Participant Information Sheet

Protocol Title: TACKLE Concussion Trial: **T**argeting **A**mateur **C**oncussions using **K**now**L**edge from neuroimaging and biomarkers to **E**nhance diagnosis and prevent long-term sequelae of Concussions.

Short Title: TACKLE Concussion Trial

Protocol Number: v 7.0

Administering Institution: University of Queensland

Chief Investigators: Fatima Nasrallah, Gary Mitchell, Martin Raftery, Brett Robinson, Warren MacDonald, Jason Ross, Wayne Leifert, Matt Trau.

1. Introduction

You are invited to participate in this study as you are a student at one of the participating schools, 14-19 years old and play rugby or basketball competitively within the schools' sports club. You are invited to take part as a control participant if you swim within the schools' sports club and DO NOT regularly participate in any contact sports. This Participant Information Sheet tells you more about the research project. It also explains in more detail the various tests involved. Knowing what is involved will help you decide if you want to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or would like to know more about. Before deciding whether or not you want to take part in the study, you might want to talk about this to a relative or friend.

Participation in this research is entirely voluntary. You can withdraw from this study at any point in time after you have been enrolled and there will be no negative consequence for you if you withdraw. If you do decide to take part in this study, you will be asked to sign the consent form if you are ≥18 years old or the assent form and your parent/guardian will be asked to sign a consent form if you are <18 years old. By signing this form, you are telling us that:

- You have read and understood the Participant Information Sheet
- You consent to your participation in this research project.
- You consent to the various tests described in this form.
- You consent to the use of your personal information as detailed in this form.

You will be given a copy of the signed consent form to keep, which also includes contact details for the research group, if you have any questions later.

2. What is the purpose of this research?

The purpose of this research is to conduct a study over 2-3 years that will help us to find a test that will allow us to diagnose when a player has had a concussion. This test will also tell us exactly when it is safe to return to play by informing us of when the brain has recovered following a concussion. By developing a method of accurately diagnosing a concussion and determining when the brain has recovered, it will become possible to manage concussions in a way that is better tailored for individual participants in the future.

3. What does participation in this research involve?

Most participants will only do each of the tests mentioned below once, when they have enrolled in the study. These are the baseline tests for all participants. Only if a head injury happens to yourself, or if you have agreed to be a control player, will you be asked to do more follow-up tests. Basketball players and swimmers will be asked to do baseline tests and some follow-up tests after they have taken part in a game/competition. Players can also be enrolled into the study on game days if they are interested in participating, or following a concussion or head knock. These players will not complete baseline testing, ,therefore an age appropriate median score will be used when analysing their data.

This study involves the following procedures (an overview is provided in the table below):

Enrolment Questionnaire - You or your parent/guardian will be asked to answer some questions to collect relevant brain-health related information. Please note that answering 'yes' to any of the questions does not exclude you from taking part in the study. Your honest answers will help the research team to identify, if the investigated biomarkers or the MRI results are influenced by any underlying medical conditions or medications. Your answers will be treated confidentially, only de-identified data will be published. The questionnaire will also collect personal details and body measurements (such as height and weight) relevant for completion of the study procedures and/or for data analysis.

Clinical/Cognitive Assessments – you will be asked to answer some questions to diagnose whether you have a concussion, using an online cognitive assessment that you can complete at home. We will use World Rugby's Head Injury Assessment (HIA) protocol to help determine whether you have had a concussion on game day. These assessments will be done once at baseline and again if you are suspected of having a concussion or head injury (HIA1), then repeated 2-3 hours later (HIA2) and then again at day 3 (HIA3). These can be done face to face or remotely via telehealth. An online cognitive test will complement the HIA process at baseline and during the recovery phase of a diagnosed concussion. At baseline, the HIA and neurocognitive data, which is collected by schools as part of their standard pre-season procedures, may also be attained from the participant's school records.

Activity/sleep tracking (actigraphy) – you will be asked to wear a smart device tracking your activity/sleep including your heart rate for two weeks at baseline. To capture the sleep changes following a concussion, participants who suffered a head injury and rugby control players will be asked to wear the smart device again from day 1 (game day) to day 13 (or up to day 21, if their symptoms persist). If you are in the basketball or swimmer control groups, you will be asked to wear the device a second time for two weeks after taking part in a game/competition. This will allow the characterization of your sleep and heart rate

without adding too much to your burden. The use of actigraphy will allow the detection of the acute and subacute effects of concussion on sleep-wake behavior.

Blood, finger-prick and saliva samples – you will be asked to provide blood, finger-prick and saliva samples at intervals which will allow us to identify concussion-specific biomarkers. When possible, blood samples are taken at baseline, and then 4 more times until 13 days after your injury, or when you are asked to act as a control for an injured player. An additional sample may be taken on day 21 if you have had persistent symptoms (injured players only). Each time 25 ml of bloods is taken. Samples will be taken by Sullivan and Nicolaides Pathology or other personnel trained in phlebotomy (e.g. a school nurse, physiotherapist or doctor).

Magnetic Resonance Imaging (MRI) scans – You will be asked as part of the study to undergo study MRI scans at baseline and up to four times after a head injury or concussion occurs (or only one additional time when you are acting as a control)). The second MRI will be at day 3 after your concussion, the third at 6 days after your concussion, and the fourth at day 13 post-concussion. If your symptoms persist on day 13 you may be asked to undergo an additional scan on day 21. The MRIs will be done at one of the specialist QScan radiology clinics (in Carindale, Clayfield, Redcliffe, Red Hill or Parkwood), participants may also attend the MRI clinic at Toowoomba Hospital. Participants and parents will have the chance to opt out of this procedure at baseline.

For participants who have a concussion or head injury:

	Clinical Assessment (HIA, SCAT5)	Biosample Collection (blood, finger-prick, saliva)	Neuroimaging (MRI)	Cognitive assessment	Activity/sleep tracking
Baseline	(if not collected from school records)✓	✓	✓ (if not opted out)	✓	✓ (2 weeks)
Day 1 (day of injury)	HIA1	✓			✓ (13-21 days)
Day 1 (within 3 hours of injury)	HIA2				
Day 3 (from date of injury)	HIA3	✓	✓	✓	
Day 6		✓	✓		
Day 13		✓	✓		

If symptoms persist beyond here:					
Day 21		✓*	✓*	✓*	

*only in players for who symptoms persist beyond Day 13

For controls in the study:

	Clinical Assessment (HIA, SCAT5)	**Biosample Collection (blood, finger-prick, saliva)**	**Neuroimaging (MRI)**	**Cognitive assessment**	**Activity/sleep tracking**
Baseline	✓ (if not collected from school records)	✓	✓ (if not opted out)	✓	✓ (2 weeks)
Day 1 (game/ competition day)		✓			✓ (basketball and swimmer controls 2 weeks; rugby controls 13 - 21 days)
Day 3 (from date of game/competition)		✓	✓	✓	
Day 6 (from date of game/competition)		✓			
Day 13 (from date of game/competition)		✓			

Duration of the project:

Your involvement in this study will be for the baseline tests and up to 21 days following your injury, or up to 14 days if you act as a control for an injured player. During this time, you will be contacted by the research team at each of the study timepoints to complete the assessments and liaise for study-related aspects. After you have fully recovered from an incident and completed all follow-up assessments, you may be asked, if you agree, to be followed-up with the same set of assessments after a potential subsequent incident. If you do not want to take part in further follow-up, you have completed the study after the first incident has been followed-up. The duration of the whole research project will be

approximately 3 years. The maximal follow-up time for any participant is till the end of the study.
There may be a larger research study following this study, and you will be asked in the assent form if you are happy to be contacted about the possibility of participating in the larger study at a later date. If you agree to be contacted, this does not commit you to take part in a future study, only to be contacted to discuss it.

Costs associated with participation:

There are no costs to you associated with participating in this research project. All tests and assessments required as part of the research project will be provided to you free of charge. When you attend an MRI scan for the study at one of the QScan facilities, the costs involved in this visit (e.g. travel) will be paid for by the study. Please send reimbursement requests for travel costs to the study coordinator (qbiconcussionstudy@uq.edu.au group).

4. What do I have to do?

The study tests, as described above, will be organised by the research team. This will include the study project coordinator, school nurse, Qscan personnel or other delegate who will contact you to arrange bookings. Taking part in this study will not restrict your diet or lifestyle in any way.

For **MRI scans**, your parent has to confirm the booking by phone or e-mail, answer some MRI specific safety questions and give their consent for you to have the MRI done. This can either be done in person, when your parent accompanies you to the scan or by signing an electronic consent (e.g. for parents/guardians of boarders, who cannot be present in person).
For the **cognitive assessment** using the ImPACT tool you will be given an access code to log onto the ImPACT testing platform. You will need to have access to a laptop or desktop computer and plan to have an undisturbed 30 minute time-slot available in which to complete the cognitive assessment. The assessment should take only 15-20 minutes, but it must be taken in one uninterrupted session for the data to be comparable between time points and participants.
The **finger prick microsampling and saliva sampling** will usually be done at school. If this is not possible, we will provide you and your parent/guardian with detailed instructions on how to take the samples. This is a simple procedure (similar to what people with diabetes do to measure their blood sugar) and can be done at home. If you visit a SNP practice for your blood sampling, please take the finger prick and saliva samples at home and bring them with you to drop off at SNP for further storage.

You will be asked to wear a **smart device tracking your activity/sleep** including your heart rate for two weeks at baseline. To capture the sleep changes following a concussion, participants who suffered a head injury and their control players will be asked to wear the smart device again from day 1 (game day) to day 13 (or up to day 21, if their symptoms persist). If you are in the basketball or swimmer control groups, you will be asked to wear the device a second time for two weeks after taking part in a game/competition.

5. Other relevant information about the research project

This study is being conducted across a number of participating schools across Queensland and aims to recruit up to 450 participants into the study. The samples and data collected, including MRI, blood biomarkers, activity/sleep tracking and cognitive assessments are all for research purposes. You will still receive standard medical care as per the standard process. In the case of any incidental findings on the study MRI scans, your general practitioner will be notified.

6. Do I have to take part in this research project?

Participation in any research project is **voluntary**. If you do not wish to take part, you do not have to do so. If you do decide to take part in the study but change your mind at a later stage, you are again **free to withdraw** from the project at any point in time. You may decide that you do not wish to participate in all the study tests, in this case your involvement would still be valued and we would only complete the tests that you feel comfortable to participate in. If you wish to withdraw from some or all study procedures we will ask you or your parent/guardian to fill in a withdrawal form in which you will be asked about the specific parts of the study you want to withdraw from.

7. What are the possible benefits of taking part?

By developing a method of accurately diagnosing a concussion and determining when the brain has recovered, it will become possible to manage concussions in a way that is better tailored for individual participants in the future. Therefore, your participation in this study may benefit other people with similar injuries in the future. There is no direct benefit to you from participating, but you may request an image of your baseline MRI scan and when you participate in baseline procedures you will receive a $50 voucher as a 'thank you' for your time.

8. What are the possible risks and disadvantages of taking part?

There are some minor risks associated with study procedures. MRI does not carry any significant risks if you are assessed as safe to undergo this. There are some conditions for ensuring your safety in MRI machines and you will be thoroughly assessed as medically fit to enter a scanning machine by Qscan or Hospital personnel every time before doing so. Having an MRI scan involves lying down, as still as possible, inside a small confined area for up to 30 min. The machine can be quite noisy and you will be provided with earphones to block the noise as much as possible. If you feel unable to enter the machine, or that once you are in there you wish to leave before the scan is finished, you can let the staff know and the MRI will be stopped.

Obtaining blood can cause pain, bleeding, bruising or swelling at the site of blood draw. Rarely a temporary loss of consciousness caused by a fall in blood pressure (i.e. syncope) or infection at the venepuncture site can occur. The necessary procedures will be performed by Sullivan and Nicolaides Pathology staff or the school nurses and sideline medical staff in case of any of the above-mentioned events. The collection of the finger prick samples can cause a temporary pain sensation but should have no side effects associated with them. There are no side effects associated with the cognitive testing or the activity/sleep tracking.

9. How do I withdraw from this research project?

If you decide to withdraw from the project, you can notify a member of the research team (qbiconcussionstudy@uq.edu.au) or any of the contact personnel at your local school including your sports coach, nurse, or administration staff. This notice will allow a member of the research team to discuss with you any special requirements linked to your decision to withdraw and you will be asked to fill out a withdrawal form. If you do withdraw your consent during the research project, the study team will not collect additional data from you. With your permission, data and samples already collected from you will be retained for inclusion in the data analysis phase of the research project, and to comply with local law and regulations. You will be asked about this in the withdrawal form. If you wish, all study data and samples collected from you for this study will be destroyed.

10. Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for reasons such as:
• The researchers becoming aware of evidence which shows the research is not valid.
• Decisions made by the sponsor or by local regulatory/health authorities.

11. What happens when the research project ends?

We expect the results of the study to be published in a medical journal, and these can be made available to you if you wish. We also expect the results to allow the development of a point-of-care diagnostic that can be used as an easy sideline test for diagnosis of concussion in the future.

12. What will happen to information about me?

By signing the consent form, you (if you are ≥18 years old) or your parent/guardian (if you are <18 years old) gives the researchers permission to collect and use data for the purpose of this research project. By signing the Assent form you also agree to this.

Once your blood samples have been collected, these will be processed and stored at Sullivan and Nicolaides Pathology and then stored and analysed in research laboratories at The University of Queensland or one of its research collaborators named in paragraph 14. If you or your parent/guardian agree, we will also store any excess biospecimen (red cells, plasma, serum finger-prick samples and saliva) for the future investigation of newly emerging concussion biomarkers and for the future development of a point of care diagnostic for concussion, which will be based on the findings of this study. Along with the electronic records for this study including your cognitive assessment and HIA data, excess biospecimens retained from this study will be destroyed after a maximum of 15 years. On the consent or assent form you will be given the option to opt out of using the biosamples for future studies and only have them analysed for this research study only.

As a participant, you will be assigned a unique study number. This unique study number will be used in any records that contain information about you that have been collected for the purposes of the research project, so that your identity (i.e. your name and any other information that could identify you) is always kept confidential.

Records linking your name to the unique study number will only be used for the purposes of the research project and will be kept on secure computer servers, and/or in a locked filing

cabinet in a locked office. They will only be made accessible to designated research project personnel, unless required otherwise by law.

Head Injury Assessment (HIA) and SCAT5 data, including identifiable data, will be recorded and stored by World Rugby in a secure encrypted cloud-based platform. World Rugby either uses the data service provider CSx Limited (New Zealand) or an Amazon Web Services (AWS) based in-house SCRM platform for data storage. In both cases your data is stored in a secure encrypted database on a server located in Ireland, in exactly the same secure way as the HIA data for professional rugby players is kept. The part of the database that contains information collected in the TACKLE study (including your data) is separate from the other data World Rugby stores and can only be accessed by delegated TACKLE study team members. Any data that is published will be de-identified, so that research results cannot be traced back to you.

Cognitive testing data, including identifiable data, will be recorded and stored in ImPACT Applications Inc.'s a secure cloud-based platform in Canada. Study participants with a testing account can access their own data only. Delegated TACKLE study team members have access, but can be restricted to see only specific data sets, for example of one study site only, to protect your privacy. Any data that is published will be de-identified, so that research results cannot be traced back to you.

MRI data will also be backed up from the RDM on tape media, remotely, for digital preservation, as is usual practice for data stored on UQ's supercomputer. Any data that is made publicly available, e.g. in publications, will be de-identified.

Activity/sleep tracking (actigraphy) data will be exported into excel sheets and uploaded and stored in UQ's secure REDCap database and/or to the data management system (RDM). These are secure password protected databases at the University of Queensland to which only the research team will have access.

Information about your participation in the research project may also be recorded in the patient records that a hospital, Medical Practice or medical service provider (such as Sullivan & Nicolaides Pathology or Qscan) collects and holds about you.

While in most cases the information collected about you during the research project will only be used and disclosed in de-identified form, your information collected during the research project may be accessed by authorised representatives of:

- the Administering Institution
- the hospital, school, medical practice or medical service provider taking part in the study procedures or providing treatment to you

This may occur for the purposes of verifying and monitoring the research study procedures and data, ensuring compliance with regulatory requirements, and as otherwise required by law. By signing the consent form, you or your parent/guardian authorise the disclosure of your information to the regulatory authorities and entities as noted above. By signing the assent form you also agree to this.

It is anticipated that the results of this project will be published and/or presented at a variety of national and international forums or platforms, including research papers, conference

presentations and/or meetings. Any personal information will be provided in such a way that you cannot be identified.

Unless specified otherwise in this section, or as permitted by law, all information about you which is collected for the research project will only be used and disclosed using the de-identified unique study number.

Regulations in Australia require all research-related data to be kept for a minimum of fifteen years. Your records will be kept for that period and may then be disposed of in line with contemporary data disposal systems.

13. Complaints and Compensation

If you suffer any injuries or complications as a result of your participation in this research project, you should contact the research team as soon as possible and you will be assisted with arranging appropriate medical treatment and care. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

14. Who is organising and funding the research and who may benefit financially?

This research project is an investigator-led study conducted by University of Queensland. The project brings together an array of partners – schools, national and international sporting bodies, and Australian companies. The partners include World Rugby, Rugby Australia, participating schools, Sullivan and Nicolaides Pathology, Qscan and Toowoomba Hospital. The neural biomarker component of this research project is being conducted by The University of Queensland (UQ), CSIRO and Trajan Scientific. The study is being funded through philanthropic funding at the Queensland Brain Institute.

At this point we do not anticipate that a financial benefit will come from the outcomes of the TACKLE research project described above. If you agree to the use of your samples and/or data for **future**, ethically approved research (this is entirely optional, and you can choose to say 'no' in the consent / assent form) this may result in the development of a **point of care diagnostic** which would help to better diagnose and manage concussion injuries in the future. In this case there may be a potential financial benefit to The University of Queensland, employees of The University of Queensland, collaborators or companies making use of the TACKLE project outcomes in future research. There will be no financial benefit to you or your family from participating in this research study.

By taking part in this research project you agree that samples of your blood or tissue (or data generated from analysis of these materials) may be provided to UQ for this research project and any subsequent activities ("Research"). UQ will store and control access to your samples in accordance with applicable research standards.

15. Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of suitably qualified individuals who form part of a Human Research Ethics Committee (HREC). This study has been reviewed and approved by the University of Queensland's HREC **[Reference number 2021/HE002696]**.

This project will be carried out according to the *National Statement on Ethical Conduct in Human Research (2007)*. This statement has been developed to protect the interests of people who agree to participate in human research studies.

16. Can I be asked to leave the study?

If you are not able to follow the requirements of the study or for any other reason, the study team may withdraw you from the study. For example, a doctor might consider it to be in your best interests to withdraw you from the study should it be judged that this would be better for your health. If you are asked to leave the study, then the reasons for this will be explained to you and you will have the opportunity to ask questions in relation to this decision.

17. Further information and who to contact.

The person you may need to contact will depend on the nature of your query.

If you want any further information concerning this project, or if you have any medical problems which may be related to your involvement in the project please contact:

Study contact person

Name	Jessie Wood
Position	Research Coordinator
Telephone	0447 470 075
Email	jessie.wood@uq.edu.au

Complaints contact person

Name	Fatima Nasrallah
Position	Lead/Principal Investigator
Telephone	(07) 3443 3004
Email	f.nasrallah@uq.edu.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	The University of Queensland HREC
HREC Executive Officer	HREC Coordinator
Telephone	(07) 3343 1657
Email	humanethics@research.uq.edu.au