PATIENT INFORMATION SHEET AND INFORMED CONSENT FORM

(for adult subjects and interventional studies)

1. **Title of study**: Remission of Diabetes with Lifestyle Intervention for Malaysian Type 2 Diabetes Mellitus patients (ReDiaL-MY) - an open label, randomised controlled study

2. **Name of investigator and institution:**

i) Prof. Dr. Winnie Chee Siew Swee, IMU University, Kuala Lumpur, Malaysia
ii) Datuk Dr. Zanariah binti Hussein, Endrocrine Unit, Hospital Putrajaya, Putrajaya, Malaysia
iii) Dr. Nazihah binti Rejab, Klinik Kesihatan Seremban, Negeri Sembilan Darul Khusus, Malaysia
iv) Prof. Dato' Dr Syed Mohamed Aljunid Bin Syed Junid, IMU University, Kuala Lumpur, Malaysia
v) Prof. Michael Lean, University of Glasgow, Scotland, United Kingdom
vi) Prof. Dato' Paduka Dr. Mafauzy Mohamed, Universiti Sains Malaysia, Kelantan, Malaysia
vii) Dr. Lee Ching Li, IMU University, Kuala Lumpur, Malaysia
viii) Dr. Farah Yasmin binti Hasbullah, IMU University, Kuala Lumpur, Malaysia

Site of study: Klinik Kesihatan Seremban & Hospital Putrajaya - Institut Endokrin

3. **Name of sponsor**: Abbott Manufacturing Singapore Pte Ltd

4. **Introduction:**

You are invited to participate in a research study because you have been diagnosed with Type 2 Diabetes that requires ongoing management of blood glucose levels. This study involves demonstrating that lifestyle intervention could induce remission of diabetes among Malaysian individuals with Type 2 Diabetes Mellitus relative to those receiving usual care. The details of the research trial are described in this document. It is important that you understand why the research is being done and what it will involve. Please take your time to read through and consider this information carefully before you decide if you are willing to participate. Ask the study staff if anything is unclear or if you would like more information. After you are properly satisfied that you understand this study, and that you wish to participate, you must sign this informed consent form. To participate in this study, you may be required to provide your doctor with information on your health history; you may harm yourself if you are not truthful with the information provided.

Your participation in this study is voluntary. You do not have to be in this study if you do not want to. You may also refuse to answer any questions you do not want to answer. If you volunteer to be in this study, you may withdraw from it at any time. If you withdraw, any data collected from you up to your withdrawal will still be used for the study. Your refusal to participate or withdrawal will not affect any medical or health benefits to which you are otherwise entitled.

This study has been approved by the Medical Research and Ethics Committee, Ministry of Health Malaysia.

5. **What is the purpose of the study?**

The purpose of this study is to demonstrate that lifestyle intervention could induce remission of diabetes among Malaysian individuals with Type 2 Diabetes Mellitus relative to those receiving usual care, similar to what has been proven in other population (UK, Middle East, India and Australia) and to assess the cost-effectiveness of lifestyle intervention in remission of Type 2 Diabetes Mellitus. Sustained weight loss of more than 10 kg can help normalise blood sugar levels (also known as blood glucose levels) leading to remission of Type 2 Diabetes in many people. This research is necessary because it provides crucial evidence on the effectiveness of lifestyle intervention in improving diabetes management and achieving remission in the Malaysian population. Additionally, it will offer insights into the economic value of such interventions, supporting more efficient resource allocation in national diabetes care strategies.

A total of 92 subjects like you will be participating in this study. The whole study will last about two (2) years and your participation will be about one (1) year.

6. **What kind of study products [or procedures] will I receive?**

If you agree to participate in the study, the doctor may need to perform some tests and examinations to determine if you are suitable for the study. If you are deemed suitable, you will be randomly (by chance, like flipping a coin) assigned to one of the treatment groups below. You have equal chance of being assigned to each of the groups. You will also be told which treatment group you are assigned to (non-blinded study).

The study products do not contain porcine or bovine ingredients.

Group 1 (Intervention group): You will begin the lifestyle intervention programme immediately. This includes a Total Diet Replacement (TDR) phase using diabetes-specific formula (DSF) of Glucerna® Control Vanilla Flavour, followed by a food reintroduction phase and a weight maintenance phase. The programme will last for a total of 12 months. During the first six months, you will receive close support from a dietitian, including regular face-to-face or virtual contact and phone follow-ups. You will also be required to record your intake of DSF and return empty bottles at each visit.

Group 2 (Wait-list control group): You will continue with your usual diabetes management for the first six months. After this period, you will begin the same lifestyle intervention programme as described above for another six months, followed by a weight maintenance follow-up similar to Group 1.

7. **What will happen if I decide to take part?**

You will be required to attend a total of **SIXTEEN (16)** in-person visits and **SEVEN (7)** follow-up phone calls throughout the 48-week study period. The study will consist of three phases: Total Diet Replacement (TDR), Food Reintroduction, and Weight Maintenance, followed by a post-exit contact.

In-person Visit sessions

Procedure/ measurements during Visit 0 (Week -1):

- You will participate in a bespoke pre-screening session, where the study staff will ask you to share your experience with diabetes and medication. You will be shown examples from a UK diabetes remission trial and the proposed Malaysian programme. You will be asked for your thoughts on the approach and whether you think it would suit you.
- The study staff will obtain your informed consent for participation in the study.
- The study team will then
    - interview you on your personal information, social history, medical history, and weight management background.
    - review your current medications and check for any prohibited medications.
    - assess your eligibility based on inclusion and exclusion criteria.
    - review your current medications (concomitant medications).
- Randomisation will take place.
- You will complete the following questionnaire:
    - Weight Management Programme Readiness Questionnaire (The Dieting Readiness Test)

Procedure/ measurements during Visit 1 (Week 0):

- The study staff will take physical measurements, including:
    - Weight, height, and waist circumference
    - Body composition (fat mass, fat-free mass, and skeletal muscle mass)
    - Blood pressure
- Your treating doctor or a qualified nurse or phlebotomist will draw 10 mL of blood (approximately 1 dessertspoon) from your arm to measure fasting glucose, HbA1C, insulin, lipid profile, and liver function test.
- The study staff will guide you in completing a 3-day food record to assess your dietary intakes.
- You will complete the following questionnaires:
    - International Physical Activity Questionnaire – Short Form (IPAQ-SF)
    - SF-12 Health Survey
    - Diet Satisfaction Questionnaire
    - Work Productivity and Activity Impairment (WPAI) Questionnaire
    - Health Utilisation Questionnaire
    - EQ-5D-5L Health Questionnaire
- You will then take part in a qualitative interview to share your initial thoughts and expectations about the ReDiaL-MY study, your motivation to participate, past weight management experiences, and how you feel about following a liquid diet. You will also be

asked about potential challenges, expected support, and your level of confidence in completing the programme.
- The study staff will distribute the study product, where you will receive Glucerna® Control Vanilla Flavour if you are assigned to Group 1, along with guidance on its use and storage.

Procedures/measurements during Visit 2 (Week 2), Visit 3 (Week 4), Visit 4 (Week 8), Visit 6 (Week 14), Visit 7 (Week 16), Visit 8 (Week 20), Visit 10 (Week 28), Visit 11 (Week 32), Visit 12 (Week 36), Visit 13 (Week 40), and Visit 14 (Week 44):
- The study staff will measure your weight and blood pressure.
- The study staff will guide you in completing a 3-day food record to assess your dietary intake.
- The study staff will assess your adherence to the study product through a self-completed adherence form.
- You will receive a new supply of the study product, along with guidance on its use and storage.

Procedures/measurements during Visit 5 (Week 12):
- The study staff will review your current medications (concomitant medications).
- The study staff will take physical measurements, including:
    - Weight, height, and waist circumference
    - Body composition (fat mass, fat-free mass, and skeletal muscle mass)
    - Blood pressure
- Your treating doctor or a qualified nurse or phlebotomist will draw 10 mL of blood (approximately 1 dessertspoon) from your arm to measure fasting glucose, HbA1C, insulin, lipid profile, and liver function test.
- The study staff will guide you in completing a 3-day food record to assess your dietary intakes.
- You will complete the following questionnaires:
    - International Physical Activity Questionnaire – Short Form (IPAQ-SF)
    - SF-12 Health Survey
    - Diet Satisfaction Questionnaire
    - Work Productivity and Activity Impairment (WPAI) Questionnaire
- You will then take part in a qualitative interview to share your experiences during this phase of the liquid diet of the ReDiaL-MY study.
- The study staff will assess your adherence to the study product through a self-completed adherence form.
- You will receive a new supply of the study product, along with guidance on its use and storage.

Procedures/measurements during Visit 9 (Week 28):
- The study staff will review your current medications (concomitant medications).
- The study staff will take physical measurements, including:
    - Weight, height, and waist circumference
    - Body composition (fat mass, fat-free mass, and skeletal muscle mass)
    - Blood pressure

- Your treating doctor or a qualified nurse or phlebotomist will draw 10 mL of blood (approximately 1 dessertspoon) from your arm to measure fasting glucose, HbA1C, insulin, lipid profile, and liver function test.
- The study staff will guide you in completing a 3-day food record to assess your dietary intakes.
- You will complete the following questionnaires:
    - International Physical Activity Questionnaire – Short Form (IPAQ-SF)
    - SF-12 Health Survey
    - Diet Satisfaction Questionnaire
    - Work Productivity and Activity Impairment (WPAI) Questionnaire
- The study staff will assess your adherence to the study product through a self-completed adherence form.
- You will receive a new supply of the study product, along with guidance on its use and storage.

Procedures/measurements during Visit 15 (Week 48):
- The study staff will review your current medications (concomitant medications).
- The study staff will take physical measurements, including:
    - Weight, height, and waist circumference
    - Body composition (fat mass, fat-free mass, and skeletal muscle mass)
    - Blood pressure
- Your treating doctor or a qualified nurse or phlebotomist will draw 10 mL of blood (approximately 1 dessertspoon) from your arm to measure fasting glucose, HbA1C, insulin, lipid profile, and liver function test.
- The study staff will guide you in completing a 3-day food record to assess your dietary intakes.
- You will complete the following questionnaires:
    - International Physical Activity Questionnaire – Short Form (IPAQ-SF)
    - SF-12 Health Survey
    - Diet Satisfaction Questionnaire
    - Work Productivity and Activity Impairment (WPAI) Questionnaire
    - Health Utilisation Questionnaire
    - EQ-5D-5L Health Questionnaire
- You will then take part in a qualitative interview to discuss your experience with the weight loss maintenance (WLM) phase.
- The study staff will assess your adherence to the study product through a self-completed adherence form.

*You are advised to fast before each blood-taking session, and all blood specimens collected will not be used for genetic research.

<u>Follow-up Phone Calls</u>

Procedures during Follow-up phone call 1 (Week 5):
- You will be asked to report your current weight and blood pressure values.

- You will take part in a qualitative interview to share your experience with the liquid diet. This includes discussion on challenges faced, strategies used, motivation, and support received.
- The study staff will review your adherence to the study product by going through your self-completed adherence form.

Procedures during Follow-up phone call 2 (Week 6), 3 (Week 9), 4 (Week 10), 5 (Week 18), and 6 (Week 22):
- You will be asked to report your current weight and blood pressure values.
- The study staff will review your adherence to the study product by going through your self-completed adherence form.

Procedures during Follow-up phone call 7 (Week 49):
- A brief follow-up call to check for any delayed effects or feedback.

8. **When will I receive the trial product and how should it be kept?**

You will be given the study product diabetes-specific formula (DSF: Glucerna® Control Vanilla Flavour) at each study visit throughout the Total Diet Replacement (TDR), food reintroduction, and weight maintenance phases of the study. You must not give the product to anyone else. The study staff will instruct you on how the product must be handled and stored. Please ensure that you keep all used, partly used, and unused DSF bottles. At each study visit, you will be required to return these DSF bottles before receiving your next supply. This is important to help the study team monitor your compliance with the intervention.

9. **What are my responsibilities when taking part in this study?**

It is important that you answer all of the questions asked by the study staff honestly and completely. If your condition or circumstances change during the study, you must tell the study doctor. When you begin your weight management treatment, all diabetes related medication will be stopped. This includes your blood pressure, diuretic (a type of medication that promotes urine production), diabetes medications. Stopping these medications is a safety measure as your blood pressure and blood glucose is likely to reduce when you are on the weight management treatment. If your blood pressure and blood glucose control are inadequate after stopping medication, the attending doctor will gradually re-introduce medication. The doctor will discuss those medications with you. You must not take any other medications without consulting your study doctor. You must inform your study doctor immediately if you make any changes to any of your current treatments, even those which you have been taking for a long time.

It is very important that your study doctor be informed very rapidly of any eventual changes to your health during your participation in the study. For your own security, it is important that you follow your study doctor’s instructions throughout the entire duration of the study.

10. **What kind of treatment will I receive after completion of study including whether the study product will continue to be given?**

    No study product will be given to you at the end of your participation in the study. Whether you complete the study or withdraw early, your doctor will discuss further health management with you. You will continue to receive standard medical care from your doctor as appropriate for your condition.

    You will be informed about the overall results of the study once it is completed, through a summary report.

11. **What are the potential risks and side effects of being in this study?**

    Given the nature of the intervention there is very low likelihood of safety concerns. Patients allocated to the intervention will be closely monitored throughout the study with review appointments 2 weekly during the total diet replacement (TDR) and food reintroduction phases. Stopping your diabetes-related and high blood pressure medications is a safety measure to prevent you from experiencing hypoglycaemia (low blood sugar) and hypotension (low blood pressure) when you adhere to the low energy diet and your weight loss progresses. You will be asked to monitor your blood glucose levels and blood pressure daily and you should contact the doctor if you feel unwell. At each appointment blood pressure and postural symptoms (symptoms such as dizziness, light-headedness or fainting when changing to an upright or standing position) will be monitored and antihypertensive therapy reintroduced if necessary according to clinical guidelines.

    Patients will be given clear guidance on detecting deteriorating glycaemia to permit hypoglycaemic agents to be reintroduced if necessary. If capillary blood glucose is $\geq$ 20 mmol/L at any appointment we will ask the participants GP check the participants HbA1C. Results will be discussed with the participants GP to allow decisions on changes to medications to be made. Any observations/results which may pose a risk to health will be discussed with the patient and their GP.

    Drawing blood may cause slight pain, infection or bruising. Precautions will be taken to minimise this risk by engaging a trained phlebotomist and using sterile technique.

    The effect of the study product on an unborn child is not known. You should not become pregnant or father a child while in this study. Women subjects should not breast feed a child while in the study as the study product may be present in the breast milk. Women who are able to become pregnant will be given a pregnancy test to confirm they are not pregnant. While in the study, if you are able to have a baby or father a child, it is important you use highly effective birth control methods consistently and correctly; the study doctor will discuss these methods with you. Notify your study doctor immediately if you think that you or your partner has become pregnant during the study. If you are pregnant, the study therapy will be discontinued immediately, and you will be removed from the study.

Please ask your study doctor if you need more information on risks and side effects. The study staff will inform you in a timely manner about any new findings or changes to the study product which may affect your health or willingness to continue in this study. Where necessary, you may be asked to reconsent to participate.

The collection of your blood specimens will not be used for future testing or research.

12. **What are the benefits of being in this study?**

By participating in this research, you will receive support from a team of health care providers trained to help people achieve remission of Type 2 Diabetes Mellitus with weight loss. You may or may not achieve remission of Type 2 Diabetes Mellitus. Information obtained from this study will help improve the treatment or management of other patients with the same disease or condition.

13. **What if I am injured during this study?**

If you are injured as a result of being in this study, you should contact your study doctor. In the event of a bodily injury or illness directly resulting from the study product or a medical procedure required for this study, treatment for such injuries will be covered by the clinical trials insurance. The sponsor is not responsible for medical expenses due to pre-existing medical conditions, any underlying diseases, any ongoing treatment process, your negligence or wilful misconduct, the negligence or wilful misconduct of your study doctor or the study site or any third parties. You do not lose any of your legal rights to seek compensation by signing this form.

14. **What are my alternatives if I do not participate in this study?**

You do not have to participate in this study to get treatment for your disease or condition.

15. **Who is funding the research?**

This study is sponsored by Abbott Manufacturing Singapore Pte Ltd who will pay for all study products and procedures. All other drugs and procedures that are not required by the study but are part of your routine medical care will have to be paid by you or your insurance. The sponsor will financially compensate the time spent by the study staff, use of facilities, etc., for including you in the study. You will be reimbursed RM100.00 per visit for your time, transportation and other incidental costs associated with your involvement in this study. There will be no other payment for participating in this study.

16. **Can the research or my participation be terminated early?**

The study doctor or the sponsor may be due to concerns for your safety, stop the study or your participation at any time. If the study is stopped early for any reason, you will be informed and arrangements made for your future care. You may be asked to attend a final follow-up visit.

17. **Will my medical information be kept private?**

All your information obtained in this study will be kept and handled in a confidential manner, in accordance with applicable laws and/or regulations. When publishing or presenting the study results, your identity will not be revealed without your expressed consent. You will not be identified, and your data will be entered using a unique participant ID only. Individuals involved in this study and in your medical care, qualified monitors and auditors, the sponsor or its affiliates and governmental or regulatory authorities may inspect and copy your medical records, where appropriate and necessary.

Your biospecimens may be sent to laboratories for testing. If this is required, your biospecimens will be coded and information that can identify you will be removed. Only your study doctor and study staff will be able to link the code with you.

Data from the study may be archived for the purpose of analysis, but your identity will not be revealed at any time.

18. **Who should I call if I have questions?**

If you have any questions about the study or if you think you have a study related injury and you want information about treatment, please contact the study doctor at your specific study location: Dr. Nazihah binti Rejab, at telephone number +6019-365 4648 at Klinik Kesihatan Seremban, or Datuk Dr. Zanariah binti Hussein, at telephone number +6012-290 7136 at Hospital Putrajaya - Institut Endokrin.

If you have any questions about your rights as a participant in this study, please contact: The Secretary, Medical Research & Ethics Committee, Ministry of Health Malaysia, at telephone number 03-3362 8407 / 8205 / 8888.

INFORMED CONSENT FORM

Title of Study: Remission of Diabetes with Lifestyle Intervention for Malaysian Type 2 Diabetes Mellitus patients (ReDiaL-MY) - an open label, randomised controlled study

By signing below I confirm the following:

- I have been given oral and written information for the above study and have read and understood the information given.
- I have had sufficient time to consider participation in the study and have had the opportunity to ask questions and all my questions have been answered satisfactorily.
- I understand that my participation is voluntary and I can at anytime free withdraw from the study without giving a reason and this will in no way affect my future treatment. I am not taking part in any other research study at this time. I understand the risks and benefits, and I freely give my informed consent to participate under the conditions stated. I understand that I must follow the study doctor's (investigator's) instructions related to my participation in the study.
- I understand that study staff, qualified monitors and auditors, the sponsor or its affiliates, and governmental or regulatory authorities, have direct access to my medical record in order to make sure that the study is conducted correctly and the data are recorded correctly. All personal details will be treated as STRICTLY CONFIDENTIAL.
- I will receive a copy of this subject information/informed consent form signed and dated to bring home.
- I agree/disagree* for my family doctor to be informed of my participation in this study. *(*delete which is not applicable)*

Subject:

Signature: I/C number:

Name: Date:

Investigator conducting informed consent:

Signature: I/C number:

Name: Date:

Impartial witness: *(Required if the subject is illiterate and contents of participant information sheet is orally communicated to the participant)*

Signature: I/C number:

Name: Date: