Version History

Version Number	Version Date	Author	List of Changes
1.0	03-Feb-2023	Emily Birthisel	N/A: initial releases

2.0	22-Mar-2024	Emily Birthisel	Alignment to 2023 National Statement
			- Definitions added for
			  ○ Burden and Inconvenience
			  ○ Discomfort
			  ○ Higher Risk Research
			  ○ Lower Risk Research
			  ○ Risk of Harm
			- Updates to Review Pathways; Negligible and Low Risk research removed, Lower Risk and Higher Risk review pathways added
			- Research including genomics added to list of project elements that aren't eligible for Lower Risk review pathway
			- Higher Risk Review risk mitigation and monitoring strategies noted

3.0	10-Oct-2024	Emily Birthisel, Natasha Schott, Tim Tang, Lori Chiampas	- *RGO-FORM Ethics Amendment / Renewal Request* requirement for amendment on ERMS submission added - Section 8 reformatted for ease of reference - Addition of Standard Approval Conditions for Lower and Higher Risk Research - Data Management Plans to be submitted to HREC - Language amendments for consistency across document - Definitions for Adverse Reaction, Affiliated research, Amendment, Annual Report, business day, chair, Close out, Consent Waiver, Data Safety Monitoring Board, Good Clinical Practice, Non interventional, non affiliated research, Opt-Out approach, participant, research, researcher, serious adverse device effect, serious adverse reaction, significant safety issue and unexpected serious adverse device events, TGA added. - "Resources for Consultation" section added - Guidance for communicating with researchers added - Additional detail for safety, annual and close out reports requiring HREC submission described

			- Addition of review checklist regarding injury compensation, data management, research conflicts of interest..

1. Purpose and Introduction

This document sets out the standard operating procedures for review of clinical diagnostic research, and related research submissions to the Nutromics Diagnostics HREC (ND HREC) to ensure that the ND HREC operates in accordance with the National Statement.

2. Definitions

Adverse Event (AE)	Any undesirable clinical occurrence in a subject whether it is device related or not, that includes a clinical sign, symptom or condition and/or an observation of an unintended technical performance or performance outcome of the device.
Adverse Reaction (AR)	An adverse reaction is a response to an investigational device which is noxious and unintended. This includes adverse reactions which arise from: • The use of a medicinal product within the terms of the marketing authorization; • The use outside the terms of the marketing authorization, including overdose, off-label use, misuse, abuse and medication errors; • Occupational exposure.
Affiliated Research	Researchers who have formal ties, such as employment or contractual agreements, with Nutromics , which provide resources and oversight of the Nutromics' RGO to ensure adherence to ND HREC governance policies and standards.
Amendment	An amendment is a formal change to the protocol or essential documents, made to adjust the research design, procedures, or criteria.
Annual Report	A document that updates on research progress, including participant data and safety information. It ensures compliance with regulatory requirements and provides transparency about the research status.
Burden and Inconvenience	Not considered a type of harm or discomfort and therefore should not be viewed as a risk. May include the time that will need to be given to each participant to participate in the research being undertaken, for filling in forms and for costs related to travel etc. in relation to their participation in relevant Research.
Business Day	Is a day that is not a Saturday, Sunday or public holiday or after 5pm in Melbourne, Victoria.
Chair	The chair of the ND HREC from time to time.
Clinical Study	Any investigation in human participants intended to discover or verify the clinical, pharmacological and/or other pharmacodynamic effects of an investigational product(s), and/or to identify any adverse reactions to an investigational product(s), and ascertaining its safety and/or efficacy.
Close Out	Close out refers to the final activity of research, where all study tasks are completed, data is finalized, and the research is officially concluded. It involves ensuring all regulatory requirements are met and all documentation is properly archived.

Consent waiver	Ethical approval that allows a study to proceed without obtaining explicit informed consent from participants. This waiver is granted when the research involves minimal risk, and obtaining consent is impractical or unnecessary for the study's objectives.
Data	Data encompasses all forms of information collected, processed, and analyzed during a research study. This includes raw data, cleaned data, transformed data, summary data, and metadata (data about data). Additionally, data can refer to research outputs and outcomes. It also includes any information collected as part of the study protocol, such as participant responses, test results, observations, and measurements.
Discomfort	Considered less serious than harm. It can involve physical or psychological impacts, for example, minor side-effects of medication, discomfort related to non-invasive examinations or tests (such as measuring blood pressure), and mild anxiety associated with an interview. However, where a person's reactions might exceed discomfort and become distress, this should be viewed as the potential for harm. Some participants may be at higher risk of harm or discomfort arising from the research being conducted. The increased risk of harm or discomfort can express itself in different ways at different times and to different degrees and can arise from: (a) the nature, design or other contextual factors of the research, such as the setting in which the research will be conducted, the social or political implications of doing the research and cultural factors or some combination of these factors; (b) specific attributes or characteristics of individual participants or of groups to which they belong; and/or (c) an interaction between (a) and (b).
Data Safety Monitoring Boards (DSMB)	Data Safety Monitoring Board (DSMB) An independent and multidisciplinary group established by researchers to review, at intervals, accumulating research data, in order to monitor the progress of research and make recommendations on whether to continue, modify or stop the research for safety or ethical reasons.
Ethical Review Management System (ERMS)	The Ethical Review Manager (ERMS) website is used for submissions to the ND HREC. The ND HREC utilizes the "Research Manager" ERMS.
Good Clinical Practice (GCP)	Good Clinical Practice (GCP) is an international ethical and scientific quality standard for designing, conducting, recording and reporting studies that involve the participation of human participants.
Human Research Ethics Committee (HREC)	A committee constituted under the guidance of the National Statement and registered with the NHMRC to conduct the ethical and scientific review of in human research.
Principal Investigator (PI)	The individual who takes overall responsibility for the research and submits the research for ethical and scientific review to the ND HREC.
Higher Risk Research	Research in which there is a risk of harm to and in which there may also be a foreseeable burden on participants in the research being conducted. The risk of harm in higher risk research may or may not be a

	risk of significant harm and may be harm to the individual, group, community, societal or global level.
Indemnity	Legal agreement where the sponsor agrees to compensate the investigator and participants for any losses or damages incurred as a result of the study. This includes protection against legal liability for harm caused during the research
Insurance	Coverage provided to protect participants, researchers, and sponsors against potential damage or loss that may occur during the study. This insurance ensures that any harm or injury resulting from participation in the research is financially covered.
Investigator's Brochure (IB)	A compilation of clinical and non-clinical data on the investigational product(s) relevant to the study of investigational product(s) in human subjects.
Lower Risk Research	Research in which: (a) there is no risk of harm, but in which there is a risk of discomfort and in which there may also be a foreseeable burden (low risk research); or research in which there is no risk of harm or discomfort, but which includes a potential for minor burden and Inconvenience (minimal risk research).
Member	An individual who is a member of the ND HREC
National Health and Medical Research Council (NHMRC)	The National Health and Medical Research Council is the main statutory authority of the Australian Government responsible for medical research.
Multi-center research	Multi-center research is research that is conducted at more than one site.
National Statement	The National Statement on Ethical Conduct in Human Research (2023), as amended from time to time..
Non-Affiliated Research	Researchers who operate independently and who are not formally tied to Nutromics, and which rely on private funding or external partnerships with less oversight and fewer resources than Affiliated Research.
Non-interventional	Refers to research where researchers collect data without altering participants' treatment or medical care. It involves observing without altering or influencing that which is being observed. These studies aim to evaluate or validate diagnostic tools. Researchers examine and report on what is happening, without controlling the course of events. Certain outcomes are measured but no attempt is made to affect the outcome (i.e. no treatment or experimental intervention is given).
Nutromics	Nutromics Operations Pty Ltd (ACN 627 168 567) and its Related Bodies Corporate (as applicable) (as defined in the *Corporations Act 2001* (Cth))
Opt-out approach	A method used in the recruitment of participants into research where information is provided to the potential participant regarding the research and their involvement and where their participation is presumed unless they take action to decline to participate.
Participant	A participant is an individual who provides data or undergoes procedures as part of the study, but their standard medical care remains unaffected by the research activities.
Protocol Departure	A minor or administrative divergence from the research protocol that does not significantly affect the participant's safety, the integrity of the research data, or the overall outcome of the research.

Protocol Violation	Any change, divergence, or departure from the study design or procedures of a research protocol that affects the subject's rights, safety, or well-being, and/or the completeness, accuracy, and reliability of the study data.

Risk of Harm	• physical harm: including injury, illness, pain or death, including but not limited to:
	  ○ psychological harm, including feelings of worthlessness, distress, guilt, anger and fear;
	  anxiety related, for example, to disclosure of sensitive information, an experience of re-traumatization, or learning about a genetic possibility of developing an untreatable disease;
	  ○ devaluation of personal worth, including being humiliated; or manipulated.
	  ○ in other ways treated disrespectfully or unjustly.
	• cultural harm: including misunderstanding, misrepresenting or misappropriating, including but not limited to: cultural beliefs, customs or practices;
	• social harm: including damage to social networks or relationships with others;
	• discrimination in access to benefits, services, employment, insurance and social stigmatization; and unauthorized disclosure of personal information;
	• economic harm: including the imposition of direct or indirect costs on participants; and
	• legal harm: including discovery and prosecution of criminal conduct.
	Any of these types of harm can be experienced individually or collectively.

Research Protocol	A document that details the objectives, design, methodology, statistical considerations and organization of research .
Research	Refers to non-interventional diagnostic clinical studies in humans, or clinical studies that support the development of diagnostic tools or methods.
Researcher	A researcher is a person involved in research, including the Principal Investigator, study team, ND HREC applicant, and delegates, who collectively ensure the study is conducted ethically and meets regulatory standards.
Safety Review Committee (SRC)	An independent data monitoring committee that may be established by the Sponsor to assess, at intervals, the progress of research, the safety data, and the critical efficacy points, and to recommend to the Sponsor whether to continue, modify, or stop the research.
Serious Adverse Device Effect (SADE)	An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

Serious adverse event (SAE)	Any adverse medical occurrence that:
	• led to a death.
	• led to a serious deterioration in health of a participant, or user, such as:
	  ○ A life-threatening illness or injury.
	  ○ A permanent impairment of body function or permanent damage to a body structure.

	○ A condition requiring hospitalization or increased length of existing hospitalization; ○ A condition requiring unnecessary medical or surgical intervention; or ○ Fetal distress, fetal death or a congenital abnormality/birth defect; • might have led to death or a serious deterioration in health had suitable action or intervention not taken place; ○ a malfunction of a device such that it has to be modified or temporarily/permanently taken out of service; or ○ Defect (deterioration in characteristics or performance) found on examination of the device.
Serious Adverse Reaction (SAR)	A serious adverse reaction corresponds to any untoward medical occurrence related to the investigational medical device and which results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly/birth defect.
Significant Safety Issue (SSI)	A safety issue that could adversely affect the safety of participants or materially impact the continued ethical acceptability or conduct of the research.
Unexpected Serious Adverse Device Events (USADE)	Serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified
Sponsor	Is the company, institution, organization, body or individual that takes overall responsibility for the conduct of Clinical Research and usually initiates, organizes and supports the Clinical Research.
Therapeutic Goods Administration (TGA)	The Therapeutic Goods Administration (TGA) is the medicine and therapeutic regulatory agency of Australia.
Therapeutic good	Defined as a good which is represented in any way to be, or is likely to be taken to be, for therapeutic use (unless specifically excluded or included under Section 7 of the *Therapeutic Goods Act 1989* (Cth). Therapeutic use means a product for use in humans in connection with: • preventing, diagnosing, curing or alleviating a disease, ailment, defect or injury; • influencing, inhibiting or modifying a physiological process; • testing the susceptibility of persons to a disease or ailment; • influencing, controlling or preventing conception; • testing for pregnancy; • used as an ingredient or component in the manufacturing of therapeutic goods; and • replacement or modification of parts of the anatomy.

3. Submission to ND HREC

Research for ND HREC review must be submitted by researchers to the ND HREC ERMS' Research Manager. Researchers must email HREC@nutromics.com to request an account be set up for their submission, after which they will be assigned an account for ERMS access.

ERMS Link: https://nutromicsdiagnosticshrec.myresearchmanager.com/

Nutromics is exempt from fees associated with review by the ND HREC. All Non-Affiliated research submissions for ND HREC review subject to the following fees:

	Service	$ Amount (inc GST)
☐	New submissions that require ND HREC review	$330
☐	ND HREC review on behalf of each additional site pertaining to the same Research	$165
☐	Review of an Amendment (including those requesting an extension of approval)	$165
☐	Further review of an amendment/requirement for resubmission of amendment (each occasion)	$165

The following documents are required for all Research and should be provided when submitting research review by the ND HREC.

- ND HREC Submission Questionnaire on ERMS
- Cover letter to describe research, listing enclosed documents and submission signed by Principal Investigator;
- Protocol;
- Participant Information Sheet and Consent Forms;
- Recruitment material (letters, posters, advertisements);
- Questionnaires and surveys;
- Any other participant documents (food diaries etc.);
- Investigator Brochure;
- Other relevant HREC approvals
    - Details of other review bodies involved;
    - Decision of other review bodies; and
    - Details of any amendments required by other review bodies;
- Insurance statements;
- Indemnity documents;
- Financial budgets;
- Researcher qualification documentation (CVs, GCP, licenses, degrees etc.).
- Researcher Conflicts of Interest
- Sample Case Report Form;
- Any other approvals or applications (for example, Institutional Biosafety Committee, Radiation Safety and Cellular Therapies Advisory Committee etc.);
- Data Management Plan;

The ND HREC will retain copies of all documentation (including any correspondence) in the form in which it was approved for 15 years following completion of the Research.

4. Resources for Consultation

Researchers and the ND HREC shall carefully review and adhere to all relevant documents and guidelines to ensure research submission, review and conduct complies with Australian regulations. This includes , and any other applicable Australian standards and guidelines.

Additionally, researchers and the ND HREC should consult the following specific ND HREC documents which can be found online at nd-hrec.org

- Terms of Reference for ND HREC
- RGO-WI HREC or Nutromics Clinical Research Centre SSA Submission
- HREC-SOP-02: HREC Operations
- RGO-FORM Protocol Departure Report
- RGO-FORM Data Breach Report
- RGO-FORM Annual Report
- RGO-FORM Safety Event or Device Deficiency
- RGO-FORM Study Close Out Report
- RGO-FORM Ethics Amendment or Renewal Request

5. Processing of submissions for review

Once received by the ND HREC via the ERMS, the research submission is assigned a unique research identification number. This unique identifier must be used by the researchers in all correspondence to the ND HREC regarding that research .

When an ethics submission is received, the ND HREC must perform a validation assessment of the submission. Validation involves determining if the submitted documents are appropriate and complete and accurate, including appropriate signatories.

If validated, the submission is assigned to a ND HREC meeting. If more information is required, a request for additional information is made to the Principal Investigator. If the submission is invalid (i.e.: not all documents were submitted), the ND HREC must give reasons why it is not valid to allow the PI to submit an alternative submission or withdraw the submission

Upon submission of submission, the ND HREC will acknowledge acceptance of the submission for scientific and ethical review by email to the Principal Investigator and/or nominated contact person within 2 working days of receipt of the Submission, which will include either an:

- Submission acknowledgement of receipt;
- Submission acknowledgement of receipt with an invitation to the ND HREC meeting;
- Submission acknowledgement of receipt and invalid submission notification; or
- Submission acknowledgement of receipt and notification of expert reviewer consultation required.

6. ND HREC review of research submissions

The ND HREC ethically assesses each submission in accordance with the National Statement and other relevant guidelines and legislation. The ND HREC must ensure that it is sufficiently informed on all aspects of a research protocol, including its scientific validity, in order to make an ethical assessment. The review will consider both scientific and ethical components of the research .

The ND HREC may also choose to refer the submission to external expert reviewer(s).

The ND HREC Chair must consider whether an advocate for any participant or group of participants should be invited to the ND HREC meeting to ensure informed decision-making. It is the responsibility of the ND HREC Chair or the Chair's delegate to act on this.

The ND HREC will endeavor to reach a decision concerning the ethical and scientific acceptability of a research by unanimous agreement. Where a unanimous decision is not reached, the decision is considered to be carried by if a majority of the Members who examined the research vote in favor of the decision. The vote including numbers for and against (and numbers of Members abstaining from voting where applicable) must be noted in the minutes.

If the ND HREC decides that further information or responses from the Principal Investigator should be considered at a further meeting of the ND HREC, the Principal Investigator (and/or their delegate) may be invited to attend the ND HREC meeting in order to provide clarification and answer any further questions raised by the ND HREC in relation to their submission.

7. ND HREC Review Pathways

The National Statement recognizes that human research involves a wide range of activities that have variable risks and potential benefits.

Researchers and the ND HREC are required to determine the existence, likelihood and severity of potential risks based on the research methodology and design, participant population and research activity proposed, including the complexity of the research to be undertaken. Monitoring arrangements should be put in place that are commensurate with relevant potential risks, and the size and complexity of the research to be undertaken as approved by the ND HREC.

Researchers are to specify the review pathway that they seek upon submission on the ERMS (i.e.: "Lower Risk Research" Review Pathway, or "Higher Risk Research" review Pathway".

7.1 Lower Risk Research - Review Pathway

Lower Risk Research is either minimal or low risk research. "Minimal risk" has no risk of harm or discomfort, but potential for minor Burden or Inconvenience, whilst "low risk research" research has no risk of harm but a risk of discomfort (+/- a foreseeable burden).

If the submission qualifies as "Lower Risk Research", the research the submission will be reviewed by the ND HREC Executive Committee and will be documented as either being

"minimal risk research" or "low risk research" with ongoing monitoring and oversight to be dictated accordingly by the ND HREC Executive Committee.

If the ND HREC decide that the research does not meet the criteria for "Lower Risk Research" research the ND HREC will advise the researcher about further steps required, such as a full review by the ND HREC.

7.2 Higher Risk Research - Review Pathway

Higher Risk Research can be considered as "Greater than Lower Risk" Research, where there is a risk of harm (with or without a foreseeable burden), or as "High Risk" where there is a risk of significant harm (with or without a foreseeable burden).

Higher Risk Research submissions shall all be subject to a full ND HREC review, with documented decision on whether the research is "Greater than Lower Risk Research" or "High Risk", with ongoing monitoring and oversight to be dictated accordingly as required by the ND HREC, and consideration of any additional conditions that the ND HREC consider necessary to put in place to ensure appropriate safety of participants. The review process by the ND HREC for "Higher Risk Research" may take longer due to the complexity of the research and the need for a thorough evaluation by the ND HREC and thus researchers should plan for a more extended approval timeline.

8. Submission of Amendments and Renewals

8.1 Submission of amendments and renewals

Proposed changes to ND HREC approved research or the conduct of the research to be undertaken (amendments) and requests for extensions to the ND HREC's approval for the Research (renewals) must be submitted by the Principal Investigator to the ND HREC for review and approval. Researchers should submit an *RGO-FORM Ethics Amendment / Renewal Request* in relation to the submission of each amendment and renewal and should include the proposed amended documentation with a description of the amendments.

All amended documents must have the changes highlighted and contain revised version numbers and dates. Two copies of the updated documents should be provided to the ND HREC – one with 'track changes' and one 'clean' copy.

8.2 Substantiality of amendments and renewals

Substantial amendments or renewals where it appears that the changes may significantly affect the scientific value of the research, for example because it modifies the recruitment targets, the selection criteria or the data analysis, should be reviewed by the full ND HREC. Amendments or renewals that are not substantial, do not require full ethical review and may be approved by the Executive Committee of the ND HREC. It is the responsibility of the Chair, in consultation with other Members (where necessary), to determine whether if an amendment is substantial.

8.3 Amendments requiring full HREC review

If research includes any of the following types of research and / or participants, it will require a full review by the ND HREC and will not be eligible for Lower Risk Research review pathway:

- Interventions and therapies, including clinical and non-clinical research and innovations of new treatment modalities;
- Human genetics;

- Human stem cells;
- Women who are pregnant and the human fetus;
- People who are highly dependent on medical care who may be unable to give consent;
- People with a cognitive impairment;
- People with an intellectual disability or a mental illness;
- Research specifically targeting Aboriginal or Torres Strait Islanders;
- People who may be involved in illegal activities; or
- Research including genomics.

However, if no information that can identify an individual is used and no linkage of data is planned in respect of the above mentioned types of research and/or participants, the research may be determined to be “Lower Risk Research” by the ND HREC and be appropriate for that review pathway.

If the ND HREC Executive Committee approves of “Lower Risk Research” research for the above-mentioned types of research/or participants the ND HREC Executive Committee will issue a formal ethics review outcome for the research with the decision noted at the next ND HREC meeting.

8.4 Further information required for review of amendment or renewal

If the ND HREC (or Chair) determines that further information, clarification or amendments are required for the consideration of the request for amendment or renewal by the ND HREC, the correspondence to the Principal Investigator must clearly articulate the reasons for this determination by the ND HREC (or Chair (as applicable) and outline the information that is required for further consideration. Where possible, requests for additional information, clarification and/or amendments should refer to the *National Statement* or relevant pieces of legislation.

When amendments are re-submitted to the ND HREC following a request from the ND HREC (or Chair) the ND HREC’s Executive Committee will review the further information, clarifications or amendments for final approval or rejection.

8.5 Urgent amendments for safety reasons

Where an urgent amendment is required for safety reasons, the Chair may review and approve of the request (with the help of an expert reviewer if necessary). In such circumstances, the amendment or renewal information is noted at the next ND HREC meeting.

8.6 Record maintenance and actions following amendment or renewal review

Any amendment or renewal requests approved by the ND HREC Executive Committee or Chair (as applicable) should be noted by the ND HREC at its next subsequent meeting.

All reviewed and approved requests for amendments and renewals must be recorded in the minutes of the meetings of the ND HREC, and the status of the research will be updated in the ND HREC ERMS.

9. Conducting HREC Review

ND HREC Members and external expert reviewers should consider the following questions to inform their review and decision making of initial submissions and any amendment/renewal requests (as applicable with respect to the nature of the submission).

Additionally, Members should also consult the National Statement for further guidance relevant to the applicable research types/areas.

General Questions to Consider:

- Does the research proposal demonstrate that the research is justifiable in terms of its
- potential contribution to knowledge?
- Is the research based on a thorough study of current literature as well as prior observation, approved previous studies, and where relevant, laboratory and animal studies?;
- Is the research proposal designed to ensure that any risks of inconvenience, discomfort or harm to participants are balanced by the likely benefit(s) to be gained?;
- What is the overarching design of this research? E.g. qualitative, quantitative, observational and/or experimental?;
- Is the proposal complete or is further information or evidence required to support the aims, hypothesis or proposed experimental methodology?;
- Are there any design or other deficiencies within the proposal that require modification?; and
- Are there points of uncertainty or ambiguity that require clarification?

Questions in relation to the Research:

- Is the hypothesis/aim clear and valid?;
- Does the literature evidence support this?;
- Is the research question useful? Is the research worthwhile?;
- Is the research likely to yield new information, enhance understanding or clarify existing uncertainty?;
- Has this, or similar research been carried out before or in the same or similar contexts?;
- Can the research proposal be supported by a systematic review of the literature that would demonstrate the importance of the research questions and that builds on the results of previous research?;
- If indicated, have the perspectives of potential participant groups, the wider community, or other disciplines been incorporated into the research proposal?;
- Does the value of the research appear to be adequate to justify its conduct with humans? (or animals if relevant?); and
- Is the rationale sound? What are the clinical implications (if any) of the expected results for this research?

Questions in respect of the researchers:

- Do the researchers have the necessary qualifications, competence and experience?

Questions in relation to the methodology and Research design:

- Are all aspects of research methodology clearly described?;
- Is the methodology appropriate to achieve the aims/intent of the research?;
- Review methodology - for example the appropriateness of design in terms of:
    - randomization/stratification;
    - sample size;
    - objectives;
    - design issues (e.g. placebo controlled, blinding, crossover, washout);
    - outcomes;
    - inclusion/exclusion criteria; and
    - analysis and statistical validity;

- Has the protocol adequately addressed research specific safety issues?; and
- How valid/effective are the participant information sheets (if any) and other documents in relation to the protocol?

9.2 Submission Requirements

9.2.1 Researcher Conflicts of Interest

Researchers should declare any conflicts of interest (actual, perceived or potential), that may influence their conducting of research, including influence over (but not limited to) the analyses of the research, recruitment or compliance.

The ND HREC will consider the declaration (in line with the relevant sections of the National Statement) and may require additional detail such as how the conflict will be managed.

9.2.2 Compensation for Injury

All PICF documentation for research within scope of the ND HREC review, must include a clause regarding compensation for injury.

"If you suffer any injuries or complications as a result of this research, you should alert the researchers as soon as possible and you will be assisted with arranging appropriate medical treatment.

There are two avenues that may be available to you for seeking compensation if you suffer an injury because of your participation in this research:

- *The medical technology industry has set up a compensation process, with which the Sponsor of this research, {Sponsor}, must comply. Details of the process and conditions are set out in the Medical Technology Association of Australia (MTAA) Guidelines for Compensation for Injury In accordance with these Guidelines, the Sponsor will determine whether to pay compensation to you, and, if so, how much. If you have any questions about the Guidelines, please ask to speak with the researchers.*
- *You may be able to seek compensation through the court."*

9.2.3 Data Management Plan

Data management plans should consider all regulatory and ethical guidelines, describing how data from research should be stored, and how privacy and confidentiality is managed. Key items that a Data Management should address are outlined below;

Data Recording and Storage
- Data are securely recorded and stored.
- Storage locations are documented.
- Published data are retained for at least five years; research data for 15 years.

Network and Data Security
- Network-connected systems ensure data security.
- Cross-border data transfers comply with Australian Privacy Principles (APP 8, HPP9).
- Overseas recipients handle personal information according to these principles and are accountable for mishandling.

Data Sourcing and Documentation
- Location of original data from limited access databases or contractual sources is documented.

- Security systems support multiple researchers and handle departures.

Personal and Health Information
- Collection, use, and disclosure of personal and health information comply with legal requirements and obtain appropriate consent.
- Future use of data/tissues complies with ethical guidelines.
- Participants understand whether their information is identifiable, re-identifiable, or non-identifiable.
- Participants are informed about health record reviews by researchers, authorities, and sponsors.
- Research publications do not identify participants.

Additional Information
- Security measures (physical, network, system, technological) are in place.
- Policies and procedures are documented.
- Contractual and confidentiality agreements are included.
- Data storage format is specified.
- Purposes for data use and/or disclosure are defined.
- Conditions for granting data access are outlined.

9.2.3.1 Wording for PICF

All PICF documentation for research within scope of the ND HREC review must include a clause regarding data management, such as:

"By signing this consent form, you agree to allow the researchers to collect and use your personal information. Any information that can identify you will remain confidential and will only be used for this research, disclosed with your permission, except as required by law.

Your personal information, including test samples, will have identifiers removed and replaced with a unique identification code. The researchers will be able to re-identify your information only if a necessary follow-up visit is required. The identification code will be stored electronically, and access to this code will require a password.

The collection, use, and disclosure of your personal and health information will comply with legal requirements and obtain your consent. Any future use of your data or tissues will adhere to ethical guidelines. The researchers have implemented comprehensive security measures. The purposes for which your data will be used and/or disclosed include [describe usage of data].

In accordance with relevant Australian and/or Victorian privacy and other relevant laws, you have the right to request access to your information collected and stored by the researcher, and to request corrections to any information with which you disagree. Please contact the researchers if you would like to access your information.

Published data will be retained for at least five years, and clinical research data for 15 years. The researchers' network-connected systems ensure data security, and any cross-border data transfers will comply with Australian Privacy Principles (APP 8, HPP9). Overseas recipients of your data will handle it according to these principles and will be accountable for any mishandling.

The results of this research may be published and/or presented in various forums, but your information will be provided in such a way that you cannot be identified, except with your express permission. If you wish to receive a copy of the published information, please request it. Research publications will not present information in a way that identifies you.

If you withdraw from the research, your personal data already collected will still be used. After your withdrawal, no new personal data will be collected or processed for the research, unless it relates to an already reported side effect."

9.2.4 Complaints About Conduct of Research

If a PICF is used in the Research, the ND HREC must ensure that it contains contact details for submitting complaints concerning matters relating to the site (site contact person) and matters relating to an aspect of the Research or the conduct of the Research .

9.2.4 Insurance and Indemnities

There must be insurance and indemnities in place to cover all research (refer to *NHMRC guidance; Indemnity and insurance arrangements for clinical trials*)

Anyone involved in human research, whether individuals or organizations, should have adequate insurance coverage to protect against potential liabilities.

Before research can commence, both the sponsor and the Principal Investigator must secure sufficient insurance coverage. The investigator's professional indemnity insurance should cover any gaps in the overall coverage. Liabilities may arise from initiating or sponsoring the research, including the development of the research protocol or conduct.

Researchers must provide an insurance certificate that covers the following:

- Named Insured: The Australian entity acting as the sponsor must be named as an insured party under the insurance policy.
- Coverage Evidence: Provide evidence that the insurance covers the conduct of the relevant research in Australia.
- Policy Validity: Provide evidence that the insurance policy will be current throughout the entire period of the research.
- Minimum Coverage: The Sponsor and Principal Investigator are responsible for ensuring the research has adequate coverage (National Statement on Ethical Conduct in Human Research, Sections 5.1.46-5.1.47).
- No-Fault Liability: The insurance must cover no-fault liability, recognizing that any injury would not have occurred without the participant's involvement in the study.

Sponsors must ensure that indemnities are established to cover the research, these may include (but not limited to);

- Medical Technology Association of Australia (MTAA) Form of Indemnity, which is an agreement between the sponsor and the Principal Investigator or site.
- The MTAA HREC indemnity, which is an agreement between the sponsor and the ND Human Research Ethics Committee (HREC).
    - Where Nutromics is the sponsor of a submission to the ND HREC, a HREC indemnity is not required.

10. Consent opt-out approach

Before approving the use of an opt-out approach for research, the ND HREC must be satisfied that:

- involvement in the research carries no more than "Lower Risk Research" to participants;
- the public interest in the proposed activity substantially outweighs the public interest in the protection of privacy;
- the research activity is likely to be compromised if the participation rate is not near complete, and the requirement for explicit consent would compromise the necessary level of participation;
- reasonable attempts are made to provide all prospective participants with appropriate plain language information explaining the nature of the information to be collected, the purpose of collecting it, and the procedure to decline participation or withdrawal from the research;
- a reasonable time period is allowed between the provision of information to prospective participants and the use of their data so that an opportunity for them to decline to participate is provided before the research begins;
- a mechanism is provided for prospective participants to obtain further information and to decline to participate;
- the data collected will be managed and maintained in accordance with relevant security standards;
- there is a governance process in place that delineates specific responsibility for the research and for the appropriate management of the data; and
- the opt-out approach is not prohibited by State, federal, or international law.

11. Consent waiver

Before deciding to waive the requirement for consent, the ND HREC must be satisfied that:

- involvement in the research carries no more than "Lower Risk Research" to participants;
- The benefits from the research justify any risks of harm associated with not seeking consent;
- it is impracticable to obtain consent (for example, due to the quantity, age or accessibility of records);
- there is no known or likely reason for thinking that participants would not have consented if they had been asked;
- there is sufficient protection of participants privacy;
- There is an adequate plan to protect the confidentiality of data;
- in case the results have significance for the participants' welfare there is, where practicable, a plan for making information arising from the research available to them (for example, via a disease-specific website or regional news media);
- the possibility of commercial exploitation of derivatives of the data or tissue will not deprive the participants of any financial benefits to which they would be entitled; and
- the waiver is not prohibited by State, Federal, or International law.

12. Review Outcomes

The ND HREC, after consideration of an submission at a meeting, will make one of the following
decisions:

- To approve the research as being ethically acceptable, with or without conditions;
- To provide provisional approval to the research with requested amendments,

- To defer making a determination in regard to the research until the clarification of information or the provision of further information is provided to the ND HREC; or
- To not approve of the research.

Any amendments submitted to address the requested changes in a provisional approval will be reviewed in the same manner as all other amendments by the ND HREC Executive committee.

In some cases, the ND HREC may approve Research classified as “Higher Risk Research” with conditions or restrictions to mitigate potential harm to participants that are proportionate to the potential harm, discomfort, Burden and Inconvenience. Researchers may need to adhere to specific guidelines or implement additional safeguards as part of the approval process by the ND HREC. Standard conditions for Lower Risk Research and Higher Risk Research proposal approvals, are described in this document, which can be amended and modified at the discretion of the ND HREC but should form a basis of initial discussion.

The conditions for Higher Risk Research approvals place greater emphasis on immediate reporting, more frequent oversight, and adherence to stricter guidelines and safeguards compared to lower Risk Research approvals. This approach ensures that research involving Higher Risks Research to participants is carefully monitored and managed throughout its duration.

a. Standard conditions for Lower Risk Research approvals

- The Principal Investigator must immediately report any adverse events or other developments that may affect the ethical approval of the research;
- The Principal Investigator must inform the ND HREC of any proposed modifications to the protocol or research documents and will submit required amendments promptly for ND HREC approval prior to implementing such modifications;
- The Principal Investigator must adhere to specific guidelines and additional safeguards as stipulated in the National Statement and ND HREC Standard Operation Procedures;
- The Principal Investigator must report on participant safety in accordance with the ND HREC’s policies and procedures;
- The Principal Investigator must provide regular updates to the ND HREC as specified in the approval and must notify the ND HREC upon completion of the research;
- If the research is terminated prematurely, the Principal Investigator must notify the ND HREC, providing reasons for discontinuation; and
- Any extension of the research beyond the approved duration must be communicated to the ND HREC, with a request for a renewal to be approved of by the ND HREC and accompanied by necessary supporting documentation in respect of the renewal request.

b. Standard conditions for Higher Risk Research approvals

- The Principal Investigator must promptly report any incidents that could necessitate a review of the ethical approval of the research;
- The Principal Investigator must notify the ND HREC of any proposed changes to the protocol or research documents and will submit required amendments promptly for ND HREC approval prior to implementing such changes;
- The Principal Investigator must adhere to additional safeguards and guidelines mandated by the National Statement and the ND HREC’s policies;

- The Principal Investigator must submit reports on participant safety in accordance with ND HREC policies and procedures;
- The Principal Investigator must provide annual reports to the ND HREC, following the specified format, and will notify the ND HREC upon research completion;
- If the research is terminated prematurely, the Principal Investigator must notify the NDHREC, providing reasons for the discontinuation; and
- Any extension of the research beyond the approved period must be communicated to the NDHREC, with a request for renewal to be approved of by the ND HREC and accompanied by requisite supporting documentation in respect of the renewal request.

13. Notification of ND HREC decisions

The Researcher will be notified in writing of the ND HREC's decision within 2 Business Days following the relevant review meeting.

If the ND HREC determines that further information, clarification or amendment is required for the consideration of a research, the correspondence must clearly articulate the reasons for the ND HREC's determination and outline the information that is required. Where possible, requests for additional information, clarification and/or amendment should refer to the *National Statement* or relevant pieces of legislation.

If the requested information is not received from the researchers within 60 days of the request for further information being sent by the ND HREC to the researchers, the research may be dismissed and the researchers may be required to re-submit the research to the ND HREC at a later date.

The ND HREC endeavors to openly communicate with researchers to resolve outstanding requests for further information, clarification or amendment of research relating to ethical issues.

The ND HREC will notify the researchers of the ethical approval of a research only when all outstanding requests for further information, clarification or amendment have been satisfactorily resolved. Notification of ethical approval is in writing, and must include the following information:

- Title of research;
- Name of the Principal Investigator for the research;
- Unique research identification number for the research;
- The version number and date of all documentation reviewed and approved by the ND HREC, including clinical protocols, patient information sheets, consent forms, advertisements and questionnaires etc.;
- The date of the ND HREC's approval; and
- Conditions of the ND HREC's approval.

If the ND HREC determines that a research is ethically unacceptable, the notification of the ND HREC's decision will include the grounds for rejecting the research with reference to the National Statement or other relevant pieces of legislation.

The status of the research will be updated on the ERMS.

14. Communication with researchers

a. Written communication

- The ND HREC must only use official ND HREC email accounts for all correspondence;
- The ND HREC Chair must sign and date all official documents before sending them to researchers.
- The ND HREC must maintain a record of all written communication in the research's ERMS record.

b. Telephone Communication

- The ND HREC Chair shall schedule telephone calls in advance whenever possible; and take notes of the key points and decisions made during the call.
- The ND HREC must summarize the telephone conversation in an email to the researcher, highlighting important points and actions; and
- The ND HREC must save the email summary in the research's ERMS record

c. Face-to-Face Communication

- The ND HREC Chair must schedule meetings with researchers through a formal invitation via email or letter, specifying the date, time, location, and purpose of the meeting;
- The ND HREC shall document key points, decisions, and action items during the meeting and send a summary of the meeting minutes to the researchers; and include any agreed-upon actions, deadlines, and responsible parties.

15. Monitoring of Approved Research

a. Research Governance Audits

The RGO monitors HREC approved research to ensure compliance with the research and relevant legislation and guidelines as per HREC approval. All ongoing research with ethics approval granted by the HREC are eligible to be audited by the RGO. Studies from all tiers of risk will be audited, however Higher Risk studies will be the focus of more audits than those considered to be lower risk. The RGO can engage with the Quality and Compliance team at the Institution to conduct audits.

Research may be selected for auditing for a variety of reasons

- Human Research Ethics Committee request
  - following approval of a new protocol;
  - as part of the approval process; or
  - due to the classification of risk.
- Random selection
- A complaint i.e. from a participant, parent, fellow researcher
- Annual report verification

b. Safety Reports

As a condition of the ND HREC's approval of each research, researchers must report significant safety issues (SSI's) and other Serious Adverse Reactions (SARs) or Unexpected Serious Adverse Device Events (USADEs) to the RGO and the ND HREC on *RGO-FORM Safety Event or Device Deficiency;*

Any adverse event that occurs as part of a research which falls into one (or more) of the categories below must be submitted to the ND HREC via the ERMS without delay:

- Is a deviation from or violation of the protocol which affects participant safety;
- May result in a claim against the site;

- Is 'unexpected' and ‘possibly’ related to the procedures of the Research;
- Requires a change in the consent form; and
- Requires a change in the conduct of the Research i.e. the protocol.

Safety reports, (SSIs, SARs or USADEs) shall include:
- A detailed description of the adverse event, including when and where it occurred, any contributing factors, and actions taken. It should assess the seriousness of the event based on its impact on participants' health, the degree of medical intervention required, and any long-term consequences identified, if any;
- Advice from the Principal Investigator as to whether, in their opinion, the adverse event was related to the protocol or in the case of a Device Clinical Research, whether the adverse event was related to the device being studied;
- Advice from the Principal Investigator as to whether, in their opinion, the adverse event necessitates an amendment to the protocol and/or the patient information sheet/consent form;
- Advice from the Principal Investigator regarding whether the event was expected or unexpected as per the protocol or for device research as per the safety profile of product; and
- Advice from the Principal Investigators to whether the event has been notified to the Independent Safety and Data Monitoring Board or Safety Review Committee (if applicable, refer to NHMRC; *Data Safety Monitoring Boards(2018)*).

c. Annual and Close Out reports

For all research assessed as Higher Risk Research by the ND HREC, the following must be provided at least annually to both the ND HREC and the ND RGO by the Sponsor:
- An annual safety report (*on RGO-FORM Annual Report*), including the Sponsor’s comments detailing any planned actions based on the reports;
- An executive summary from the Data Safety Monitoring Board (DSMB) or equivalent, if appropriate;
- Any other reports consistent with TGA Good Clinical Practice Guidelines.

Additionally, at the conclusion of the research, the researchers must submit a close-out report to both the ND RGO and the ND HREC (*on RGO-FORM Study Close Out Repor*t). The ND RGO will manage all close-out actions, while the ND HREC's role is to acknowledge the receipt of the close-out report and ensure that the Research has been appropriately concluded.

The annual/close out report should address the following:
- Research Details:
  - Description and analysis of new/relevant safety findings;
  - Implications of the safety findings on the risk and benefit of the research;
  - Describe any measures, taken or proposed to minimize risk;
  - Comments from the Sponsor;
  - Safety monitoring;
  - Has the safety monitoring plan been reviewed or adapted in the past 12 months?;
  - Has a safety monitoring plan been implemented?;
  - Does the research have a Safety Review Committee?;
  - How many times has the Safety Review Committee reviewed the research in the past 12 months?;
  - Comments on safety monitoring;
  - Investigator’s Brochure;

  - Has the investigator's brochure been reviewed?; and
  - Does the investigator's brochure require an update to include any with new and relevant information?
- Site Research Investigators:
  - List any investigators who have joined the research team in the past 12 months or since the date of the previous Annual Report. Indicate whether each new investigator is listed in any amendment.
- Good Clinical Practice (GCP) Training
  - List of investigators who have completed GCP training in the past 12 months or since the date of the previous Annual Report.
- Research Commencement:
  - Research commencement/initiation date at site; and
  - If the research has not commenced, an explanation should be provided.
- Research Status
  - Current status of research at the site;
  - Expected date of completion;
  - Brief summary of the research research's status; and
  - Is extension of ethical approval required past the current approval date?
- Audit
  - Has the research been subject to an audit at the site in the past 12 months (or since previous report)?;
  - Date of any audit; and
  - Name of auditor.
- Protocol
  - Is the research being conducted according to the protocol?; and
  - Are all conditions of the ND HREC's approval being met?
- Recruitment at site
  - Recruitment target;
  - Recruitment to date;
  - Withdrawals to date;
  - Is recruitment on target?;
  - Provide reason(s) for participant withdrawals; and
  - If recruitment is not on target, provide an explanation.
- Consent
  - Did ND HREC waive the informed consent requirement?
- Safety Issues
  - Have there been any AEs, SAEs, or USADEs that have raised safety issues in relation to the research , which occurred in the past 12 months (or since the previous report) and are yet to be reported to the reviewing ND HREC?
- Funding
  - Status of research budget.
- Insurance
  - Is the insurance certificate in respect of the research current?; and
  - If a current insurance certificate (or extract) for the next 12 months is not attached, an explanation should be provided.

d. Protocol Departures and Violations

All protocol departures and violations are to be reported to the ND HREC/ND RGO in a timely manner by the Principal Investigator using *RGO-FORM Protocol Departure Report* and must provide a detailed description of what occurred, and the steps taken to resolve/address the issue or prevent future re-occurrences.

e. Data Breaches

A data breach, refers to an incident where any data from Research is accessed, disclosed, or lost without authorisation from the HREC, participant, the Researchers or the institution as appropriate. The breach must be reported in compliance with the Australian Privacy Principles and the Research Code of Conduct on *RGO-FORM Data Breach Report.*

16. Suspension or Withdrawal of ND HREC Approval

Where the ND HREC (or the ND HREC Chair) finds reason to believe that continuance of a research will compromise participants' welfare, or that a research is not being or cannot be conducted in accordance with its ND HREC ethical approval, it should immediately seek to establish whether its ethical approval for the research should be suspended or withdrawn.

The ND HREC may suspend or withdraw its ethical approval if it is satisfied that circumstances have arisen such that a research is not being or cannot be conducted in accordance with its ethical approval and that, as a result, the welfare and rights of participants are not or will not be protected. Includes when the ND HREC concludes that the adverse event/s and/or monitoring reports requires the immediate suspension or discontinuation of its ethical approval of the research .

Suspension or withdrawal of the ND HREC's approval shall be reported to the ND RGO without delay, and the ND HREC should immediately notify the Principal Investigator of the suspension or discontinuation of the ND HREC's approval for the research.

The Principal Investigator cannot continue with any research if the ND HREC's ethical approval has been suspended or discontinued and must comply with any special conditions imposed by the ND HREC. The research may not be resumed unless either:

- The Principal Investigator subsequently establishes to the ND HREC that continuance will not compromise participants' welfare and/or is to be conducted in accordance with its ethical approval; or
- The research is modified to provide sufficient protection for participants, the amendment is ethically reviewed, and the modified research is approved by the ND HREC.

The ND HREC, after consideration at a meeting, makes the final decision with regards to reinstatement or withdrawal of its ethical approval (in its sole discretion). The Principal Investigator (and Research contact) must be notified in writing of the decision within 2 Business Days.

The status of the research will be updated in the ERMS.