

**CONFIDENTIAL REPORT**

**Ref: AV-MK01-TD-JR08**

**NON INTERVENTIONAL TRIAL**

**EVALUATION OF THE EFFICACY OF**

**A MEDICAL DEVICE AGAINST HEADACHES**

**THROUGH:**

■ **SELF-ASSESSMENT QUESTIONNAIRE**

**TEST PRODUCT REFERENCE:**

**CEFALY®**

Study Sponsor:

**STX-Med Sprl Belgique**  
**4 rue des Chasseurs Ardennais**  
**B-4031 ANGLEUR**  
**BELGIUM**

Investigator:

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Operating licence issued by:



French Health Products Safety Agency  
for cosmetic products (n° 06055C)  
for dietary supplements (n° 06055S)

**MAY 2008**



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2. Self-assessment questionnaire
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## 2. SUMMARY OF THE STUDY

### 2.1 Objective

The objective of this study is to evaluate the in-vivo efficacy of a medical device against headaches coded:

**Test product reference: CEFALY®**

The evaluation is performed using:

■ **SELF-ASSESSMENT QUESTIONNAIRE**

The study lasts 28 days following the first use of the product.

### 2.2 Population

33 subjects were recruited at T0, 32 included for the study.  
The subjects selected for this study are healthy females (27 subjects) and males (5 subjects), between 18 and 54 years of age.

These subjects are selected according to the inclusion / non inclusion criteria listed in paragraph 3.1.

### 2.3 Study Schedule and Duration

Preinclusion: 13/02/08  
Beginning of the study: 14-15/02/08  
End of the study: 14/03/08  
Final results are sent by e-mail: 03/04/08

A CD-Rom of the report is also supplied.

Scheduled Procedures:

	<b>Preinclusion</b>	<b>T0</b>	<b>T+28 days</b>
Dates	<b>13/02/08</b>	<b>14/02/08 15/02/08</b>	<b>14/03/08</b>
<b>MEETING WITH THE GENERAL PRACTITIONER</b>	■		
<b>INITIATION SESSION UNDER A TECHNICIAN CONTROL TO INSURE THE GOOD USE OF THE DEVICE</b>		■	
<b>SELF-ASSESSMENT QUESTIONNAIRE</b>			■

### 2.4 Study design

- Open study.
- Non comparative study.
- Subjects serve as their own reference.

### 3. STUDY PROTOCOL

#### 3.1 Subject selection

Spincontrol's subject panel is composed of subjects selected on the basis of a questionnaire filled in on a computer, prior to the study, that provides details of their medical history, possible allergies, skin-care and make-up habits, as well as a certain amount of administrative information. The inscriptions are made by a certified beautician.

The selection procedures are elaborated in order to guarantee that the subjects receive all possible information about the aims of the study and the consequences of their participation.

This selection procedure includes:

- a preliminary interview, during which the following points are explained to the subjects: the study's modalities, its practical considerations, possible payment, as well as any possible cosmetic benefits, inconveniences or potential risks;
- the information form which is specific to the study, including all essential information is then read.
- the consent form is read, approved, and signed by the subject to substantiate the fact that they freely accept the conditions of the study which has been described to them;
- this consent form which was filled in freely and intentionally by the subject after it had been fully explained to them, in the event of any claims for damages, enables them to benefit from the terms of the insurance policies taken out by both the investigator and by the study sponsor as soon as the subject is accepted onto the study by the study manager.

The subjects selected for the study are chosen under the supervision of the investigator and study manager, on the basis of the inclusion/non inclusion and proscription/restriction criteria listed below.

A selection of 33 subjects is made for this study.

The results given include all of the present and assessable subjects at each examination.

##### 3.1.1 Inclusion criteria

###### **Standard criteria**

- Female (20+2 subjects) and Male (10+1 subjects);
- Healthy.
- Between 18 and 65 years of age.
- Available for the entire duration of the study (28 days).
- Motivated to freely participate in the study.
- Skin at assessed area is healthy (free of psoriasis, eczema, erythema, œdema, scars, wounds or lesions).
- Willing to follow the full product-application procedure.
- Able to justify a permanent address.
- Able to understand the French language (i.e. French-speaking subjects able to read the documents presented to them and to adhere to the participation conditions).
- Benefiting from Social Security medical cover.

### **Specific criteria**

- Having chronic headache more than once a week.
- Having recurrent headache for more than 2 years.
- Having anterior headache.
- Taking regularly analgesic.

### **3.1.2 Non-inclusion criteria**

#### **Standard criteria**

- Failing to meet the aforementioned inclusion criteria.
- *For the female subjects:* Being pregnant or breastfeeding in the past 3 months;
- *For the female subjects:* Intending to become pregnant during the study;
- Having changed their cosmetic habits in the 14 days preceding the start of the study or intending to change them during the study.
- Being in remanence, at the beginning of the study, on the studied area(s), following another cosmetic, dermatological, or medical test.
- Having undergone any major surgery in the previous year.
- Having undergone plastic surgery on the studied area(s).
- Having cutaneous hypersensitivity or a skin allergy to cosmetic products.
- Taking part or intending to take part in another study liable to interfere with this study.
- Following or intending to follow a chronic medicinal treatment comprising any of the following products taken orally: anti-histamines, corticotherapy;
- Being diabetic.
- Being chronically asthmatic.
- Failing to heed Article L1124-4 (new legislative part) of the amended law dated 20 December 1988, relating to:
  - the proscription of simultaneously participating in different biomedical research projects offering no direct individual benefit.
  - the non-inclusion period during which the subject cannot participate in any other biomedical research projects offering no direct individual benefit.
- Having participated in skin or peri-ocular tolerance testing in the past two weeks and/or in sensitisation trials in the past four months.
- Individuals sentenced to imprisonment by a court decision or in need of urgent care due to serious illness (Article L1121-5).
- Minors, as well as individuals of age, who are wards of the court, or mentally or physically handicapped individuals unless the study can be carried out in some other manner (Article L1121-6).
- The refusal to give their assent by signing the consent form.

#### **Specific criteria**

- Having posterior headache.
- Having chronic sinusitis.
- Having untreated medically arterial high blood pressure.
- Following or intending to follow an anti-depressant medication;
- Following or intending to follow an anti-migraine medication of type “triptan” (Imigrane®, Imiject®, Zomig®, Naramig®, Relpax®, Almogran®);
- Meniere’s disease;
- Recent facial or cranial traumatism;
- Flu-like, infectious condition or high infectious rhinitis;

### 3.1.3 Proscriptions and restrictions

#### **Standard criteria**

- The use of any of the following products taken orally is proscribed for the entire duration of the study: anti-histamines, corticotherapy, anti-depressants, anti-migraine medication and neuroleptics.

## 3.2 The products

### 3.2.1 Presentation of the products

The test product is supplied free of charge by the study sponsor.

The product is an electric medical device IIA class with a CE medical marking complying with the directive 93/42 CEE.

The product is packaged in a case with its notice and 6 electrodes.

For the preparation of the session, wipes are also supplied to clean the area before the use of the CEFALY®.

The study sponsor is in charge of product manufacturing and packaging. He/She is responsible for product identification, purity determination, composition, innocuousness, and any other characteristics of each product to be tested prior to the beginning of the study.

**The study sponsor must supply a certificate of innocuousness for the tested product.**

The study sponsor is responsible for supplying the exact amount of product needed to carry out the test(s).

**The product should be delivered to the study manager one week prior to the beginning of the study at the latest.** Should there be a delay in this delivery time, due to the responsibility of the study sponsor, another time must be arranged between the two parties.

For this study, the study sponsor agrees to supply:

- The appropriate quantity of the product required to treat all of the subjects;
- A sufficient quantity of the product for any additional subjects participating in the study;
- One product unit per reference and per batch to be retained in the sample cabinet.

Products are stored in an ambient temperature away from light.

At the end of the study, the products used by the volunteers or the left over products can be sent back to the promoter if he has asked for it on the document attached to the quotation or by mail, sent at the beginning of the study.

On the other hand, the investigator proceeds to eliminate the remaining products according to the method of their choice described in their procedures.

The costs of resending or destroying the products by the investigator are charged to the promoter.

### 3.2.2 Product application

The application is carried out by the subjects:

Product	Application areas	Frequency of application	Application duration	Conservation
CEFALY®	Forehead	<b>Initiation session at T0</b> <b>1 session at T+1 day</b> <b>1 session during every painful event</b> (maximum supportable intensity)	<b>28 days</b>	<b>At ambient temperature</b>

#### **Session modalities:**

- ✓ Preparation of the session:
  - Clean the lower and central part of the forehead and the glabella area with the wipe.
  - Apply the PATCH onto this area (the narrow part of the patch on the bottom of the glabella).
- ✓ Apply the DEVICE with the central electric part on top of the PATCH, and then align the electric part with the press stub.
- ✓ Use the DEVICE for a FULL SESSION under the maximum supportable intensity (for 20 minutes)
- ✓ Take off the DEVICE and the PATCH (5 uses per patch)

### 3.3 Study design

- This is an “open study”. Both the participating subjects and the investigator are aware of the type of product being applied.
- This is a non-comparative study.
- The subjects serve as their own reference.

### 3.4 Study procedures: Self-assessment questionnaires

The subjects are asked to answer self-assessment questionnaire. This questionnaire is designed in agreement with the study sponsor.

The questionnaires are filled out in SPINCONTROL's offices.

These documents are drawn up using Scan' Bac software (3SI company). Answers are read by means of a Canon printer and data acquired via the Scan' Bac software. A descriptive analysis is undertaken using Excel (Microsoft).

A copy of this questionnaire is available in Appendix 4 of the protocol.

### 3.5 Examination schedule

The effect of the product is evaluated over a 28-day period. The scheduled measurement procedures are as follows:

#### **Preinclusion**

- Checking of the inclusion/non inclusion criteria;
- Clinical observation and description of the quality of the skin at the measuring areas;

#### ***At T0 before the application of the product:***

- Acknowledgement, reading and signature of the consent form;
- Initiation session under a technician control to insure the good use of the device;
- Distribution of the test product and of the information form.

#### ***At T+1 day:***

- Session at home even in the absence of pain to get used to the treatment

#### ***At T+28 days:***

- Checking of the proscriptions and restrictions;
- Discussion about the volunteer's tolerance towards the product;
- Clinical observation of the quality of the skin at the measuring areas;
- Self-assessment questionnaire;
- End of test-product application. Subjects are indemnified.

### 3.6 Data analysis and statistics

The analysis involves establishing frequency tables that take into account the number of responses and calculate the frequency of the different possible answers (given as percentage) to each qualitative question. For each question, results are shown in tabular form (number of individuals and frequency).

To evaluate the efficacy and the appreciation of the products for each item, percentages are calculated. As a pilot study there is no control group and no statistical analysis was performed.

## 4. ETHICAL AND LEGAL CONSIDERATIONS

### 4.1 Study personnel

The investigator assures that the study manager and everyone who participates in this study have the required qualifications and abilities to carry it out.

### 4.2 Data archiving

Dual archiving is ensured by using both paper and IT storage media.

Paper files are archived in locked premises, located near a fire extinguisher. Electronic backup on DAT tapes are also stored for 10 years.

The investigator keeps a copy of the protocol signed by both himself and by the Study Sponsor, as well as the original “observation records”, questionnaires and all associated documents, the participation consents, and all project-related documents of any type for a 10-year period following delivery of the final report.

All these documents are accessible upon request for inspection by the study sponsor, their representative or by administrative authorities. The investigator informs the study sponsor of his intention to proceed with their destruction after the 10-year period.

### 4.3 Insurance

The study sponsor insures this study by taking out a policy with:

**ETHIAS n°04/044 45.168.947**

The investigator is insured for civil liability under the terms of the following policy:

**AXA n° 000 000 2270 670 004**

The investigator and the study sponsor have both taken out separate insurance policies to cover their civil liability with regards to the subjects.

Excerpt of modified law n°88-1138, dated December 1988, regarding the protection of individuals taking part in biomedical research trials (Article L1121-7):

“With regard to biomedical research without any direct individual benefit, the study sponsor assumes responsibility for compensating an injured participant and their eligible beneficiaries for prejudicial consequences resulting from the study, even without being at fault and without it being possible to blame third parties or the withdrawal of the individual who had initially volunteered to take part in the research”.

### 4.4 Declaration to the CNIL

In compliance with the law on “Information technology and freedom” dated January 6<sup>th</sup>, 1978, the existence of the database that Spincontrol refers to for all of its studies has been declared to the CNIL (Commission Nationale de l’Informatique et des libertés).

The promoter of the study cannot have access to the confidential data relative to the subjects registered in the data base of Spincontrol.

#### 4.5 Anonymity of the subjects

The subjects are identified for the study sponsor using a five-character alphanumeric code and a number. The investigator makes a commitment not to raise the anonymity of the subjects.

#### 4.6 Consent to participate in the study

An information form is given to each subject providing full details about the study and:

- its objectives, methods, and duration;
- possible expected benefits, constraints, and potential risks (especially should the study be discontinued);
- the non-inclusion period, the amount of the payment, the right of access to data files and their later destruction.

This information enables the subjects to sign their participation consent form freely and unequivocally, in the knowledge that they are fully aware of the testing details.

#### 4.7 Confidentiality

All the information, data, and results of the study are confidential.  
Everyone having access to such data are informed of their confidentiality.

Medical information about the subjects obtained before the study by the investigator during the recruitment and admission procedures is handled confidentially in compliance with the Penal Code's Article 226-13 and subsequent ones, as well as with the Medical Ethics Code (Decree n°95-1000, December 6th, 1995).

In all cases, nominal information of this type shall not be transmitted to the study sponsor.

“The investigator, as well as individuals conducting the testing, are bound by professional secrecy concerning the nature of the products under study, the trials, the volunteers, and the final results” (excerpt from Article R 5120 of Decree n°90-872 dated September 27th , 1990, that comes under modified law n°88-1138, dated December 20th 1988, regarding the protection of human biomedical-research subjects: Huriet law).

#### 4.8 Quality Assurance

The entire file (protocol, results, final report, and study-related documents) is subject to quality assurance procedures in compliance with regulatory recommendations. Verifications of data generated in this study are performed in accordance with the **POS-ASQ-AU03-Procédure de Contrôle qualité des documents d'étude**.

The investigator cooperates in ensuring any additional auditing required by the study sponsor with regards to the protocol or the current procedures.

## **4.9 Regulations**

This study, which has no direct therapeutic purpose, is undertaken according to the most recent recommendations given by the World Medical Association (Helsinki Statement 1964, amended in Edinburgh, Scotland, 2000).

As it does not fall under the field of application of French law n° 88-1138 dated December 20, 1988, modified by laws n° 90-86, dated January 23, 1990 and n° 94-630, dated July 25, 1994, as is indicated in the “legislative and regulatory text guidebook” (B.O.M.S n° 91/13 b), concerning the protection of subjects participating in biomedical research, no information is communicated to the National file of subjects participating in biomedical research without direct individual benefit and the counsel of the Advisory Board is not sought.

However, the spirit of Decree 90-872 dated September 27th, 1990, concerning the application of this law is heeded.

## **4.10 Practical Considerations**

A preliminary agreement between the Investigator and the study sponsor, concerned by the present contract, is necessary for any publication or communication directly concerning the two parties. They must both take the initiative to inform each other if a change is to occur.

## 5. RESULTS

### 5.1 Deviations from the study the protocol

The protocol was respected as a whole.

### 5.2 Cutaneous reactions

No cutaneous reaction was noted by the subjects during the study.

### 5.3 Absences and withdraws from the study

#### Withdraw at T0:

- Subject n°23: PAPGI: she did not tolerate the device.

The data for this subject at T0 was not exploited, the subject was removed from the study panel.

### 5.4 Population considered in the expression of the results

#### **At T0, 33 subjects were recruited, 32 included:**

Considering the information previously mentioned in the paragraphs 5.1 to 5.3, the number of subjects considered in the expression of the results, are presented in the following table :

Technique \ kinetic	T+28 days
SELF ASSESSMENT QUESTIONNAIRE	32

### 5.5 Description of the exploited panel at T0

At T0 the exploited panel consisted of **27 women** and **5 men** between 18 and 54 years of age (**Mean age: 33 years old**, see detail in appendix 1), having anterior chronic and recurrent headache more than once a week, for more than 2 years and taking regularly analgesic.

## 5.6 Self assessment questionnaire

The detail of the results of the self evaluation is presented in appendix 2.

### 5.6.1 Results tables

The following table summarises the agreement percentages recorded for each suggested item at T+28 days.

PROPERTIES	Evaluation at 28 days
	% Agreement
<b>Questionnaire to evaluate the change in pain whilst using the device during the painful episode:</b>	
Using the device during the painful episode makes the pain go away:	66%
The device is simple to use:	94%
The sensation produced by the device during a session is pleasant:	44%
The sensation produced by the device during a session is not painful:	66%
<b>Questionnaire to evaluate the change in pain in the two hours following a session with the device:</b>	
In the two hours that followed the session of treatment with the device, the pain disappeared:	56%
<b>Questionnaire on the preventive effect frequency of painful episodes</b>	
During the test, the frequency of painful episodes decreased:	59%
<b>Questionnaire on the preventive effect intensity of painful episodes</b>	
During the test, when you had painful episodes, they were less painful than normal:	56%
<b>Questionnaire on taking medication</b>	
During the test your consumption of pain relief medication decreased:	63%
<b>Questionnaire on general state (well-being) :</b>	
During the test, your « well-being » was better than normal:	47%
During the test, your quality of life was better than normal:	44%
<b>Overall opinion</b>	
I am satisfied with the treatment:	63%
I wish to keep and continue to use the device:	63%

### 5.6.2 Results analysis

After 28 days of use, the most recognized item is « **The device is simple to use** » with **94% of favourable opinion**.

The agreement percentages are very good: **3 items out of 10** obtained percentages of agreement **more than 63%** (“Using the device during the painful episode makes the pain go away”, “The sensation produced by the device during a session is not painful” and “During the test your consumption of pain relief medication decreased”) and **3 items** out of 10 **more than 56%** (“In the two hours that followed the session of treatment with the device, the pain disappeared:”, “During the test, the frequency of painful episodes decreased” and “During the test, when you had painful episodes, they were less painful than normal”). Then only 3 items obtained a positive opinion inferior to 50%.

**Concerning the overall opinion**, 63% of the subjects are “satisfied with the treatment” and they “wish to keep and continue to use the device”.

## 6. CONCLUSION

The use of the medical device CEFALY®, for 28 days, by a panel of 32 subjects between 18 and 54 years of age, lead to, through self evaluation questionnaires, the following results:

The device received a **very good reception from the panel**, both on its:

- **The practical aspect.** « The device is simple to use » which obtained the best percentage of agreement with 94%

and on :

- **The effectiveness after 28 days of use** with a majority of items with percentage of positive opinion from 56% up to 66% (*“Using the device during the painful episode makes the pain go away”, “The sensation produced by the device during a session is not painful”, “During the test your consumption of pain relief medication decreased”, “In the two hours that followed the session of treatment with the device, the pain disappeared:”, “During the test, the frequency of painful episodes decreased” and “During the test, when you had painful episodes, they were less painful that normal”*).

Overall, **63 % of the subjects are “satisfied with the treatment” and they “wish to keep and continue to use the device”** which confirms the excellent reception of the product by the panel.

***APPENDIX 1***  
**Panel characteristics at T0**

## ***APPENDIX 2***

### **Self assessment questionnaire**

***APPENDIX 3***  
**Copy of the study protocol**