



CHECKING THE ACCEPTABILITY AND EFFICACY OF A TOOTH WHITENING PRODUCT AFTER USING UNDER NORMAL CONDITIONS OF USE

In use test with clinical control by a dentist

June 23rd, 2005

Investigator: Ds. E. Jacquemyns

Co-investigator: Ph. T. Verhaeghe
Ph. D. P. Lombaert

Study Site: Dental Practice
Oude Houtlei 126
B- 9000 Gent
Belgium

Sponsor: Remedent N.V.

I. AIM OF THE STUDY

This study intended to check the mouth and tooth acceptability and efficacy of a tooth whitening product after using the product under normal conditions for 10 days:

The acceptability was:

- checked every day, by the volunteers themselves
- controlled after visual examination of the mouth and tooth acceptability by the investigator and after questioning of the volunteers.

The efficacy of the product was assessed, at the end of the study, by using Vitapan® Classical Shadeguide* (B1, A1, B2, D2, A2, C1, C2, D4, A3, D3, B3, A3.5, B4, C3, A4, C4). Tooth stain was evaluated on the facial surfaces of the front teeth.

II. STUDY SPECIFICATIONS

Ethics

The study is aiming at a better knowledge of the mouth and tooth tolerance and the efficacy of the test product. Taking into account that the foreseeable risk incurred by the volunteers who took part in the study being minor, there was a suitability between the aim of the study and its possible risks.

Methodological approach

The experimental conditions adopted (experimental area, frequency and duration of the applications, formula, product design...) reproduced the normal conditions of use advocated and the test performed on a "reproducible scale", reflected the use by future consumers.

The observance of the experimental conditions by the volunteers who took part in the study was assessed by a questionnaire at the end of the study and by a control of the product consumption. The acceptability and efficacy were controlled by the investigator who has an appropriate experience. The investigator, Ds. Jacquemyns, graduated in 1980 from the R.U. Gent (Belgium), she is the former president of the B.A.E.D. and member of several academies of esthetic investigatory and has been performing whitening procedures for more than 15 years.

Panel

The panel corresponded to the population likely to use the product: the inclusion criteria corresponded to the target market of the product.

The number of volunteers defined in the protocol was sufficient to check the acceptability and the efficacy of the test product.

Results

The results were expressed as descriptive and statistical data.

The data on efficacy were expressed in percentage improvement on the Vitapan® Classical Shadeguide.

The method is based on a relative scale referring to the initial teeth color and the maximum result that could be obtained (=B1).

If the acceptability and the efficacy of test product, under the experimental conditions, would be sufficient, the extrapolation of the data would result into a safe and efficient product for human teeth when applied, under normal conditions, by a major number of consumers.

* The VITAPAN® shade guide was ordered in terms of brightness as recommended by the manufacturer

III. TYPE OF STUDY

This study is an open study with control by a dentist.
The subjects were used as their own control.

IV. INVESTIGATION CENTRE AND TECHNICAL STAFF

Investigator: Doctor E. Jacquemyns (dentist)

Study Site: Dental Practice
Oude Houtlei 126
B- 9000 Gent

Co-investigators: Ph. D. Pol Lombaert
Ph. Tim Verhaeghe (toxicologist)

V. DATES OF PERFORMANCE OF THE STUDY

- Beginning on: June 3rd, 2005
- End on: June 13th, 2005

VI. TEST PRODUCT

1. Identification of the test product

Denomination	Meta Foam strips
Reference	MT
Batch number Meta Foam strips	MTX1
Content of the samples	1 Metatray and 20 Meta Foam strips

2. Information concerning the test product

The Metatray[®] product and the Meta[®] Foam strips form a dental system for professional use. The Metatray[®] is a portable system that combines a tray and patented technology. The technology uses light and heat energy to catalyse the whitening reaction of the additional foam strips. The Metatray[®] uses special Meta[®] Foam strips as whitening device.

VII. VOLUNTEERS

1. Number of volunteers

The number of volunteers whose data had to be exploitable at the end of the study was 20.
No volunteers discontinued and no exclusion was decided by the investigator.
The risks and benefits of participating in the study were explained to each potential subject prior to entering the study.

2. Inclusion criteria

- Ability to understand and provide informed consent,
- General good health Male and female adults, ages 18 to 55, inclusive,
- Availability for the full duration of the study,
- Minimum of twenty-four natural, uncrowned teeth. No fillings, veneers or other restorations in frontal teeth (8 upper, 8 lower arch),
- Ability to comply with all study requirements,
- For women: using a contraceptive method to avoid to be pregnant during the study,
- Covered by social security

3. Exclusion Characteristics

- Presence of any orthodontic appliances or severe malocclusion,
- Soft or hard tissue tumors of the oral cavity,
- Presence of extensive caries or severe calculus,
- Intrinsic stains on frontal teeth due to medications, trauma, secondary dentin deposition or dental procedures,
- Acute periodontal disease characterized by the presence of pain, purulent exudates, or severe tooth mobility requiring immediate treatment intervention,
- Subjects who are pregnant or nursing,
- Involvement in any concurrent study, the nature of which may affect the parameters being investigated in this study,
- Use of any medications that affect the flow of saliva or previous oral or maxillofacial radiation that might affect salivation,
- Use of chew tobacco,
- Teeth whitening treatment within 6 months before the beginning of the study,
- Forecast of tooth care during the study
- Treatment with topical anti-inflammatory drugs or antibiotics must be stopped 8 days before entering the study.

VIII. METHODOLOGY

1. Experimental conditions of use

See annex I

2. Constrains of the study and precautions of use

Constrains imposed on the volunteers were the following ones:

- Using of the usual toothbrush and no change of toothbrush and toothpaste during the study
- Full respect of the conditions of use of the test product
- No eating of products containing pigments or coloring agents like red wine, coffee, beetroots,...
- No tobacco during the test period
- No tooth care during the study
- No wearing of dental prosthesis or brace during the study
- No anti-aggregating, anti-coagulating nor analgesic treatment

The precautions of use were the following ones (as stated in the notice see annex I)

- Keep the product out of reach of children
- Keep the product in a cool dry place and away from direct sunlight
- If the product would be in contact with the eyes, rinse with water
- Avoid contact with clothes
- In the case of dental hypersensitivity contact the investigator
- In the case of abnormal discoloration of the teeth contact the investigator before stopping the treatment

3. Control of observance of the modalities of the protocol

Volunteers were questioned at the end of the study about the functionality and the way they used the product. The investigator assessed the importance of the possible deviations in comparison with the experimental conditions required at the beginning of the study.

All the deviations from the protocol were analyzed and the investigator assessed their effect on the validity of the results. If major deviations would occur they explicitly noted in the conclusion.

4. Checking of the efficacy: scoring of the shade of the teeth and photographs

On Day1= D1 (T0) before the treatment and on D10 after 10 days of use of the test product, the investigator scored the shade of the frontal teeth, according to the Vitapan® Classical Shadeguide*. For each volunteer, the score of each tooth obtained on D1 was compared to the score obtained on D10. According to the result, a conclusion was noted per volunteer concerning the whitening effect of the product.

Furthermore at D1 and D10 one photograph per volunteer was taken of the face (when smiling) and one close-up of the upper arch.

* The VITAPAN™ shade guide was ordered in terms of brightness as recommended by the manufacturer

5. Checking of the acceptability

Frequency of the examinations

The volunteers were requested to note every day any reaction, sensation or discomfort observed during the study on an individual observation sheet that was given at the beginning of the study. A tooth and mouth examination was performed by the investigator.

Expression of the results

The volunteers were questioned and examined by the investigator: the gathered information during the questioning was compared to the one that was noted every day by the volunteer on his individual observation sheet

IX. RESULTS

1. Checking the acceptability

Types of clinical signs reactions due to the test product	Percentage of volunteers exhibiting clinical signs due to the test product	Types of sensations of discomfort due to the test product	Percentage of volunteers exhibiting sensations of discomfort due to the test product
None	0%	Slight stinging Sensitivity to the gums Sensitivity of the lips Sensitivity of the tongue	25%

Note:

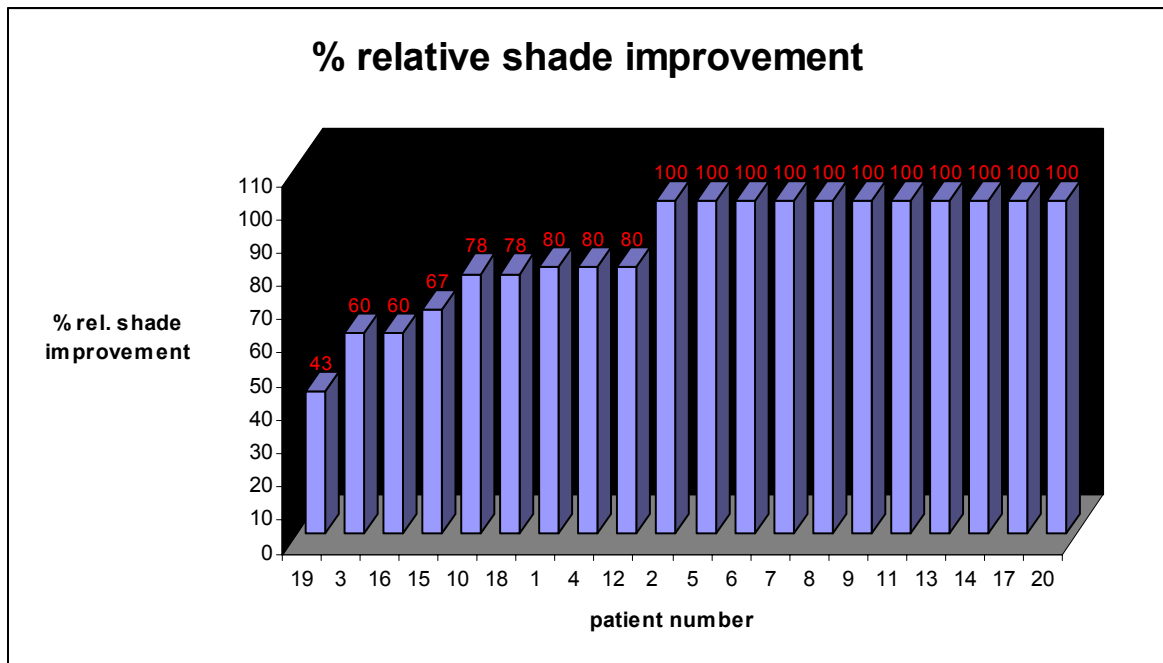
Five volunteers (vol. 2, vol. 5, vol. 6, vol. 7 and vol. 17) expressed slight sensations of discomfort but they were judged as minor and normal by the investigator after a dental control. None of these volunteers had to stop the treatment due to major side effects or discomfort directly related to the test product.

2. Scoring of the percentage relative shade improvement of the teeth

Patient nr.	Sex	Initial C	End C	% Rel. shade improvement
1	F	C1	A1	80
2	F	B2	B1	100
3	F	C1	B2	60
4	M	C1	A1	80
5	F	C2	B1	100
6	F	A1	B1	100
7	F	A1	B1	100
8	M	A1	B1	100
9	M	C2	B1	100
10	F	D3	B2	78
11	F	A2	B1	100
12	F	B3	B2	80
13	M	A1	B1	100
14	M	B2	B1	100
15	F	C2	B2	67
16	F	C1	B2	60
17	F	B2	B1	100
18	F	D3	B2	78
19	F	A4	A3	43
20	F	C1	B1	100

3. Checking the efficacy

3.1. Overview results



3.2. Best result

Patient number 5

Before



After



X. CONCLUSION

According to the experimental conditions adopted and taking into account the grading scale established by the investigator; the Meta® Foam strips, batch MTX1, reference MT, has a **correct and good acceptability on the mucous membrane**. No problems of major buccal intolerances were noted.

According to the experimental conditions adopted and taking into account the grading scale established by the investigator; the Meta® Foam strips, batch MTX1, reference MT, has a good efficacy. The data on efficacy were expressed in percentage relative shade improvement on the Vitapan® Classical Shadeguide*. The method is based on a scale referring to the initial teeth color and the maximum result that could be obtained (=B1).

The **average percentage relative shade improvement** of the Meta® Foam strips, batch MTX1, reference MT, was **86, 3 %**. Eleven patients had a percentage relative shade improvement of 100%.

* The VITAPAN™ shade guide was ordered in terms of brightness as recommended by the manufacturer

Annex I

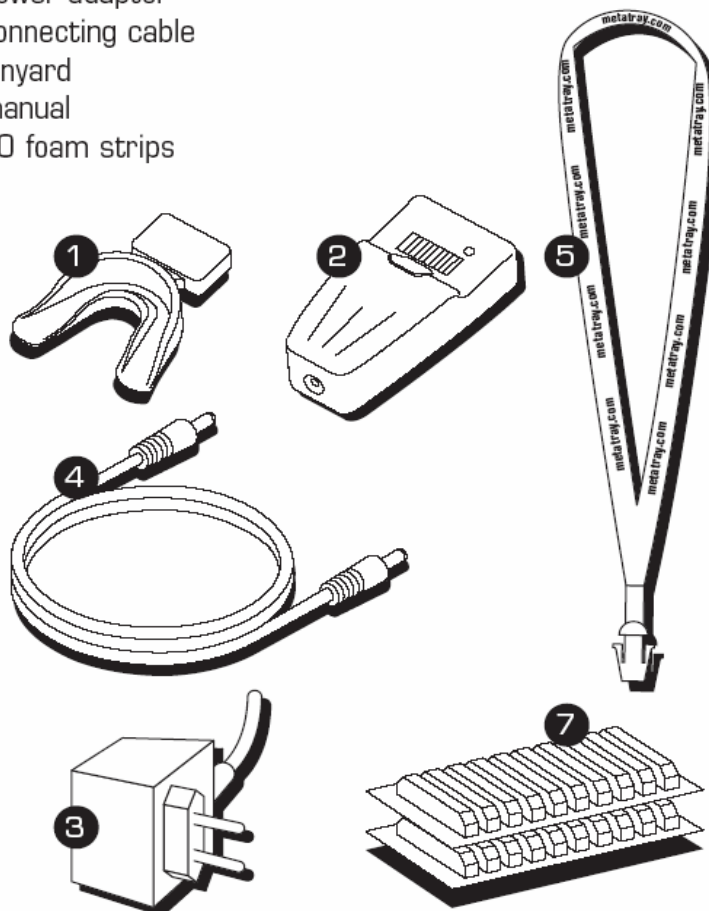
Metatray Operating Instructions UK

Before operating the unit and for optimum performance, please read these instructions carefully. Please retain this manual for future reference

A. Introduction

Parts:

1. mouthpiece
2. controller
3. power adapter
4. connecting cable
5. lanyard
6. manual
7. 20 foam strips



1

B. Getting Started

Charging the battery

The Metatray controller battery must be charged before you use the Metatray. Connect the power adapter to the socket at the bottom of the controller and to a wall outlet. Charge the battery for at least 3 uninterrupted hours.

During charging, the indicator LED (top right) will flash (green) until charging is complete. The controller is fully charged when the indicator LED stops flashing and is illuminated constantly (green).

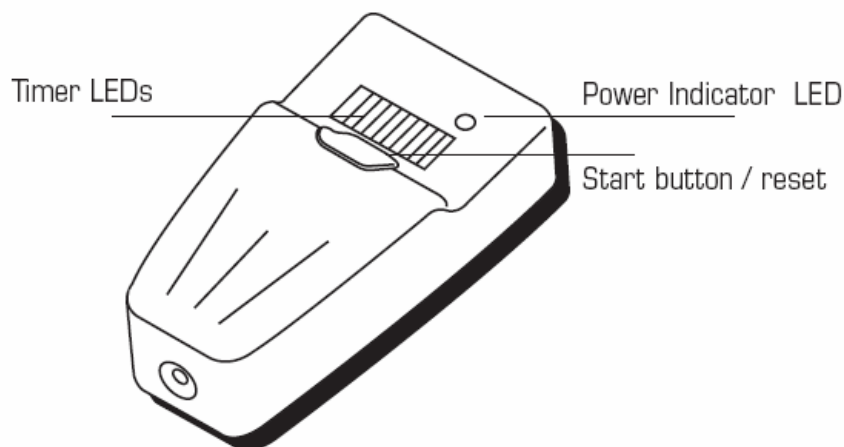
Important:

A display of 10 green LEDs shows the remaining usage time of the controller (each LED is equivalent to 2 minutes).

A fully-charged controller provides sufficient power for a complete upper and lower teeth treatment.

The controller should be recharged after each complete treatment of the top and bottom teeth (see below in the instructions for use).

Start the treatment when the indicator LED on the controller remains constantly green.

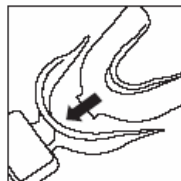
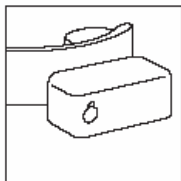


If the power indicator LED at the top right of the display flashes red during or before treatment, this means that the battery power is running low. If this happens, you can charge the controller during treatment by connecting it directly. This allows you to charge the device during use.

Instructions for use

- Wipe the mouthpiece thoroughly clean before first use and before every subsequent use. Use a small quantity of warm water and a minimal quantity of mild household detergent. Also bear in mind the following guidelines:

Important:



Make sure that the sealing valve on the mouthpiece remains closed.

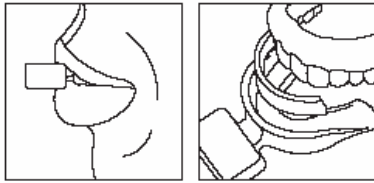
Do NOT immerse the mouthpiece in water or other liquid.

Remove the rubber sleeve from the mouthpiece and clean thoroughly.

Hold the mouthpiece firmly on the rectangular part and clean ONLY the curved tray.

Do not use solvent-based cleaners.

- Connect the connecting cable between the top socket on the controller and the mouthpiece.
- Take the blister pack of foam strips and follow the instructions below:
 - a. Clean your teeth before applying the product.
 - b. Tear off 1 individual blister pack.
 - c. Open the foil of the individual blister pack.
 - d. Remove the foam strip from its individual blister pack using the supplied tweezers and place it immediately in the tray. Position the



foam strip vertically in the tray with the long side down and the impregnated side (blue) towards the teeth. Avoid touching the foam strip with your fingers if at all possible.

- e. For your upper teeth, place the tray in your mouth facing the roof of your mouth; put your lips over the tray and carefully close your mouth. Make sure that the tray fits closely around your top teeth without sucking on the tray. Do not bite or press too hard as liquid may come out of the impregnated foam strip. Avoid swallowing the liquid.
- f. Activate the tray by pressing the push button on the controller once.
- g. One treatment per upper or lower arch of teeth lasts 20 minutes. It is inadvisable to remove the mouthpiece during the treatment; however, it is permissible for a short period under certain circumstances (e.g. in the event of excess saliva). The treatment is automatically stopped after 20 minutes with a beep. Remove the tray and discard the foam strip immediately.
- h. Brush and rinse any remaining liquid from your teeth and gums.
- i. Rinse the tray with a small quantity of warm water (see cleaning guidelines above).
- j. Repeat the treatment for your bottom teeth, this time placing the tray facing down.
- k. Clean the mouthpiece and rubber sleeve thoroughly (see above). Now your Metatray is ready for storage and future use.

C. Precautions

Device

- Only use the supplied power adapter for the intended purpose and only charge the controller with the supplier power adapter.
- Do not connect any other device or power source to the mouthpiece.
- Do not change the shape of the mouthpiece.

- Do not flatten or bend the mouthpiece.
- Do not bite or chew on the mouthpiece.
- Do not expose the parts to temperature extremes.
- Do not expose the parts to fire.
- Do not attempt to dismantle the parts.
- Keep the parts away from dirt and dust.
- Do not allow children to play with the parts.

Foam Strips

- Do not lie down while carrying out the treatment.
- Keep the product in a dry, cool place away from heat and direct sunlight. Storage above 21 °C will reduce the effectiveness of the product.
- Keep out of reach of children.
- Not recommended for use in excess of 20 minutes per arch.
- Not recommended for children under the age of 14.
- Not recommended for use if you are pregnant or breast-feeding.
- Not recommended for extended contact with human skin.
- Products containing peroxide do not affect fillings or crowns.
- Discontinue the treatment if you experience pain or excessive sensitivity.
- Rinse thoroughly with water in the event of contact with the eyes.
- Use of the product is inadvisable if you have known allergic reactions to peroxide.
- Avoid getting the product on clothing.
- For optimum results, avoid tobacco, coffee, red wine, fruit juice and other staining substances during the treatment period.
- Do not use this product if you suffer from gum problems.
- Visit your dentist every 6 months.

Annex II: Patient information sheet

Patient's Name:	M/F
Date of Treatment:	
Date of Birth:	
 Patient's Consumption Pattern:	
• Tobacco:	Y / N
• Tea:	Y / N
• Coffee:	Y / N
• Cola:	Y / N
• Red Wine:	Y / N
• Other colouring substances:	Y / N
 Patient's Medical History:	
• Antibiotics as a child:	1 / 2 / 3
• Fluor Tablets as a child:	1 / 2 / 3
• Fluorosis:	1 / 2 / 3
• Trauma:	Y / N
• Other internal discolouration:	Y / N
 Initial Colour Determination (Vitapan Classical Shadeguide[*])	
B1, A1, B2, D2, A2, C1, C2, D4, A3, D3, B3, A3.5, B4, C3, A4, C4	
← lighter shades – darker shades →	
 End Colour Determination (Vitapan Classical Shadeguide[*]):	
B1, A1, B2, D2, A2, C1, C2, D4, A3, D3, B3, A3.5, B4, C3, A4, C4	
← lighter shades – darker shades →	
 Comments:	

^{*} The VITAPAN™ shade guide was ordered in terms of brightness as recommended by the manufacturer