Full Ethical Assessment Form

APPLICATION FOR ETHICAL APPROVAL OF A RESEARCH PROJECT FROM FACULTY ETHICS COMMITTEE

This application form is to be used by **STAFF** and **PGR STUDENTS** seeking ethical approval for an individual research project where preliminary ethical assessment has indicated that full ethical review is required.

A completed version of this document should be emailed to the Secretary of your appropriate Faculty Ethics Committee in the University. *Applications must be completed on this form; attachments will not be accepted other than those requested on this form. This form has been designed to be completed electronically; no handwritten applications will be accepted.*

Research must NOT begin until approval has been received from the appropriate Faculty Ethics Committee.

Section 1: Applicant Details

Applicant Name	[redacted]
Contact Email	[redacted]
Academic Unit	School of Agriculture, Food & Rural developments/ Human Nutrition Research Centre.
Applicant Type	□Staff □Undergraduate □Postgraduate Taught *X* Postgraduate Research

Section 2: Project Details

Project Title	**Growth of lettuce with different content of inorganic nitrate as a feeding strategy for placebo-controlled nutritional interventions to test the effects of inorganic nitrate on human health**
My Projects Reference	
Already has ethical approval	□Yes *X* No
Project Funder(s)	The Higher Committee For Education Development in Iraq (HCED)
Other organisations involved	NO
Proposed Start / End Date (dd/mm/yyyy)	Start Date 12/01/2015 End Date 01/09/2015
Category	□ Staff Research *X* Postgraduate Research □ Course
Preliminary Ethical Flag(s)	□ Animals □ Environment □ International (non EEA) □ NHS □ Data *X* Humans Non-Clinical
Supervisor (Student Research projects only)	[redacted]
Who is responsible for the overall management of the research? Name & post.	[redacted]
Who designed the research? Name & post.	[redacted]

	[redacted]
Who is conducting the research? Name & post.	[redacted]
Is this a re-approval of an existing project?	□Yes X No
Project type: Please mark the predominant nature of this project (one only).	□ Questionnaire / Survey x Experiments □ Observational □ Data based □ Other- define: The study is an experimental study design. The study is a one day nutritional intervention investigating the bioavailability of nitrate from lettuce produced with treatments that result in high or low nitrate content, and relate this to effects on blood pressure in young adult subjects.
Has Peer Review taken place	X Yes By: [redacted] □ No

Section 3: Project Outline & Proposed Research methods

Project outline & aims

Briefly describe the aims of this research, including the anticipated benefits and risks. This description must be in everyday language. If any jargon, technical terms or discipline-specific phrases are used, these should be explained. Please use no more than 500 words.

Background: The chemical composition of vegetables is dependent on several growing conditions. This effect relates to nitrate and phytochemical compounds including secondary metabolites and other bioactive non-nutritional compounds. Nitrate is important in vasodilation (relaxation of blood vessels) as a precursor of the potent vasodilator nitric oxide (NO). NO is released in the blood vessel wall and causes rapid relaxation of the blood vessel and a fall in BP.
Leafy vegetables are a natural source of dietary nitrate, which may reduce blood pressure (BP). However until now no appropriate placebo treatment has been available, so it is not possible to meet the criteria for randomised placebo-controlled intervention trials of highest quality. The effect of processed products such as juice may be different from that of fresh vegetables, e.g. due to conversion of nitrate to nitrite in the mouth during chewing.

Aim: to investigate whether two sets of lettuce specifically grown with different nitrate content but otherwise similar composition show sufficiently different effects on nitrate uptake in humans that they can be used in human intervention studies to investigate the effect of intake of nitrate in vegetables on blood pressure (BP).

Methods: This will be tested by growing lettuce with different fertiliser compositions resulting in high and low nitrate content and then investigating the bioavailability and short-term effect on BP in healthy young volunteers in a double-blind cross-over design. Eligible subjects will consume one meal each of either low or high nitrate lettuce. Urine, blood and saliva samples will be collected at baseline, for 6 hours after the ingestion and then again after 24hr. Blood Pressure BP will be measured continuously for 24 hours starting at baseline. The volunteers will repeat the intervention with the second treatment.

Screening: A series of questions regarding the study's inclusion/exclusion characteristics will be completed during an interview to define if participants are able to take part. The eligibility of each

subject will be then be confirmed at the first visit by measuring their body mass index. Measurements of height, weight and waist circumference will be taken for correlation with blood pressure measurements.

Proposed research methods (Experimental design)

Please provide an outline, in layman's terms, of the proposed research methods. Specify whether the research will take place outside of the UK or in collaboration with partners based outside the UK, and/or if research will take place using the internet. Present an outline of the method in a step-by-step chronological order, and avoid using jargon and technical terms as much as possible. Ensure you describe the key tasks including how data will be collected and used. Please do not exceed 500 words.

This is an educational project contributing to the award of Doctorate of Philosophy in Food Quality and Health.

The study will be conducted at the NU-Food - Food and Consumer Research Facility of the School of Agriculture, Food & Rural Development. After an initial screening visit, participants will be randomly assigned to receive two 50g-portions of lettuce (one with low and one with high nitrate content) on separate days. The duration of the study is about 4 weeks including the visits (6 times) and a washout period (3 weeks) between experimental day 1 and 2. In addition, participants will be asked to self-measure their resting BP and to collect additional urine and saliva samples at their house. A description of the proposed research methods is provided below:

Study Design and Subjects: This study is designed as a double-blind, randomized, crossover, intervention trial in which thirty healthy young volunteers (BMI: 20-25 kg/m2), non-smoking subjects (age: 18-35 years) will be recruited. In each of two intervention periods, subjects will be asked to eat 50g of either high nitrate lettuce or low nitrate lettuce (placebo) on a single occasion (the second visit) with dietary restriction for 3 days prior to the second visit and in the 24 hr period following after the consumption, concluded with a third visit, with at least 3 weeks washout period before the second 2-day intervention period. Urine, saliva and blood samples will be collected during a 6-hour period during the second visit. Urine samples will be collected during 24h from consumption until the third visit, to assess the pharmacokinetics and bioavailability and compliance to the interventions (details in the diagram of human trial).

The primary outcomes are 24-hour BP and nitrate content in urine, plasma and saliva. Samples will be collected into tubes and then analysed in the laboratory for the nitrate content (NO_3^-) by gas chromatography-mass spectroscopy (GCMS). Participants will follow specific dietary and lifestyle instructions to minimise confounding effects.

Participant will receive a small honorarium after the study and reasonable travel expenses will be reimbursed.

Dietary Interventions: Participants will be asked to arrive fasting in the morning of the second (main) visit and will consume a standard meal (Chicken Hotpot from ASDA) with the same drink water at the evening before and the evening after the visit, as well as following a diet that excludes a list of specific foods containing high nitrate (rocket, spinach, other leafy vegetables, radish and beet root), cured meat, cured seafood and cured fish, mature cheese for 24hr prior to the study and fasting on the morning of the study.

Anthropometry: we will measure body weight, height and waist circumference according to standardised protocols. Procedures are safe, not invasive and induce minimal discomfort for the participants.

Body Composition: This includes the measurement of body fat and muscle using a non-invasive technique called bio impedance analysis using a leg-to-leg bioelectrical impedance device (TANITA 300 MA). The procedure is safe, non-invasive and induces minimal discomfort for the participant. The duration of the measurement is of approximately 3-5 minutes.

24-hr BP monitoring: participants will be fitted with an automated portable device to measure BP over a 24-hr period. Participants will be instructed on how to safely operate the device. The measurement are safe and minimally invasive. BP readings will be recorded every 30 minutes during day time and every hour during the night to minimise the potential impact on sleep quality.

Urine samples: the morning void will be collected at home (pre supplementation) and after arrival full urine samples (all that the volunteer is able to produce) at set times before and after the supplementation (between baseline and 6hr) at NU-Food research facility. Subsequent collections afterwards (between 6-12hr and 12-24 hr) will take place at home in appropriate plastic containers and the samples will be collected at the final visit 24hr after the consumption. After measuring the volume of each sample, subsamples will be stored for analysis and for calculation of pharmacokinetics.

Saliva samples: a small saliva sample (~2ml) will be collected in disposable plastic containers at baseline and at every hour for 6 hours at NU-Food research facility; and then after 9 and 12 hour at home, with the final sample taken after 24 hr.

Blood Samples: Capillary tube (finger prick) or venous blood methods will be tested in a pilot study, since I am not able to take venous blood samples myself. We will compare the methods, and if the finger prick give us the sufficient amount of blood sample with good quality results, then we will choose the finger prick method.
If the finger prick method is appropriate, blood samples (~0.5 ml) will be collected at baseline, three and six hours post supplementation of treatments and then again after 24 hr.

Section 4: Environment

(Complete this section only if the project was flagged 'environment' at preliminary review.)
Please provide the locations in which your research will take place, together with the anticipated risks (destruction of habitat or artefacts/emissions, etc.), potential damage and mitigating measures planned. Please use no more than 700 words.

Section 5: Human participants in a Non-Clinical Setting

(Complete this section only if the project was flagged 'Human Participants in a Non-Clinical Setting' at preliminary review)

Participant Details

Does this research specifically target participants recruited by virtue of being (select all that apply):	*X* Students or staff of this University *X* Adults (over the age of 18 years and competent to give consent) □ Children/legal minors (anyone under the age of 18 years) □ Persons incapable of giving informed consent

	□ People from non-English speaking backgrounds □ Welfare recipients □ Prisoner or parolee
Does the study involve recruiting participants through a gatekeeper?	□Yes X No
Number of participants required for the study	30
Source and means by which participants are to be recruited:	Participants of this study will be healthy young volunteers recruited from among the general public via advertising. We will advertise our protocol among the university staff as well as in public places such as the city library, through email and posters. Volunteers responding to advertisements will be interviewed to assess their suitability using a standardised health questionnaire

Participant Information

	YES	NO
Will you inform participants that their participation is voluntary?	X	☐
Will you inform participants that they may withdraw from the research at any time and for any reason?	X	☐
Will you inform participants that their data will be treated with full confidentiality and that, if published, it will not be identifiable as theirs?	X	☐
Will you provide an information sheet that will include the contact details of the researcher/team?	X	☐
Will you obtain written consent for participation?	X	☐
Will you debrief participants at the end of their participation (i.e., give them an explanation of the study and its aims and hypotheses)?	☐	X
Will you provide participants with written debriefing (i.e., a sheet that they can keep that shows your contact details and explanations of the study)?	X	☐
If using a questionnaire, will you give participants the option of omitting questions that they do not want to answer?	X	☐
If an experiment, will you describe the main experimental procedures to participants in advance, so that they are informed about what to expect?	X	☐
If the research is observational, will you ask participants for their consent to being observed?	☐	☐

Participant consent

Please describe the arrangements you are making **to inform potential participants**, before providing consent, of what is involved in participating in your study and the use of any identifiable data, and whether you have any reasons for withholding particular information. Due consideration must be given to the possibility that the provision of financial or other incentives may impair participants' ability to consent voluntarily. (No more than 300 words)

In this study we propose to seek informed consent from participants after having been duly informed about the study. Participants expressing an interest in participating to the research project will be contacted in face to face to discuss their involvement in the study as well as check their eligibility.
Participants will have the opportunity to ask questions, clarify doubts about the study such as duration, reimbursements or risks. Participants will also be reassured that their participation is voluntary and that they are free to withdraw at any time. If volunteers are found to be eligible for the study they will be sent an information sheet by post or email which contains detailed information about the study. Participants will be invited to read the document carefully and discuss any of its content with members of the research team. Participants still interested in taking part will then be invited to the NU-Food - Food and Consumer Research Facility of the School of Agriculture, Food & Rural Development to attend their first visit.

Participants should be able to **provide written consent**. Please describe the arrangements you are making for participants to provide their full consent before data collection begins. If you think gaining consent in this way is inappropriate for your project, please explain how consent will be obtained and recorded. (No more than 300 words)

Informed consent from participants will be obtained only by a member of the research team. After having read the information sheet, and been briefed about the study, each participant will be given again the opportunity to ask questions and clarify doubts. Participants will then be asked to read the consent form and together with the researcher clarify any doubts before signing it. Specifically, they will be informed that they can withdraw from the study at any time and they will be asked if:

1) they consent to be informed of their clinically relevant results, 2) they are willing to give permission that their samples taken as part of the protocol of this study may be stored and used in further research studies, 3) they give permission that their samples taken as part of this study may be analysed in another laboratory outside of AFRD school and 4) they will be reassured that all samples will be linked-anonymised. Participants will be provided with a copy of the form to keep. The consent will be taken in a private quiet room to ensure confidentiality and minimise any discomfort to the participants when discussing potentially sensitive topics.

Please attach a copy of the information to be provided to the participant(s) to enable informed consent. This should include the 'Consent Form' & 'Participant Information Sheet' on appropriately headed paper.

Participant debriefing
It is a researcher's obligation to ensure that all participants are fully informed of the aims and methodology of the project, that they feel respected and appreciated after they leave the study, and that they do not experience significant levels of stress, discomfort, or unease in relation to the research project. Please describe whether, when, and how participants will be debriefed. (No more than 300 words)

There is no continued provision of any of the intervention at the end of the study. Participants may receive advice on how to increase nitrate consumption by consuming other vegetables if they wish to do so. After the study is completed, the participants will receive a written debriefing sheet explaining the aims, design and results of the study.

Please attach a copy of any debriefing sheet that you may provide on appropriately headed paper.

Potential risk to participants and risk management procedures

Identify, as far as possible, all potential risks (small and large) to participants (e.g. physical, psychological, etc.) that may be associated with the proposed research. Please explain any risk management procedures that will be put in place and attach any risk assessments or other supporting documents. Please answer as fully as possible. (No more than 300 words)

The screening questionnaire includes questions which some people may find sensitive. The questionnaire will be asked in person in a private environment and the interviewer will make sure that the participant will be comfortable in completing the questionnaire. If not, a more convenient time for the participant will be arranged. All information provided during the study will be kept confidential. Measurements that need be obtained in a fasted state will be carried out as early as possible in the morning, and participants will be offered a breakfast immediately afterwards. Participants will be asked to collect a urine sample for 24h and 2 times saliva samples at home which may potentially involve some brief discomfort. Participants will be reminded of this procedure and to increase fluid intake to facilitate the collection of the sample. Participants will commit to make a few changes that will modify their lifestyle in some degree. This will not have any effect on the participant health and they will be made aware of it. Medical supervision will be available if any adverse events occur during the study.

Section 6: Data

Please attach a copy of your data management plan (if available) or alternatively note where appropriate: whether consent will be sought, how data will be accessed, how participants' confidentiality will be protected, and any other relevant considerations. Information must be provided on the full data lifecycle, from collection to archive. If you do not have a data management plan, funder-specific plans are available from the Digital Curation Centre. See https://dmponline.dcc.ac.uk/

Data generated from each of these measurements will be anonymized and stored in password protected computer systems accessible only by members of the research team. Paper forms will be stored in locked filing cabinets. The urine and saliva samples will be stored in AFRD School refrigerators and freezers. The research team will implement and maintain an audit trail system to track the progress of samples from collection and storage to analysis. Access to samples will be limited to those involved in the processing and analysis of the samples. Participants' names will not be used to identify any samples; Samples will be stored in vials, identifiable by ID codes (link anonymized). Publications will not contain identifiable personal data.

Section 7: Permissions (Inc Overseas)

Overseas: For any research conducted outside the EEA the researcher is responsible for ensuring that local ethical considerations are complied with and that the relevant permissions are sought. If relevant please complete the table below otherwise move on to the permissions table.

Is the research to be conducted outside the EEA?	□Yes *x* No
If 'Yes' please state the location(s):	
Have the appropriate local ethical considerations been complied with and relevant permissions sought?	□Yes (awarded) – Please note in table below □Yes (pending) – Please note in table below □ No

Permissions: Please use the table below to record details of licenses or permissions required and / or applied for e.g. LEA, governing body, etc along with the reference, status and the date when it was granted.

Permission / License	Award Body	Reference Number	Date of Permission	Status e.g. Granted / Pending

Section 8: Risk Considerations & Insurance

Newcastle University must have in place appropriate insurance cover for its legal liabilities for research studies. Dependent upon the nature of the research and how it is governed cover will either come under Clinical Trials Insurance or Public Liability Insurance. Please refer to the supplementary guidance "When does the Insurance Office need to be notified of a research proposal?" for clarification.

Potential risk to researchers and risk management procedures

What are the potential risks to researchers themselves? This may include: personal safety issues, such as those related to lone or out of normal hours working or to visiting participants in their homes; travel arrangements, including overseas travel; and working in unfamiliar environments. Please explain any risk management procedures that will be put in place and attach any risk assessments or other supporting documents. (No more than 300 words)

The risk for the members of the research team are minimal as all the activities will take place at the purpose-built NU-Food - Food and Consumer Research Facility of the School of Agriculture, Food & Rural Development.

Please attach a risk assessment or any other appropriate documents as required.

Section 9: Supporting documentation

Please supply copies of any applicable and documents in support of your answers. Ensure that attached files have appropriate file names.

Document	Attached
Participant consent form	X
Participant information sheet	X
Participant debriefing document	*Since this will be based on the outcome of the study this will not be available until after the study has been completed*
Questionnaire(s)	X
Outline protocol	X
Project risk assessment	X
Travel risk assessment	☐
Original ethical assessment (re-approval only)	☐

Full Ethical Assessment Form

Data management plan	☐
Peer review evidence (Internal / non funded)	Yes by [redacted]
Local permissions / licenses (non EEA)	☐
Other ethical review forms	☐
Others (please list):	☐

Section 10: Declaration

I certify that the information contained in this application is accurate. I have attempted to identify the risks that may arise in conducting this research and acknowledge my obligations and the rights of the participants. I confirm that the research will be conducted in line with all University, legal and local ethical standards.

Name of Principal Investigator:	[redacted]
Signed:	
Date:	22/01/2015

If you have any queries on this form, please contact your Faculty Ethics Coordinator or visit the website at http://www.ncl.ac.uk/res/research

Please email or send this form to the appropriate Faculty Ethics Coordinator

For office use only:

The appropriate Ethics Committee has considered the ethical aspects of this proposal. The committee recommends that the programme/project be:

☐ Approved ☐ deferred (for reasons attached) ☐ not approved

Name of Committee Member:	
Ethics Committee Concerned:	
Signed:	
Date:	