study Design: Describe the study design (e.g., single/double blind, parallel, crossover, etc.). Indicate whether or not the subjects will receive placebo medication at some point in the research procedures. Also, indicate whether or not the subjects will be randomized in this study. You may reference sponsor's protocol pages and attach as an appendix in the E-IRB "Additional Information" section. (Including the study design table from a sponsor's protocol is helpful to IRB members.)

Community-Based Participatory Research: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.

Research Repositories: If the purpose of this submission is to establish a research repository describe the repository design and operating procedures. For relevant information to include, see question 22 of the UK IRB "Frequently Asked Questions (FAQs) on the Return of Research Results or Incidental Research Findings" [PDF].

Forty patients with previously diagnosed DMII and referred to the Kentucky Neuroscience Institute Neuromuscular Laboratory for nerve conduction velocity studies (NCVs) will be asked to participate in the study. Because this is a pilot study, every effort will be made to select a broad distribution of patients who are mildly to severely symptomatic based on NCVs. • Informed consent will be obtained from patients who have obtained NCVs as standard-of-care and are interested in participating. After those individuals sign an IRB-approved informed consent, data will be collected including duration of DMII diagnosis, current medications, height and

weight (to calculate body mass index [BMI]), family history of neuropathy, and results of blood tests if obtained within the previous 6 months to include comprehensive metabolic profile, complete blood count, lipid profile, vitamin B12, and thyroid stimulating hormone to help exclude other common causes of peripheral neuropathy. Participants will then undergo a skin biopsy taken from the volar forearm using a standardized kit and vibratory sensation will be measured over the tip of the 2nd digit (index finger) quantified using a Rydel-Seiffer 128 Hz tuning fork), and venipuncture for blood samples utilizing the UK Healthcare Clinical Laboratories. Blood samples will be collected for measure of RBC amylin (performed in Dr. Despa's laboratory) and HbA1c (UK Healthcare Clinical Laboratories), as well as those measures not performed in the previous 6 months to include metabolic profile, complete blood count, vitamin B12, and thyroid stimulating hormone. Skin biopsies will be collected and stored in formalin. The formalin-fixed skin biopsy will be paraffin embedded and sectioned for staining with an anti-amylin antibody as previously described (15). RBCs will be harvested from collected samples. Cells will by lysed, protein concentration will be determined, and amylin will be detected by immunofluorescence using enzyme-linked immunosorbent assay (ELISA) (14,15). The positive control for the amylin antibody is the pancreatic tissue from a patient with type-2 diabetes. Negative controls for the amylin antibody are pancreatic and liver tissues from amylin knockout (AKO) rats. Immunohistochemical staining and co-staining of the skin tissue with anti-amylin and anti-collagen IV antibodies will be performed to assess the level of amylin deposition in the skin sample and the localization of amylin deposition with respect to the blood vessel wall. To assess the density of the blood vessels that have amylin deposition, the tissue will be co-stained with anti-amylin and anti-collagen IV antibodies; co-localization will be analyzed using immunoconfocal microscopy (14). One week after NCV, biopsy, and venipuncture, participants will be scheduled for Pain Tests (see below) conducted at the Straus Behavioral Science Building, UKMC. Statistical analysis: The two measures of amylin will be compared using the Bland Altman procedure to determine how well the less invasive measure obtained from RBCs agrees with the more invasive punch biopsy measure. Then each amylin measure will be correlated with the Hba1c and NCV/sensory examination measures to determine how well these levels correlate with a measure of glucose control and with severity of neurologic disease. Correlations will be based on Pearson's correlation coefficient. With a sample size of 40 patients this will have 80% power to detect a correlation at least as large as 0.414 at the 0.05 level of significance. The statistical design has been discussed with Dr. Richard J. Kryscio, consulting statistician for UK COM.

Attachments

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Study Population: Describe the characteristics of the subject population, such as anticipated number, age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion. Explain the rationale for the use of special classes such as fetuses, pregnant women, children, institutionalized, adults with impaired consent capacity, prisoners or others who are likely to be vulnerable. If women or minorities are included, please address how the inclusion of women and members of minority groups and their subpopulations will help you meet your scientific objectives. Exclusion of these groups requires clear and compelling rationale that shows inclusion is inappropriate with respect to the health of the subjects or that inclusion is inappropriate for the purpose of the study. Cost is not an acceptable reason for exclusion except when the study would duplicate data from other sources. Women of childbearing potential should not be excluded routinely from participation in clinical research.

Provide the following information:

• A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
• A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
• The proposed dates of enrollment (beginning and end);
• The proposed sample composition of subjects.

You may reference grant application/sponsor's relevant protocol pages and attach as an appendix using the below attachment button.

Forty patients, age 18 years or older, with previously diagnosed DMII and referred to the Kentucky Neuroscience Institute Neuromuscular Laboratory for nerve conduction velocity studies (NCVs) will be asked to participate in the study. Because this is a pilot study, every effort will be made to select a broad distribution of male and female patients, regardless of ethnicity, who are mildly to severely symptomatic based on NCVs.

Attachments

Subject Recruitment Methods & Privacy: Describe plans for the identification and recruitment of subjects, including how the population will be identified, and how initial contact will be made with potential subjects by those having legitimate access to the subjects' identity and the subjects' information. Describe the setting in which an individual will be interacting with an investigator. If applicable, describe proposed outreach programs for recruiting women and minorities as participants in clinical research.

Please note: Based upon both legal and ethical concerns, the UK Medical Institutional Review Board (IRB) will not approve finder's fees for research studies.

Subjects will be identified from the patient population that has been previously diagnosed with DMII and who were referred to the Kentucky Neuroscience Institute Neuromuscular Laboratory for nerve conduction velocity studies (NCVs). The assessment for eligibility will be done by Stephen Ryan, MD who will ask potential participants if they would like to be part of a research study of patients with DMII who have been referred for NCVs. Patients deemed eligible for the study and interested in participating will be approached to undergo participation in this study by a member of the research staff qualified to consent patients for the study. Forty patients with previously diagnosed DMII and referred to the Kentucky Neurological Institute (KNI) Neuromuscular Laboratory for nerve

conduction velocity studies (NCVs) will be asked to participate in the study. Initially all patients with a diagnosis of DMII referred for NCVs will be asked to participate. After 20 participants have been recruited, an interim analysis of upper extremity NCV data will be reviewed by Dr. Ryan, who will then selectively recruit if necessary based on NCV data to insure a broad distribution of participants with range of NCVs from normal to severe. Information related to participants will be treated in strict confidence to the extent provided by law. Their identities will be coded with a unique number and will not be associated with any published results. The code number and identity will be securely kept in a locked office by the study coordinator.

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Advertising: Specify if any advertising will be performed. If yes, please see "Advertisements - Application Instructions" for instructions on attaching copies of the information to be used in flyers or advertisements. Advertisements must be reviewed and approved by the IRB prior to use. For additional details, see topic "Recruitment" or "Advertising" on ORI's IRB Survival Handbook web page for the PI Guide to Identification and Recruitment of Human Subjects for Research [D7.0000] document [PDF]. If you will be recruiting subjects via advertising at non-UK owned or operated sites, you should include a copy of written permission from that site to place the advertisement in their facilities.

Not Applicable

Attachments

Informed Consent Process: Describe the consent/assent procedures to be followed, the circumstances under which consent will be sought and obtained, the timing of obtaining informed consent, whether there is any waiting period between informing the prospective subject and obtaining consent, who will seek consent (Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application), steps taken to minimize the possibility of coercion or undue influence, the method used for documenting consent, and if applicable who is authorized to provide permission or consent on behalf of the subject. Describe, if applicable, use of specific instruments or techniques to assess and confirm potential subjects' understanding of the nature of the elements of informed consent (i.e., research involving adult subjects with impaired consent capacity) and/or a description of other written materials that will be provided to participants or legally authorized representatives. If you have a script, please prepare it using the informed consent template as a guide, and submit it on a separate page. For additional information, see the "Informed Consent Standard Operating Procedures (SOPs)" [PDF].

Informed Consent for Research Involving Emancipated Individuals
If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **when preparing the IRB application and prior to submitting the application to the IRB**. Include legal counsel's recommendations (legal counsel's recommendations may be attached in the E-IRB "Additional Information" section as a separate document, if necessary). For a complete definition of emancipated minors, see the section on *Emancipated Individuals* in the Informed Consent SOP [PDF].

Informed Consent for Research Involving Non-English Speaking Subjects
If you are recruiting non-English speaking subjects, the method by which consent is obtained should be in language in which the subject is proficient. Describe the process for obtaining informed consent from prospective subjects in their respective language (or the legally authorized representative's respective language). In order to ensure that individuals are appropriately informed about the study when English is their second-language, describe a plan for evaluating the level of English comprehension, and the threshold for providing a translation, or explain why an evaluation would not be necessary. For additional information on inclusion of non-English speaking subjects, or subjects from a foreign culture, see Instructions for Recruiting Non-English Speaking Participants or Participants from a Foreign Culture.

Research Repositories
If the purpose of this submission is to establish a research repository describe the informed consent process. For guidance regarding consent issues, process approaches, and sample language see the "University of Kentucky Issues to be Addressed and Sample Consent Language for Tissue/Specimen Repositories or Individual Studies Banking Material for Future Use" [PDF].

Informed consent will be obtained at the Kentucky Neuroscience Institute Neuromuscular Laboratory from patients who have been previously diagnosed with DMII and have had NCVs as standard-of-care and are interested in participating. Prior to entering the study, the risks and benefits of participating will be explained to potential subjects. Patients will be given sufficient time to review and read through the consent form and ask questions. All questions will be answered to the patients' satisfaction. A copy of the signed informed consent will be placed in each subject's medical record. The original, signed informed consent form will be retained by the investigator. The study subject will receive a copy of the informed consent form.

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Research Procedures: Describe the research procedures that will be followed. Identify all procedures that will be carried out with each group of subjects. Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project.

After signing an IRB-approved informed consent, all research subjects will have: • skin biopsy, 3 mm in diameter, taken from volar forearm using a standardized kit and vibratory sensation measured over the tip of the 2nd digit (index finger) quantified using a Rydel-Seiffer 128 Hz tuning fork),. Skin biopsies will be collected and stored in formalin. • venipuncture for blood samples utilizing the UK Healthcare Clinical Laboratories (total volume = 30-60 ml). Blood samples will be collected for measure of RBC amylin (performed in Dr. Despa's laboratory) and HbA1c (UK Healthcare Clinical Laboratories), as well as those measures not performed in the previous 6 months to include metabolic profile, complete blood count, vitamin B12, and thyroid stimulating hormone (UK Healthcare Clinical Laboratories). • pain/sensory testing will be conducted (as described below) to assess sensory responses. Pain/Sensory Testing Procedures: These assays have been safely implemented in our previous research studies (as indicated below) and are designed not to cause and tissue damage. a. Pressure Algometer Test: The pressure algometer test will be conducted using a computerized system (Medoc AlgoMed, U.S.A, Durham, N.C.). Pressure is applied at the rate of 40 kilopascals/sec with an algometer device will be applied to the thenar eminence (the area just below the thumb) on the palm side of the dominant hand. Two trials will be conducted, with at least 5 minutes separating each application. The main outcome measures for this test are 1) first detection of pressure sensation (sensory threshold) and 2) first detection of a painful sensation (pain threshold) (measured in kPa). We have safely used this procedure in previous studies (Protocols # 14-0769-F3R, 11-0816, 11-0980). b. Cold Pressor Test: Participants immerse their non-dominant forearm in a warm water (room temperature) bath for a total of 2 minutes. After the 2 minutes is complete, the participant is assisted in placing his/her forearm in a cold water bath (1.0°C ± 0.5°C) and is instructed to not touch the side or bottom of the water bath. Participants will report when they begin to feel pain (pain threshold) and will remove their arm from the water when they can no longer tolerate the pain (pain tolerance). Cold water immersion will last for a maximum of 5 min (a predetermined safety cut-off to prevent numbness or tissue damage). Pain threshold and tolerance (seconds of immersion) will be recorded manually. Our laboratory has previous experience safely using this procedure (IRB Protocols #14-0769-F3R , 06-0605, 11-0816, 11-0980). c. Cold Thermode Testing: A thermode will be applied to on the dorsal surface of the hand. The temperatures will start at approximately room temperature (approx. 35°C) and will steadily decrease (lowest possible temperature is 0° C). Volunteers will indicate when they begin to feel a cold sensation (sensory threshold) and the thermode will be removed when the participant reports the sensation of pain (pain threshold). If the participant does not report any pain, the thermode will be removed when the temperature reaches 0°C. Sensory and pain threshold are the main outcome measures and will be measured in temperature (e.g., the temperature at which they begin to feel

cold and the temperature at which they detect the pain). Our laboratory has previous experience safely using this procedure (IRB Protocols #14-0769-F3R). d. Heat Thermode Test: A thermode will be applied to the skin of the arm. Thermode temperature will begin at approximately room temperature (approx. 35°C) and will steadily increase (highest possible temperature is 53° C). Volunteers will indicate when they begin to feel a hot sensation (sensory threshold) and the thermode will be removed when the participant reports the detection of pain (pain threshold). If the participant does not report any pain during a given trial, the thermode will be removed when the maximum temperature is reached (53° C). Two applications will be conducted during trial. Sensory and pain thresholds are the main outcome measures and will be measured in temperature (e.g., the temperature at which they begin to feel a hot sensation and the temperature at which they begin to feel pain).

Attachments

Data Collection: List the data or attach a list of the data to be collected about or from each subject (e.g. interview script, survey tool, data collection form for existing data).

If the research includes survey or interview procedures, the questionnaire, interview questions or assessment scales should be included in the application (use attachment button below).

The data collection instrument(s) can be submitted with your application in draft form with the understanding that the final copy will be submitted to the IRB for approval prior to use (submit final version to the IRB for review as a modification request if initial IRB approval was issued while the data collection instrument was in draft form).

The following data will be collected: • Results from relevant laboratory analyses • Results from sensory examination • Results from peripheral nerve conduction velocities (NCVs) • Data from your medical record including duration of DMII diagnosis, current medications, height and weight • No other areas will be examined

Attachments

Resources: Describe what resources/facilities are available to perform the research (i.e., staff, space, equipment). Such resources may include a) staffing and personnel, in terms of availability, number, expertise, and experience; b) psychological, social, or medical services, including counseling or social support services that may be required because of research participation; c) psychological, social, or medical monitoring, ancillary care, equipment needed to protect subjects; d) resources for subject communication, such as language translation services, and e) computer or other technological resources, mobile or otherwise, required or created during the conduct of the research. Please note: Some mobile apps may be considered mobile medical devices under FDA regulations (see FDA Guidance). Proximity or availability of other resources should also be taken into consideration, for example, the proximity of an emergency facility for care of subject injury, or availability of psychological support after participation.

Research activities conducted at performance sites that are not owned or operated by the University of Kentucky, at sites that are geographically separate from UK, or at sites that do not fall under the UK IRB's authority, are subject to special procedures for coordination of research review. Additional information is required (see ORI's Off-Site Research web page); supportive documentation can be attached in the E-IRB "Additional Information" section. Provide a written description of the role of the non-UK site(s) or non-UK personnel who will be participating in your research. The other site may need to complete its own IRB review, or a cooperative review arrangement may need to be established. Contact the Office of Research Integrity at (859) 257-9428 if you have questions about the participation of non-UK sites/personnel.

If the University of Kentucky is the lead site in a multi-site study, or the UK investigator is the lead investigator, describe the plan for managing the reporting of unanticipated problems, noncompliance and submission of protocol modifications and interim results from the non-UK sites.

Patient recruitment and consenting will be done at Kentucky Neuroscience Institute Neuromuscular Laboratory. Venipuncture for RBCs and HgA1c utilizing the UK Healthcare Clinical Laboratories. Storage of RBCs and skin biopsies, as well as their analyses for amylin, including all immunohistochemical staining and confocal-microscopic analysis will be done by Florin Despa, PhD (Co-Investigator) at his lab located in Room 459, Charles T. Wethington Building. Pain testing sessions will occur at the Straus Behavioral Science Building.

Potential Risks: Describe any potential risks or likely adverse effects of the drugs, biologics, devices or procedures subjects may encounter while in the study. Please describe any physical, psychological, social, legal or other risks and assess their likelihood and seriousness.

• Skin Biopsy: A skin biopsy is a generally safe procedure, but complications can occur, including bleeding, bruising, scarring and rarely an infection. The site may be sore afterwards. If an infection does occur, it can be treated. • Venipuncture: The risks of having blood drawn include slight pain, a bruise and/or bleeding at the site of the needle stick. Occasionally, a person may feel faint when blood is drawn. The site may be sore afterwards. Rarely, an infection may develop. If an infection does occur, it can be treated. • Pain Tests: The participants will feel acute painful sensations, but these resolve quickly and do not cause any tissue damage. Side effects may include skin redness, tenderness and irritation,. Participants have safely tolerated the proposed pain tests in previous studies and no serious adverse events have occurred (IRB Protocols #14-0769-F3R)

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Safety Precautions: Describe the procedures for protecting against or minimizing any potential risks, *including risks of breach of confidentiality or invasion of privacy*. Where appropriate, discuss provisions for ensuring necessary medical or professional intervention in the event of adverse events, or unanticipated problems involving subjects. Also, where appropriate, describe the provisions for monitoring the data collected to ensure the safety of subjects. If vulnerable populations other than adults with impaired consent capacity are to be recruited, describe additional safeguards for protecting the subjects' rights and welfare.

There will be no interventions, no changes in medications, and no "safety" risks to subjects.

Benefit vs. Risk: Describe potential benefits to the subject(s); include potential benefits to society and/or general knowledge to be gained. Describe why the risks to subjects are reasonable in relation to the anticipated benefit(s) to subjects and in relation to the importance of the knowledge that may reasonably be expected to result. If you are using vulnerable subjects (e.g., impaired consent capacity, pregnant women, etc…), justify their inclusion by describing the potential benefits of the research in comparison to the subjects' vulnerability and the risks to them. For information about inclusion of certain vulnerable populations, see the IRB/ORI Standard Operating Procedure for Protection of Vulnerable Subjects [C3.0100] [PDF].

Subjects may not receive any direct benefit from participating in this study. This pilot study will provide preliminary data to fuel a larger, potentially multi-center, clinical trial investigating the utility of peripheral amylin or RBC amylin as a quantitative biomarker of microvascular disease that would include monitoring the effect of potential therapies.

Available Alternative Treatment(s): Describe alternative treatments and procedures that might be advantageous to the subjects, should they choose not to participate in the study. This should include a discussion of the current standard of care treatment(s).

Not Applicable

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Research Materials, Records and Privacy: Identify the sources of research material obtained from individually identifiable living human subjects. Indicate what information (specimens, records, data, genetic information, etc.) will be recorded and whether use will be made of existing specimens, records or data. Explain why this information is needed to conduct the study.

Return of Research Results or Incidental Findings (if applicable):
If research has the potential to identify individual results or discover incidental findings that could affect the health of a subject, describe plans to assess, manage, and if applicable disclose findings with individual subjects or provide justification for not disclosing. For IRB expectations, refer to the UK IRB "Frequently Asked Questions (FAQs) on the Return of Research Results or Incidental Research Findings" [PDF].

The investigative team maintains the right to keep, preserve, use and dispose of the findings of this investigation in accordance with Health Insurance Portability and Accountability Act (HIPAA), and National Institute of Health (NIH) guidelines. The National Institute of Health (NIH) maintains the right to inspect the records of the study at any time. Investigational records from this study will be maintained in a confidential manner, subject names will not be associated with any published results.

Confidentiality: Specify where the data/specimens will be stored and how the researcher will protect both the data and/or specimens with respect to privacy and confidentiality. Address physical security measures (e.g., locked facility, limited access); data security (e.g., password-protection, data encryption); safeguards to protect identifiable research information (e.g., coding, links, certificate of confidentiality); and procedures employed when sharing material or data, (e.g., honest broker (if applicable), written agreement with recipient not to re-identify). If you plan to procure, store, and/or share material (tissue/specimens/data) expressly for use in current or future research, describe measures that you will take to secure and safeguard confidentiality and privacy.

Provide a time table for destroying the data/specimens and identify how they will be destroyed, or provide rationale for perpetual maintenance [Note: The investigator is responsible for retaining the signed consent and assent documents and IRB research records for at least six years after study closure as outlined in the Study Closure SOP [PDF]. If the research falls under the authority of FDA or other regulatory agency, the investigator is responsible for retaining the signed documents and IRB records for the period specified if longer than six years after completion of the study]. For multi-site studies, the PI consults the study sponsor regarding retention requirements, but must maintain records for a minimum of six years after study closure. Also, specify who will access the identified data/specimens, and why they need access. If applicable, describe what measures will be taken to ensure that subject identifiers are not given to the investigator. If applicable, describe procedures for sharing data/specimens with entities not affiliated with UK.

> *NIH-funded genomic research*: The National Institutes of Health (NIH) Genomic Data Sharing (GDS) Policy sets forth expectations that ensure the broad and responsible sharing of genomic research data consistent with the informed consent of study participants from which the data was obtained. If you are submitting genomic data to an NIH data repository, describe your NIH data sharing plan.

Please note: The IRB expects researchers to access the minimal amount of identifiers to conduct the study and comply with applicable HIPAA and Family Educational Rights and Privacy Act (FERPA) requirements. If data are going to be collected, transmitted, and/or stored electronically, for appropriate procedures please refer to the guidance document "Confidentiality and Data Security Guidelines for Electronic Data" [PDF].

Also please note that storage of data on cloud services may not be appropriate and is subject to applicable university policies regarding the use of cloud services. If deemed too sensitive or inappropriate to be stored or collected using cloud services, the IRB

may require an alternate method of data storage in accordance with applicable university policies and the electronic data security guidance document referenced above.

If a research protocol involves the creation and/or use of a computer program or application, mobile or otherwise, please specify whether the program/application is being developed by a commercial software developer or the research team and provide any relevant information regarding the security and encryption standards used, how data is stored and/or transmitted to the research team, what information about the subjects the program/application will collect, etc. The IRB may require software programs created or used for research purposes be examined by a consultant with appropriate Internet technology expertise to ensure subject privacy and data are appropriate protected.

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During and after this study, the subjects' identify will be kept confidential to the extent permitted by law. Patients will be identified by a code, and, except as set forth below, personal information from subjects' records will not be released to any third party without written permission. Subjects will not be personally identified in any publication or presentation about this study. However, the records may be reviewed, under the guidelines of the Health Insurance Portability and Accountability Act (HIPAA), and the National Institute of Health (NIH). Additionally, local site personnel, agents of the University of Kentucky, the Office to Research Integrity and the Institutional Review Board may review the study records including those with identifying information. The information may be disclosed if the recipients described above are not required by law to protect the privacy of the information. To protect confidentiality, access to the paper records will be limited to research staff. All paper records will be maintained in locked file cabinets within locked offices. Electronic data files will be password protected on password-protected, HIPAA-compliant computers maintained on a password-protected, HIPAA-compliant server in a secure environment. When the study has closed, paper records will archived at the Department of Neurology. Paper records will be held for a minimum of six years. Patient confidentiality will be preserved by HIPAA regulations and awareness of subject participation in this study will be confined to research personnel.

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Payment: Describe the incentives (e.g., inducements) being offered to subjects for their time during participation in the research study. If monetary compensation is offered, indicate how much the subjects will be paid and describe the terms and schedule of payment. (It is IRB policy that provision should be made for providing partial payment to subjects who withdraw before the completion of the research. Monetary payments should be prorated or paid in full.)

Participants will be paid $25 for the pain test visit.

Costs to Subjects: Describe any costs for care associated with research (including a breakdown of standard of care procedures versus research procedures), costs of test drugs or devices, and research procedure costs that are the subject's responsibility as a consequence of participating in the research. Describe any offer for reimbursement of costs by the sponsor for research related injury care.

There are no anticipated costs to the subject for care associated with this research.

Data and Safety Monitoring: The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research, clinical research, or NIH-funded/FDA-regulated clinical investigations.

If you are conducting greater than minimal risk research, clinical research, or your clinical investigation is NIH-funded/FDA-regulated, describe your Data and Safety Monitoring Plan (DSMP). Click here for additional guidance on developing a Data and Safety Monitoring Plan.

If this is a *non-sponsored investigator-initiated* protocol considered greater than minimal risk research, clinical research, or your clinical investigation is FDA-regulated, *and* if you are planning on using a Data and Safety Monitoring Board (DSMB) as part of your DSMP, click here for additional guidance for information to include with your IRB application.

When participants appear for sensory testing at the UK Robert Straus Behavioral Science Laboratory, 845 Angliana Avenue, Lexington, KY on or about 1 week after venipuncture and skin biopsy, the sites will be examined by study personnel. If evidence of continued inflamation, infection or other abnormal appearance, Dr. Slevin will examine site and treat as he opines medically appropriate. On or about 1 week after sensory testing, participants will be called and asked if they have any residual discomfort or other symptoms pertaining to the study. If a positive response, Dr. Slevin will be informed and take action based on his best medical judgement.

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Subject Complaints: Describe procedures (other than information provided in consent document) for handling subject complaints or requests for information about the research. The procedures should offer a safe, confidential, and reliable channel for current, prospective, or past research subjects (or their designated representative) permitting them to discuss problems, concerns and questions, or obtain information.

Requests for information about the research or complaints will be addressed directly to the principal investigator, Dr. Slevin. Each subject will be allowed access to any information derived from the study that will affect overall health or may be useful in future medical care.

Does your research involve **Non-English Speaking Subjects or Subjects from a Foreign Culture**?

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Describe how information about the study will be communicated to potential subjects appropriate for their culture, and if necessary, how new information about the research may be relayed to subjects during the study.

Include contact information for someone who can act as a cultural consultant for your study. The person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted. The consultant should not have any direct involvement with the study. If you do not know someone who would be willing to act as your cultural consultant, the Office of Research Integrity will try to find someone to fill this role (this may delay the approval process for your protocol). Please include the name, address, telephone number, and email of the person who will act as the cultural consultant for your study. For more details, see ORI's help page on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

For recruitment of Non-English speaking subjects, the consent document needs to be in the subject's native language. Download the informed consent template available in the E-IRB "Informed Consent/Assent Process" section and use it as a guide for developing the consent document. (Note: Your translated consent document can be attached to your application in the "Informed Consent" section; **be sure to save your responses in this section first**.)

If research is to be conducted at an international location, identify local regulations, laws, or ethics review requirements for human subject protection. If the project has been or will be reviewed by a local Ethics Committee, attach a copy of the review to the UK IRB using the attachment button below. You may also consult the current edition of the International Compilation of Human Research Standards

Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis C, etc…)**?

○ Yes ◉ No

HIV/AIDS Research

If you have questions about what constitutes a reportable disease and/or condition in the state of Kentucky, see ORI's summary sheet: "Reporting Requirements for Diseases and Conditions in Kentucky" [PDF].

HIV/AIDS Research: There are additional IRB requirements for designing and implementing the research and for obtaining informed consent. Describe additional safeguards to minimize risk to subjects in the space provided below.

For additional information, visit the online IRB Survival Handbook to download a copy of the Medical IRB's requirements for Protection of Human Subjects in Research Involving HIV Testing, and visit the Office for Human Research Protections web site for statements on AIDS research, or contact the Office of Research Integrity at 859-257-9428.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

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1) involves testing a Nonsignificant Risk (NSR) Device, or
2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?

○ Yes ◉ No

PI-Sponsored FDA-Regulated Research

If the answer above is yes, then the PI assumes the regulatory responsibilities of both the investigator and sponsor. The Office of Research Integrity provides a summary list of sponsor IND regulatory requirements for drug trials, IDE regulatory requirements for SR device trials, and abbreviated regulatory requirements for NSR device trials. For detailed descriptions see FDA Responsibilities for Device Study Sponsors or FDA Responsibilities for IND Drug Study Sponsor-Investigators.

- Describe your (the PI's) experience/knowledge/training (if any) in serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if you have transferred any sponsor obligations to a commercial sponsor, contract research organization (CRO), contract monitor, or other entity (provide details or attach FDA 1571).

IRB policy requires mandatory training for all investigators who are also FDA-regulated sponsors (see Sponsor-Investigator FAQs). A sponsor-investigator must complete the applicable Office of Research Integrity web based training, (drug or device) before final IRB approval is granted.

Has the PI completed the mandatory PI-sponsor training prior to this submission?

○ Yes ○ No

If you (the PI) have completed equivalent sponsor-investigator training, you may submit documentation of the content for the IRB's consideration.

Attachments

HIPAA

Is HIPAA applicable? ◉ Yes ○ No

(Visit ORI's Health Insurance Portability and Accountability Act (HIPAA) web page to determine if your research falls under the HIPAA Privacy Regulation.)

If yes, check below all that apply and attach the applicable document(s):

☐ HIPAA De-identification Certification Form
☐ HIPAA Waiver of Authorization

Attachments

STUDY DRUG INFORMATION

The term drug may include:

- FDA approved drugs,
- unapproved use of approved drugs,
- investigational drugs or biologics,
- other compounds or products intended to affect structure or function of the body, and/or
- complementary and alternative medicine products such as dietary supplements, substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease, or clinical studies of e-cigarettes examining a potential therapeutic purpose.

Does this protocol involve any use of a drug in a human other than the use of an approved drug in the course of medical practice?

○ Yes ◉ No

If yes, complete the questions below. Additional study drug guidance [HTML]

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Note: Inpatient studies are required by Hospital Policy to utilize the Investigational Drug Service (IDS). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with drug accountability good clinical practices.

Indicate where study drug(s) will be housed and managed:

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

Is the study being conducted under a valid Investigational New Drug (IND) application?

○ Yes ○ No

If Yes, list IND #(s) and complete the following:

IND Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Checkmark this if the study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND).

- FDA's Expanded Access Program Information (e.g., treatment IND)
- Guidance and definitions: "Expanded Access SOP" [PDF]

Please also complete and attach the Study Drug Form (required):

[PDF]

Attachments

STUDY DEVICE INFORMATION

A DEVICE may be a:

- component, part, accessory;
- assay, reagent;
- software or computer/phone application;
- other instrument if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease; or
- a homemade device developed by an investigator or other non-commercial entity and not approved for marketing by FDA.

For additional information, helpful resources, and definitions, see ORI's Use of Any Device Being Tested in Research web page.

Does this protocol involve testing (collecting safety or efficacy data) of a medical device including an FDA approved device, unapproved use of an approved device, humanitarian use device, and/or an investigational device?

○ Yes ◉ No

[Note: If a marketed device(s) is only being used to elicit or measure a physiologic response or clinical outcome, AND, NO data will be collected on or about the device itself, you may answer “no” above, save and exit this section, (Examples: a chemo drug study uses an MRI to measure tumor growth but does NOT assess how effective the MRI is at making the measurement; an exercise study uses a heart monitor to measure athletic performance but no safety or efficacy information will be collected about the device itself, nor will the data collected be used for comparative purposes against any other similar device).]

If you answered yes above, please complete the following questions.

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

Is the study being conducted under a valid Investigational Device Exemption (IDE) or Humanitarian Device Exemption (HDE) application? See UK HUD SOP [PDF] for guidance.

○ Yes ○ No

If Yes, list IDE or HDE #(s) and complete the following:

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment or Compassionate Use IDE under the Food and Drug Administration (FDA) Early Expanded Access program.

- FDA's Early Expanded Access Program Information
- Guidance and definitions: "Medical Device Clinical Investigations, Compassionate Use, and Treatment IDE SOP" [PDF]

Does the intended use of any device used in this study meet the regulatory definition of Significant Risk (SR) device?

○ Yes. Device(s) as used in this study presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential

for serious risk to the health, safety, or welfare of a subject.

No. All devices, as used in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Please also complete and attach the Study Device Form (required):

[PDF]

Attachments

RESEARCH SITES

In order for this section to be considered complete, you must click "SAVE" after ensuring all responses are accurate.

A) Check all the applicable sites listed below at which the research will be conducted. If none apply, you do not need to check any boxes.

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☑ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☐ UK Hospital

Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

***Fayette Co. School systems, as well as other non-UK sites, have additional requirements that must be addressed. See ORI's Off-site Research Instructions web page for details.**

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Norton Healthcare
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Veterans Affairs Medical Center
- ☐ Other Hospitals and Med. Centers

- ☐ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

List all other non-UK owned/operated locations where the research will be conducted:*

*A letter of support and local context is required from non-UK sites. Click HERE for more information.

Attachments

B) Is this a multi-site study for which you are the lead investigator or UK is the lead site? ○ Yes ◉ No

If **YES**, you must describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites in the E-IRB "Research Description" section under *Resources*.

If the non-UK sites or non-UK personnel are *engaged* in the research, there are additional federal and university requirements which need to be completed for their participation, such as the establishment of a cooperative IRB review agreement with the non-UK site. Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

RESEARCH ATTRIBUTES

Indicate the items below that apply to your research. Depending on the items applicable to your research, you may be required to complete additional forms or meet additional requirements. Contact the ORI (859-257-9428) if you have questions about additional requirements.

☐ Not applicable

Check All That Apply

- ☐ Academic Degree/Required Research
- ☐ Aging Research
- ☐ Alcohol Abuse Research
- ☐ Cancer Research
- ☐ Certificate of Confidentiality
- ☐ CCTS-Center for Clinical & Translational Science
- ☑ Clinical Research
- ☐ Clinical Trial
- ☐ Clinical Trial Multicenter(excluding NIH Cooperative Groups)
- ☐ Clinical Trial NIH cooperative groups (i.e., SWOG, RTOG)
- ☐ Clinical Trial Placebo Controlled Trial
- ☑ Clinical Trial UK Only
- ☑ Collection of Biological Specimens
- ☐ Collection of Biological Specimens for Banking
- ☐ Community-Based Participatory Research
- ☐ Data & Safety Monitoring Board
- ☑ Data & Safety Monitoring Plan
- ☐ Deception
- ☐ Drug/Substance Abuse Research
- ☐ Educational/Student Records (e.g., GPA, test scores)
- ☐ Emergency Use (Single Patient)
- ☐ Genetic Research
- ☐ Gene Transfer
- ☐ GWAS (Genome-Wide Association Study) or NIH-funded study generating large scale genomic data
- ☐ International Research
- ☐ Internet Research
- ☐ Planned Emergency Research Involving Waiver of Informed Consent
- ☐ Pluripotent Stem Cell Research
- ☐ Recombinant DNA
- ☐ Survey Research
- ☐ Transplants
- ☐ Use of radioactive material, ionizing radiation, or x-rays [Radiation Safety Committee review required]
- ☐ Vaccine Trials

Click applicable listing(s) for additional requirements and/or information:

- Cancer Research (MCC PRMC)
- Certificate of Confidentiality
- CCTS (Center for Clinical and Translational Science)
- Clinical Research
- Clinical Trial

*Reminder: Ensure compliance with clinicaltrials.gov registration requirements for applicable clinical trials

- Collection of Biological Specimens for Banking
- Collection of Biological Specimens
- Community-Based Participatory Research
- Data & Safety Monitoring Board
- Data & Safety Monitoring Plan
- Deception*

*For deception research, also go to the Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- Emergency Use (Single Patient) [attach Emergency Use Checklist]
- Genetic Research
- Gene Transfer
- HIV/AIDS Research
- Screening for Reportable Diseases [E2.0000]
- International Research
- Planned Emergency Research Involving Waiver of Informed Consent*

*For Planned Emergency Research Involving Waiver of Informed Consent, also go to the Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"

- Use of radioactive material, ionizing radiation or x-rays for research

FUNDING/SUPPORT

If the research is being submitted to, supported by, or conducted in cooperation with an external or internal agency or funding program, indicate below all the categories that apply.

☐ Not applicable

Check All That Apply

- ☑ Grant application pending
- ☐ (HHS) Dept. of Health & Human Services
  - ☐ (NIH) National Institutes of Health
  - ☐ (CDC) Centers for Disease Control & Prevention
  - ☐ (HRSA) Health Resources and Services Administration
  - ☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
- ☐ (DoJ) Department of Justice or Bureau of Prisons
- ☐ (DoE) Department of Energy
- ☐ (EPA) Environmental Protection Agency
- ☐ Federal Agencies Other Than Those Listed Here
- ☐ Industry (Other than Pharmaceutical Companies)
- ☐ Internal Grant Program w/ proposal
- ☐ Internal Grant Program w/o proposal
- ☐ National Science Foundation
- ☐ Other Institutions of Higher Education
- ☐ Pharmaceutical Company
- ☐ Private Foundation/Association
- ☐ U.S. Department of Education
- ☐ State

Other:

Click applicable listing(s) for additional requirements and/or information:

- (HHS) Dept. of Health & Human Services
- (NIH) National Institutes of Health
- (CDC) Centers for Disease Control & Prevention
- (HRSA) Health Resources & Services Administration
- (SAMHSA) Substance Abuse & Mental Health Services Administration
- Industry (Other than Pharmaceutical Companies) [IRB Fee Info]
- National Science Foundation
- (DoEd) U.S. Department of Education
- (DoJ) Department of Justice or Bureau of Prisons
- (DoE) Department of Energy
- (EPA) Environmental Protection Agency

Specify the funding source and/or cooperating organization(s) (e.g., National Cancer Institute, Ford Foundation, Eli Lilly & Company, South Western Oncology Group, Bureau of Prisons, etc.):

Internal Neurology Grant Proposal

Add Related Grants

If applicable, please search for and select the OSPA Account number or Electronic Internal Approval Form (eIAF) # (notif #) associated with this IRB application:

Add Related Grants

Grant/Contract Attachments

Attach Type	File Name
GrantContract	DMII_Amylin-Research_Grant_References_09-20-2017.pdf
GrantContract	Slevin Neurology Research Proposal v2.pdf

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other DoD resources. (See DoD SOP [PDF] for details).

○ Yes ◉ No

Using the “attachments” button (below), attach applicable materials addressing the specific processes described in

the DoD SOP.

DOD SOP Attachments

Additional Certification: (If your project is federally funded, your funding agency may request an Assurance/ Certification/Declaration of Exemption form.) Check the following if needed:

☐ Protection of Human Subjects Assurance/Certification/Declaration of Exemption (Formerly Optional Form – 310)

OTHER REVIEW COMMITTEES

If you check any of the below committees, additional materials may be required with your application submission.

Does your research fall under the purview of any of the other review committees listed below? [*If yes, check all that apply and attach applicable materials using the attachment button at the bottom of your screen.*]

○ Yes ◉ No

☐ Institutional Biosafety Committee
☐ Radiation Safety Committee
☐ Radioactive Drug Research Committee
☐ Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)
☐ Graduate Medical Education Committee (GME)
☐ Office of Medical Education (OME)

Additional Information

- Institutional Biosafety Committee (IBC)--Attach required IBC materials
- Radiation Safety Committee (RSC)-- For applicability, see instructions and/or upload form [WORD] [RTF]
- Radioactive Drug Research Committee (RDRC)--information
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)**--Attach MCC PRMC materials, if any, per instructions
- See requirement of Office of Medical Education (OME)
- See requirement of Graduate Medical Education Committee (GME)

Attachments

**** If you are proposing a study involving cancer research, be sure to have "Cancer Research" marked in the E-IRB "Research Attributes" section.** If your study involves cancer research, ORI will provide a copy of your research protocol to the Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC). The MCC PRMC is responsible for determining whether the study meets the National Cancer Institute (NCI) definition of a clinical trial and for issuing documentation to you (the investigator) which confirms either that PRMC approval has been obtained or that PRC review is not required. Your IRB application will be processed and reviewed independently from the PRMC review.

ADDITIONAL INFORMATION/MATERIALS

Do you want specific information inserted into your approval letter? ○ Yes ◉ No

Approval Letter Details (e.g., serial #):

Submission Description: If you wish to have specific details included in your approval letter (e.g., serial #, internal tracking identifier, etc…), provide that information here as you wish it to be seen on the approval letter. These details will be automatically merged into a field at the top of the approval letter when it is generated. If these details need to be changed as a result of revisions or modifications to the application, you are responsible for updating the content of the field below accordingly.

Protocol/Product Attachments - For each item checked, please attach the corresponding material.

- ☐ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☐ Drug Documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.)
- ☐ Device Documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.)
- ☑ Other Documents

Protocol/Product Attachments

NOTE: Instructions for Dept. of Health & Human Services (DHHS)-approved protocol [HTML]

If you have password protected documents, that feature should be disabled prior to uploading to ensure access for IRB review.

Additional Materials:

If you have other materials you would like to include in your application for the IRB's consideration, please attach using the Attachments button below.

[To view what materials are currently attached to your application, go to "Application Links" in the menu bar on the left and click "All Attachments".]

Attachments

Attach Type	File Name
AdditionInfoConsiderations	McGill Questionaire.pdf
AdditionInfoConsiderations	Protocol Sheets_.xls
AdditionInfoConsiderations	Online_Deviation_ViewReportable.pdf
AdditionInfoConsiderations	DMII_Amylin-Research_Grant_References_09-20-2017.pdf
AdditionInfoConsiderations	42732_DEVIATION_APPROVAL_LETTER_ID _ 218__11-29-2017.pdf

SIGNATURES (ASSURANCES)

On all IRB applications there is a requirement for additional assurances by a Department Chairperson (or equivalent) [hereafter referred to as "Department Authorization"], and when applicable, a Faculty Advisor (or equivalent), which signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans.

For a list of responsibilities reflected by signing the Assurance Statement, download the guidance document "What does the Department Chairperson's Assurance Statement on the IRB application mean?"

Required Signatures:

First Name	Last Name	Role	Department	Date Signed	
John	Slevin	Principal Investigator	Neurology	09/25/2017 11:53 AM	View/Sign
Larry	Goldstein	Department Authorization	Neurology	09/22/2017 05:00 PM	View/Sign

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects and I agree:

1. To comply with all IRB policies, decisions, conditions, and requirements;
2. To accept responsibility for the scientific and ethical conduct of this research study;
3. To obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent/assent form;
4. To report to the IRB in accord with IRB/IBC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to subjects;
5. To complete, on request by the IRB for Full and Expedited studies, the Continuation/Final Review Forms;
6. To notify the Office of Sponsored Projects Administration (OSPA) and/or the IRB (when applicable) of the development of any financial interest not already disclosed;
7. Each individual listed as study personnel in this application has received the mandatory human research protections education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

☑ Furthermore, by checking this box, I also attest that I have appropriate facilities and resources for conducting the study. If applying for an exemption, I also certify that the only involvement of human subjects in this research study will be in the categories specified in the Protocol Type: Exemption Categories section.

*You will be able to "sign" your assurance after you have sent your application for signatures (use Submission section). Please notify the personnel required for signing your IRB application after sending for signatures. Once all signatures have been recorded, you will need to return to this section to submit your application to ORI.

Department Authorization

☑ This is to certify that I have reviewed this research protocol and that I attest to the scientific validity and importance of this study; to the qualifications of the investigator(s) to conduct the project and their time available for the project; that facilities, equipment, and personnel are adequate to conduct the research; and that continued guidance will be provided as appropriate. When the principal investigator assumes a sponsor function, the investigator is knowledgeable of the additional regulatory requirements of the sponsor and can comply with them.

*If the Principal Investigator is also the Chairperson of the department, the Vice Chairperson or equivalent should complete the "Department Authorization".

SUBMISSION INFORMATION

Each Section/Subsection in the menu on the left must have a checkmark beside it indicating the Section/Subsection has been completed; otherwise your submission for IRB review and approval will not be able to be sent to the Office of Research Integrity/IRB.

If your materials require review at a convened IRB meeting which you will be asked to attend, it will be scheduled on the next available agenda and a message will be forthcoming to notify you of the date.

Modification Request Information

Select One:

- ◉ This modification does not increase risk to study participants.
- ○ This modification may or will increase risk to study participants.

Is this modification request due to an Unanticipated Problem/Adverse Event, or Protocol Violation?

- ○ Yes ◉ No

In your professional opinion, does this modification involve information that might relate to a subject's willingness to continue to take part in the research?

- ○ Yes ◉ No

If yes, state how the information will be communicated to subjects (i.e., re-consent, send letter, etc.):

For each proposed modification, include a justification.

Example: Jane Doe, MD, is being added as co-investigator because she has expertise with the subjects on this protocol. She has completed human subject protections training, and is authorized to obtain consent.

Study Personnel adding Alcala.

Your protocol has been submitted.

Save Only **The PI must login to submit this protocol.**

	Document Type	File Loaded	Document Description	File Size	Modified By	Mod Date
	Stamped Consent Form	IRB Memo Amylin Study.pdf		0.079	jlkear0	1/25/2018 10:31:51 AM
	Stamped Consent Form	IRB Memo Amylin Study Modification #2.pdf		0.064	jlkear0	1/25/2018 10:31:51 AM
	Stamped Consent Form	Clean_DMII_Amylin-Form_C_Med_and_HIPAA_1.5.2018.....pdf		0.101	jlkear0	1/25/2018 10:31:51 AM
	Stamped Consent Form	IRB Memo Amylin Study Modification #3 SP Add Alcala.pdf		0.060	jlkear0	1/25/2018 10:31:51 AM
	ApprovalLetter	ApprovalLetter.pdf		0.057	jlkear0	1/25/2018 10:31:50 AM
	CoverLetter	IRB Memo Amylin Study Modification #3 SP Add Alcala.pdf	Cover Memo SN#03 SP Add Alcala	0.048	samo222	1/24/2018 3:58:11 PM
	AdditionInfoConsiderations	42732_DEVIATION_APPROVAL_LETTER_ID_ 218__11-29-2017.pdf	Deviation Approval Letter	0.058	samo222	1/11/2018 12:02:22 PM
	Informed ConsentHIPAA Combined Form	Clean_DMII_Amylin-Form_C_Med_and_HIPAA_1.5.2018.....pdf	Clean_DMII_Amylin_Form_C_and_HIPAA__1.5.2018	0.059	samo222	1/11/2018 10:57:29 AM
	InformedConsent_HighlightedChanges	Tracked_DMII_Amylin-Form_C_Med_and_HIPAA_1.5.2018.pdf	Tracked_DMII_Amylin-Form_C_Med_and_HIPAA	0.071	samo222	1/11/2018 10:51:37 AM
	GrantContract	DMII_Amylin-Research_Grant_References_09-20-2017.pdf	DMII_Amylin-Research_Grant_References_09_20_2017	0.085	samo222	1/10/2018 12:12:50 PM
	CoverLetter	IRB Memo Amylin Study.pdf	Cover Memo	0.060	samo222	1/10/2018 12:07:21 PM
	GrantContract	Slevin Neurology Research Proposal v2.pdf	DMII_Amylin-Slevin Neurology Research Proposal v2	0.128	samo222	1/10/2018 11:40:07 AM
	AdditionInfoConsiderations	DMII_Amylin-Research_Grant_References_09-20-2017.pdf	DMII_Amylin-Research_Grant_References_09-20-2017	0.085	samo222	1/10/2018 11:39:28 AM
	AdditionInfoConsiderations	Online_Deviation_ViewReportable.pdf	42732 Protocol Deviation Information	0.073	samo222	1/10/2018 11:37:53 AM
	AdditionInfoConsiderations	Protocol Sheets_.xls	Protocol Sheets	0.095	samo222	1/5/2018 9:28:41 AM
	AdditionInfoConsiderations	McGill Questionaire.pdf	Patient Questionnaire	0.088	samo222	1/5/2018 9:28:23 AM
	CoverLetter	IRB Memo Amylin Study Modification #2.pdf	Cover Memo Modification #2	0.050	samo222	1/5/2018 9:24:48 AM

Protocol Changes

Protocol Number: 42732

No Changes
There are no recorded changes tracked for this protocol.

Study Personnel Changes:

00009290	
Name	Alcala, Ramona
Email	ramona.alcala1@uky.edu
Role 1	SP
Role 2	Study Coordinator
Is Contact	N
Room	
Dept Code	
Dept Desc	
SFI	N
Is PIRN	