Trial Protocol

Title: "Longitudinal trial assessing cellulite in women wearing a new compression garment - one side with ink printed micro-pads ("Vari-pads") and one side without."

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Protocol Identifying Number: TWC-SM-2023-01

Protocol version number & date: v 1.1 28 June 2023

Ethics: Not required according to HRA Decision Tools (see Result - England Ethics 21-May-2023) – and confirmed by e-mail from MHRA.

NCT: To be registered on ClinicalTrials.gov on confirmation of Ethics position

Background:

Cellulite is a very common condition that affects up to 90% of women.[1] It is much less commonly found in men. It presents as a dimpling principally of the skin of the buttocks and thighs, with the appearance having been described as resembling "orange peel", "cottage cheese" or a "quilt". In women who are affected, it usually appears after puberty. It occurs in all races, but is thought to occur more commonly in Caucasians.[1]

The product being tested:

The product being tested is to be a retail (non-medical) product presented as standard compression shorts with a pattern of small, raised pads ("Vari-pads") of different heights printed on the inner aspect. A previous trial that we have performed has suggested that wearing these for eight hours a day can reduce the appearance of cellulite.[2] In addition, subjects found these compression pants to be very comfortable.[2]

In this trial, we want to see whether the subjective and objective improvement is due to the compression alone, or whether the Vari-pads on the inside of the product enhance the subjective or objective impression of cellulite. As such, we have asked the manufacturer to produce pairs of pants where the Vari-pads are printed onto the inner aspects as per usual on one side only, but not on the other side.

Subjects will then be asked to wear the apparel for at least eight hours a day, at times most suitable for themselves.

If and when they notice a difference between the appearance of cellulite between the two sides, they will notify us and we will then swap them into the 'normal' garments with Vari-pads on both sides, which they are then welcome to continue to wear.

Subjects:

We will be asking for volunteers of who are adult women (over the age of 18 years old), who are able to walk normally and have cellulite of their buttocks and/or upper thighs. We will ask them to check the inclusion and exclusion criteria and, if they believe that they are able to be part of the trial, they will be given an appointment to see the trial coordinator.

Inclusion Criteria:

- Women, over the age of 18 years old, who are able to walk normally and who have cellulite on their buttocks and/or upper thighs.

Due to having to produce special garments for this trial where only half of the garment has the Vari-pads, there will be for following restrictions:

Total number = 60

Volunteers will be asked their sizes (Small, Medium, Large and Extra-large) and will only be invited to attend if there are available places in that size category.

Sizes:

- Small = 15
- Medium = 15
- Large = 15
- Extra-large = 15

Exclusion Criteria:

- Women under 18 years of age.
- Women who are pregnant or who intend to get pregnant in the next 6 months.
- Women with no discernible cellulite on initial examination.
- Women undergoing any other treatment which aims to reduce the appearance of cellulite.
- Women who are unable to complete at least 3 months of this trial.

The Trial:

Volunteers will be asked to email their interest in the trial and will be asked to check that they fit the inclusion and exclusion criteria. If they do, they will be given a free of charge appointment.

Potential volunteers will then be sent the subject information sheet by email so they have ample opportunity to both read about the trials but in addition, to ask any questions before their first appointment. These can be answered by email. In this way, we hope that most volunteers will be suitable to proceed with the trial. We will stop recruitment when a maximum 60 subjects have been enrolled.

The garments will be worn for at least 8 hours per 24 hours. For hygiene reasons, we suggest that briefs/pants are worn under the garment. However, to increase the area of contact between garment and cellulite, we suggest wearing a thong, "high thigh", or similar panties.

There will be 4 visits required:

1] First Visit - Start of trial
2] 3 Months Visit
3] 6 Months Visit - End of trial
4] Variable end-point visit - whenever the subject can tell that there is a difference between the left and right sides - if the subject does not reach this end point, they will only have 3 visits and will not need the garment with Vari-pads on both sides.

First Visit (day zero):

Subjects will be asked to sign a consent form if they have asked sufficient questions and have decided to go ahead with the trial.

- Their cellulite will be graded as per the Nürnberger F, Müller grading system[3]

Grading Scale	Description
0	No alteration to the skin surface - NO CELLULITE SO THESE SUBJECTS will be EXCLUDED
1	Skin is smooth whilst subject is standing/lying, but alterations can be seen by pinching the skin, or by muscle contraction
2	'Orange-peel' or mattress appearance is evident upon standing without the use of any manipulation (pinching or muscle contraction)
3	Alterations seen in grade two presented together with raised areas and nodules

- Standard high-resolution photographs will be taken of their buttocks from behind, side and obliquely in the standing position with the muscles relaxed. The same will then be performed for the thighs. [Subjects will not be photographed in any way so as to be able to identify them.]
- Subjects will have height and weight measured and noted.
- Localised transcutaneous water content measurement using LymphScanner (Delfin Technologies, Finland) - this is a non-invasive device passed over the skin to determine the electrical conductance of the skin and sub-cutaneous tissues.
- They will be given a Celluqol® Quality of life questionnaire (long version - see appendix)[4] to complete.
- They will then be given the garment (x2) with one side covered with the Vari-pads, with the other side without any raised pads.

Variable End-point Visit:

When subjects can see or feel a significant difference in the cellulite of their buttocks and/or thighs between the sides, they will contact us and return for assessment.

At this visit, the following will be performed:

- Weight
- Photographs
- Questions as to the routine of garment wearing – how many hours per 24 and when
- Transcutaneous water content buttocks and thighs
- Celluqol® QOL Questionnaire
- They will be given 2 new garments with Vari-pads on BOTH sides.

3 Months Visit.

At this visit, the following will be performed:

- Weight
- Photographs
- Questions as to the routine of garment wearing – how many hours per 24 and when
- Transcutaneous water content buttocks and thighs
- Celluqol® QOL Questionnaire

6 Months Visit - end of trial and £100 paid if all visits completed. The subject can keep the x2 bilaterally padded garments.

At this visit, the following will be performed:

- Weight
- Photographs
- Questions as to the routine of garment wearing – how many hours per 24 and when
- Transcutaneous water content buttocks and thighs
- Celluqol® QOL Questionnaire

Primary endpoint:

- The time taken for patients to notice a self-determined significant difference between their right and left side and request the full garment.

Secondary endpoints:

- Quality of life changes by Celluqol® questionnaire 0, 3 and 6 months.
- Changes in photographs 0, 3, 6 months as assessed by 2 'blinded' observers
- Changes in transcutaneous water measurements

Interim Analysis:

We will perform an initial analysis when all of the results are in from the 1 month and 3 months visit.

Consent form: Please see attached.

Subject information sheet: Please see attached.

Insurance: The Whiteley Clinic has full insurance cover for clinical trials.

Payment: Subjects who complete the trial to 6 months will be allowed to keep the compression garments (worth £90.00 each) and will be given £100 in compensation for their time and travel.

References:

1 - Arora G, Patil A, Hooshanginezhad Z, Fritz K, Salavastru C, Kassir M, Goldman MP, Gold MH, Adatto M, Grabbe S, Goldust M. Cellulite: Presentation and management. J Cosmet Dermatol 2022; 21: 1393-1401.

2- Kiely MJ, Poulsen A, Muschamp SD, Sallis C, Whiteley MS. Participant Reported Improvement in Cellulite by Vari-pad Apparel and Objective Measurements – a "First Use" Pilot Study. Retrieved from osf.io/preprints/coppreprints/a3uq9 (accessed 13 June 2023)

3 - Nürnberger F, Müller G. So-called cellulite: an invented disease. J Dermatol Surg Oncol. 1978;4(3):221-229.

4 - Hexsel D, Weber MB, Taborda ML, Dal'Forno T, do Prado DZ. Celluqol® - a quality of life measurement for patients with cellulite. Surgical and Cosmetic Dermatology 2011 (Jan);3(2):96-101

CONSENT FORM

Identification Number for this trial:_____

Study Title: "Longitudinal trial assessing cellulite in women wearing a new compression garment - one side with ink printed micro-pads ("Vari-pads") and one side without."

Please initial/tick each box:

1. I confirm that I have read and understand the information sheet provided for the above study, including the process of assessment and photography. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected. ☐
3. I understand they my personal data is confidential and protected, and I agree to the potential publication of my anonymised results and images. ☐
4. I understand that relevant sections of my medical notes and data collected during the study may be looked at by individuals from regulatory authorities or from an NHS trust, where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records. ☐
5. I agree to take part in the above study and confirm that I believe that I meet the inclusion criteria ☐

Participant Name: _____ Signature:_____

Date: _____

Researcher Name: _____ Signature:_____

Date: _____

<u>OPTIONAL:</u> If you would like to be contacted to receive a summary of the study results, please write your email, OR home address, in the form below:

E-mail: **Home Address:**