UNIVERSITY OF OXFORD

PARTICIPANT INFORMATION SHEET

A ketone drink (ΔG®) to increase cerebral ATP in Parkinson's disease

You are being invited to take part in a research study as you have expressed an interest in doing so. Before you decide to participate, it is very important for you to understand why the research is being done and what it will involve. You can decline to participate in this study at any point.

Please take time to read the following information carefully.

This participant information leaflet is split into two parts:

Part 1

Describes the purpose of this study and what will happen to you if you decide to take part.

Part 2

Has more detailed information about how we will conduct the study.

Please make sure you ask us if there is anything that is not clear or if you would like more information.

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Part 1

The purpose of the study and what will happen to you if you take part.

1. Why have I been invited?
Because you expressed to one of our investigators your interest in volunteering for this trial.

2. What is the purpose of the study?
To investigate the hypothesis ketone bodies increase ATP levels in the brains of patients with Parkinson's disease and, thereby, ameliorate the energy deficit that contributes to the death of Parkinson's-sensitive neurons.

3. Do I have to take part?
No, it is up to you to decide whether to take part. If you do, you will be given this information sheet to keep and will be asked to sign a consent form. You are free to withdraw at any time without giving a reason. A decision to withdraw, or a decision not to take part, will not affect the standard of any medical care that you may need in the future.

4. What will happen to me if I take part?
Your participation in this study would involve two visits to the John Radcliffe Hospital and a total of roughly 3 hours.

During the first visit, we will ask you some questions to check whether you are eligible for the study and, if you agree to participate, you will be asked to sign a consent form.

For the second visit you will be asked to come in before breakfast. We will perform magnetic resonance imaging (MRI) to measure the levels of ATP in your brain and take blood samples to measure levels of glucose, insulin, free fatty acid, and beta-hydroxybutyrate. You will then be asked to consume a drink containing 350mg/kg of a ketone ester and to wait for one-hour before we repeat the MRI and blood tests. The MRI scans will not cause any discomfort and the estimated volume of collected blood is less than 30 ml (or about two tablespoons).

5. What else do I have to do?
Apart from the tests described above, there is nothing else that you need to do.

6. What is the drink that is being tested?
The ketone ester is called ΔG® and is transformed into ketone bodies after being digested. These substances are not normally found in the human diet but are produced by the liver during carbohydrate starvation as an alternative energy source for the brain.

7. What are the potential side effects drinking the ketone ester ΔG®?
ΔG® is generally well tolerated. You may experience none, some, or all mild episodes of the symptoms listed below:

- Diarrhoea

- Abdominal distension
- Nausea
- Headache
- Dizziness

Published studies, in rodents and healthy human subjects, support ΔG®'s safety and tolerability for longer-term use. In collaborations with UK Sport, numerous studies have been performed on ~250 athletes to determine the effects of single drinks on physical endurance and cellular metabolism without problems. The HVMN ΔG® drink has FDA approval and is commercially available in the United States as a sports supplement.

The tested dose is among the lowest studied. Daily doses six times greater than this have already proven to be safe. Participants will receive advice on how to minimise the bad taste of the drink.

8. What are the other possible disadvantages and risks of taking part?
Some participants find cannula insertions painful or have difficult to access veins. To minimise these problems, all cannula placements will be performed by experienced personnel.

9. What are the possible benefits of taking part?
There are no expected potential benefits of participating in this study.

10. What if there is a problem?
Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. Contact information is provided below.

11. Will my taking part in this study be kept confidential?
Yes. All the information about your participation in this study will be kept confidential. More details about this are included in Part 2.

12. Will I receive reimbursement for taking part in this research?
Yes. Participants who complete the study will receive £50 and reasonable travel expenses.

13. Who do I contact if I have problems?
If you wish to complain about any aspect of the way in which you have been approached or treated during this study, you should contact the investigators directly at 07444 054375 or nicholas.norwitz@dpag.ox.ac.uk. You may also contact the University of Oxford Clinical Trials and Research Governance (CTRG) office at 01865 572224 or the head of CTRG at ctrg@admin.ox.ac.uk.

Alternatively, you can contact Chief Investigator, Professor Michele Hu, at michele.hu@ndcn.ox.ac.uk.

The Patient Advisory Liaison Service (PALS) is a confidential NHS service that can provide you with support for any complaints or queries you may have regarding the care you receive as an NHS patient. PALS is unable to provide information about this research study.

If you wish to contact the PALS team, please contact:
PALS Office
Churchill Hospital
Old Road, Headington
Oxford OX3 7LE
Tel: 01865 235855
Email: PALSCH@ouh.nhs.uk

TΔS® Ltd, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this study. NHS indemnity operates in respect of the clinical treatment which is provided.

This completes Part 1 of the Information Sheet.
If the information in Part 1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

More detailed information about how we will conduct of the study

1. What will happen if I don't want to carry on with the study?
You can withdraw from the study at any point.

2. Will my taking part in this study be kept confidential?
All the information is entirely confidential. None of the information stored on computers will be identifiable with your name. We will replace your name, initials, and date of birth with a participant number to make sure you remain anonymous.

Responsible members of the University of Oxford may be given access to data for monitoring and/or audit of the study to ensure that the research is complying with applicable regulations.

4. What will happen to the samples that I give?
The samples you provide will be kept secure and anonymised.

5. Will any genetic tests be done?
No genetic tests will be performed as part of this study.

6. What will happen to the results of the research study?
At the end of the study, the results will be presented at regional, national, and international meetings and published in medical journals. All published results and information will be anonymised.

7. Who is organising and funding the research?

Research is organised by Department of Physiology, Anatomy and Genetics (DPAG) of the University of Oxford and is funded by TΔS® Ltd.

8. Who has reviewed the study?
This study has been given a favourable ethical opinion for conduct in the NHS by XXXX

This study is part of an educational project that will contribute towards doctoral degrees in Physiology, Anatomy, and Genetics for DPhil (PhD) candidates Nicholas Norwitz and Dr. Adrian Soto.

If you would like to be part of this study, or would like more information, please contact Nicholas Norwitz.
Email: nicholas.norwitz@dpag.ox.ac.uk
Mobile number: 07444 054375