Trial number	KF10004/08	
Title of trial	Lidocaine 5% medicated plaster for the topical treatment of localized chronic postoperative neuropathic pain	
Trial design	Randomized, multi-center, double-blind, placebo-controlled, parallel group, Phase II proof-of-concept trial	
Development phase	Phase II	
EudraCT number	2009-016337-10	
Publication number	761541	
Indication	Localized chronic postoperative neuropathic pain (PoNP)	
Trial sponsor	Grünenthal GmbH, 52099 Aachen, Germany	
Coordinating investigator	[redacted] 75019 Paris, France [redacted]	
Trial sites	22 active sites in France	
Trial period	First subject enrolled:	24 Aug 2010
	Last subject completed:	27 Nov 2012
	Early trial termination:	15 Oct 2012

Objectives

Primary objective:

- To assess the analgesic efficacy of lidocaine 5% medicated plaster in comparison to placebo in subjects with moderate to severe localized chronic PoNP.

Secondary objectives:

- To evaluate the effect of lidocaine 5% medicated plaster on quality of life, allodynia, and various symptoms of localized neuropathic pain in subjects suffering from localized chronic PoNP.
- To evaluate the safety and tolerability of lidocaine 5% medicated plaster in subjects suffering from localized chronic PoNP.

Investigational medicinal products

Lidocaine 5% medicated plaster, batch number 19132 (expiry date 31 Dec 2011) and batch number 60082 (expiry date 31 May 2013); placebo plaster visually not distinguishable from lidocaine 5% medicated plaster, batch number 19081 (expiry date 31 Dec 2011) and batch number 60081 (expiry date 31 May 2013).

Treatments

Subjects in the Lidocaine Plaster Arm applied lidocaine 5% medicated plaster once daily on a daily basis for 4 weeks. Subjects in the Placebo Plaster Arm applied placebo plasters once daily on a

daily basis for 4 weeks. The most appropriate daily time period for plaster application and removal (taking the typical daily variation of pain into consideration, e.g., any increase/decreases in pain) was identified individually for each subject at enrollment and was not to be changed during treatment.

At the Randomization Visit, subjects were allocated to either lidocaine 5% medicated plasters or placebo plasters (ratio of 1:1). Depending on the size of the painful area, 0.5, 1, 1.5, 2, 2.5 or 3 lidocaine 5% medicated plasters or placebo plasters were applied on the painful skin area for between 12 hours and 18 hours per day. The number of plasters applied per day was defined individually for each subject by the investigator at Visit 2 to ensure that the most painful PoNP area was fully covered; this number had to remain unchanged during the Double-blind Treatment Period. The plasters had to be applied to healed skin (no skin disease, skin irritation, inflammation or injury, such as active herpes zoster lesions, atopic dermatitis, wounds, was allowed). If plaster adhesion problems emerged (e.g., for subjects with pain in the knee), the plasters had to be fixed in position using suitable mesh bandages. When needed, plasters could be cut into smaller sizes with scissors prior to removal of the release liner.

The use of rescue medication (tablets containing paracetamol 500 mg, ≤3 g/day) was allowed if an unbearable worsening of pain occurred between enrollment and the Final/Withdrawal Visit.

Trial population

Male or female subjects aged ≥18 years were enrolled who gave their informed consent and who were suffering from moderate to severe localized chronic PoNP following surgery, i.e., pain present for ≥6 months. Localized chronic PoNP was defined as chronic neuropathic pain in a single cutaneous area neurologically related to the site of prior surgery and following surgery (e.g., thoracotomy, total knee replacement, cholecystectomy, mastectomy, inguinal hernia repair, varicose vein stripping). The surgery leading to PoNP had to be performed ≤24 months prior to enrollment. At enrollment, subjects had to have a typical daily pain intensity of ≥5 on an 11-point numeric rating scale (NRS) and a score of ≥4/10 on the "Douleur neuropathique en 4 questions" (DN4) questionnaire. Furthermore, the size of the affected painful and healed skin area had to be smaller or equal to the size of 3 plasters.

Subjects with PoNP related to a surgery due to neoplasia were not enrolled if they were undergoing chemotherapy or radiotherapy for treatment of their neoplasia or if they had suspected residual neoplasia or metastases. Subjects with other painful conditions in the area of PoNP or infectious or non-infectious, inflammatory, or neuropathic causes, conditions representing a complication of the previous surgical procedure, with a diagnosis of complex regional pain syndrome type 1, with presence of total anesthesia in the neurological area of localized chronic PoNP, or with any topical treatment with capsaicin within the 6 months prior to enrollment were also excluded.

Methodology

The overall trial duration per subject was about 7 weeks (maximally 8 weeks) and included a 1-week Enrollment Period, a 4-week Double-blind Treatment Period, and a 2-week Follow-up Period. During the Double-blind Treatment Period, the subjects visited their trial site on the first day (Randomization Visit, Visit 2), after 1 week of treatment (Interim Visit, Visit 3), and after 4 weeks of treatment (Final Visit, Visit 4). All subjects attended a Follow-up Visit (Visit 5),

subjects who prematurely terminated their trial participation were asked to attend a Final/Withdrawal Visit (Visit 4) and Visit 5.

At the Enrollment Visit (Visit 1), a clinical diagnosis of neuropathic pain was made and included a neurological examination (e.g., dynamic mechanical allodynia [brush testing] and hypoesthesia testing). Subjects completed the Neuropathic Pain Symptom Inventory (NPSI) and recorded their typical daily pain. The investigator completed the DN4 questionnaire and recorded demographic data, prior and concomitant medication/treatment, medical and surgical history (including history of chemotherapy or radiotherapy and information on presence of neoplasia or metastases if applicable), vital signs, and body weight and height. Subjects had to be either treatment naïve, be receiving a stable oral treatment for localized chronic PoNP, or using a non-stable pain medication either as monotherapy or in combination with their stable pain treatment. They were allowed to continue taking their previous stable oral pain medication until the Final/Withdrawal Visit. Any non-stable or topical pain medication or topical treatment on the affected area had to be discontinued. A physical examination and a skin check at the anticipated site of plaster application were performed. Blood samples were taken for laboratory investigations (in total about 18 mL per subject). Rescue medication (paracetamol 500 mg) was dispensed.

Electronic diaries (eDiaries) were used to record pain intensities and rescue medication use. From enrollment until Visit 2, subjects assessed their pain right now (NRS-N) at the time points corresponding to the planned plaster application (at t = 0 h; NRS-N_0) and removal (at t = ≥12 h; NRS-$N_{\geq 12}$). The average and worst pain intensities over the last 24 hours (NRS-A and NRS-W) were assessed at the time points of planned plaster removal (i.e., at t = ≥12 hours).

At Visit 2, the investigator checked inclusion/exclusion criteria, the outcome of the laboratory investigations including pregnancy test, the subject's documented pain intensity and rescue medication entries, performed a drug accountability on the rescue medication used, recorded adverse events which occurred since enrollment, vital signs, and concomitant treatment, performed a skin check and allodynia testing, and requested the completion of the NPSI, Hospital Anxiety and Depression Scale (HADS), and the EuroQol-5 Dimension (EQ-5D) quality of life questionnaires. Subjects who had an average NRS-A7 of ≥5 (for the Enrollment Period, calculated over 7 days) and fulfilled all eligibility criteria were allocated to 1 of the 2 treatment arms. They received IMP/rescue medication and were instructed on use of IMP (e.g., number of plasters, application times). The subjects continued to record their pain assessments and IMP/rescue medication use.

At Visit 3 and Visit 4, diaries were checked for pain assessments, IMP application, and rescue medication use; drug accountability was performed. Allodynia was assessed. Adverse events, any changes in concomitant treatment, results of a skin check at the site of plaster application, and vital signs were recorded. Subjects completed the NPSI questionnaire.

At Visit 4, subjects additionally completed the HADS, Patient's Global Impression of Change questionnaire (PGIC), EQ-5D, and Treatment Satisfaction Questionnaire for Medication (TSQM). The investigator performed a physical examination and completed the Clinical Global Impression of Change questionnaire (CGIC). Blood samples were taken for laboratory investigations and pregnancy testing.

During the Follow-up Period, subjects did not receive rescue medication or IMP. They were allowed to continue their concomitant treatment and to use any additional pain medication required.

At Visit 5, a follow-up was made on all adverse events reported as ongoing at the last visit, newly occurring adverse events since the last visit were recorded, concomitant treatments were documented, the subject's skin at the site of plaster application was checked, and the outcomes of laboratory investigations (blood samples taken at Visit 4) were assessed.

Data collected

Efficacy and quality of life

Subject-documented pain intensity (NRS-A, NRS-W, NRS-N_0 and NRS-$N_{\geq 12}$), dynamic mechanical allodynia testing (brush test), NPSI, HADS, PGIC, CGIC, TSQM, EQ-5D scores.

Safety

Adverse events, vital signs (diastolic blood pressure, systolic blood pressure, and pulse rate, weight and height), physical examination results, laboratory blood test results including pregnancy tests and calculated glomerular filtration rate/creatinine clearance, subject-documented use of IMP and rescue medication, skin check outcome.

Other

Subject-documented typical daily pain, DN4 questionnaire scores, and testing of anesthesia at enrollment; demographic data, medical and surgical history, and prior and concomitant treatment.

Statistical methods

For this proof-of-concept trial, about 150 subjects were planned to be enrolled to allow the randomization of 100 subjects (50 per treatment arm). However, in 2012 it was decided to terminate this trial prematurely due to slow enrollment. Only about half of the planned number of subjects was allocated to treatment. All statistical analyses were performed in an explorative manner and inferential statistics should be regarded as hypothesis generating rather than confirmatory.

All data collected were presented by means of location parameters and measures of dispersion statistics (n, mean, standard deviation, minimum, 1st quartile, median, 3rd quartile, maximum) or absolute and relative frequencies as appropriate.

Safety analyses

The analysis of safety and tolerability data (e.g., adverse events, diastolic blood pressure, systolic blood pressure, and pulse rate, and laboratory parameters) was performed for the Safety Set (subjects allocated to treatment who applied any amount of IMP). Adverse events were coded using the Medical Dictionary for Regulatory Activities (MedDRA) Version 15.1. Treatment emergent adverse events (TEAEs) were summarized for each treatment group by primary system organ class (SOC) and preferred term (PT). For laboratory parameters, diastolic and systolic blood pressure, and pulse rate, descriptive statistics for the absolute values and the differences from baseline values (i.e., values at Visit 1) were calculated.

Efficacy analyses

The analyses of all primary and secondary efficacy parameters were performed on the Full Analysis Set (FAS) which consisted of all subjects of the Safety Set who had at least 1 valid post-baseline average 24-hour daily pain intensity assessment (NRS-A) (i.e., an assessment linked to a confirmed application/removal of plaster). Additionally, all analyses were performed on the Per Protocol Set (PPS, subset of subjects in the FAS who had no major protocol deviations during the trial). For the

primary endpoint, the last observation carried forward (LOCF) principle was applied to missing data for subjects who prematurely discontinued the trial. Additional methods were applied for assessing the robustness of this imputation strategy, e.g., Baseline Observation Carried Forward (BOCF) and Worst Observation Carried Forward (WOCF). The primary efficacy endpoint was summarized by descriptive statistics grouped by treatment and analyzed by means of an analysis of covariance including treatment as factor and the baseline pain intensity score as a covariate. For the primary efficacy endpoint, the baseline mean average pain intensity and the mean average pain intensity at the end of the Double-blind Treatment Period were calculated as the mean of the average 24-hour daily pain intensity (eDiary entries) over the last 7 days of the Enrollment Period or over the last 7 days of treatment with IMP (before the Final Visit or the Withdrawal Visit, respectively). If the Enrollment Period was shortened to 5 days (due to unbearable pain), the mean average pain intensity was calculated from those pain assessments which were recorded during this shortened Enrollment Period.

Summary of results

Subject disposition

A total of 74 subjects were enrolled in 22 sites with active recruitment, with 1 to 11 subjects per site. Twenty-two of 74 subjects were not allocated to treatment; all subjects but 1 were considered enrollment failures. For 1 subject there was a technical issue at Visit 2 and the subject could not be allocated to treatment. Overall, the subjects allocated to treatment (N = 52) were equally distributed among the treatment arms with 26 subjects per arm (Safety Set).

Population	Placebo N (%)	Lidocaine N (%)	Overall N (%)
Subjects planned			150
Subjects enrolled			74
Subjects enrolled but not randomized			22
Enrollment failure			21
Other reasons [a]			1
Randomized subjects/Safety Set	26 (100.0)	26 (100.0)	52 (100.0)
Subjects completing trial	25 (96.2)	21 (80.8)	46 (88.5)
Full Analysis Set	25 (96.2)	25 (96.2)	50 (96.2)
Per Protocol Set	20 (76.9)	21 (80.8)	41 (78.8)
Subjects randomized and prematurely discontinued	1 (3.8)	5 (19.2)	6 (11.5)
Adverse event [b]	1 (3.8)	0	1 (1.9)
Lack of efficacy	0	1 (3.8)	1 (1.9)
Protocol deviation	0	2 (7.7)	2 (3.8)
Other reasons [c]	0	2 (7.7)	2 (3.8)

a) Reason: technical issue at Visit 2 – randomization not possible.

b) The subject experienced a non-treatment emergent adverse event during the Enrollment Period, which led to trial discontinuation during the Double-blind Treatment Period.

c) For 1 subject, Visit 4 was planned 1 week in advance by mistake. One subject was not compliant: all visits had to be postponed and the IMP was not correctly used.

Six subjects prematurely discontinued their participation during the course of the Double-blind Treatment Period due to adverse events, lack of efficacy, other reasons (e.g., non-compliance with respect to IMP use, wrongly scheduled visit) or were withdrawn from the trial because of protocol deviations. No subject withdrew the informed consent, no subject died during the course of the trial, and no pregnancy was reported. A total of 46 subjects completed the Double-blind Treatment Period and attended the Follow-up Visit.

Demographics

A total of 52 subjects (34 women and 18 men) aged 22 years to 83 years were included in the Safety Set of the trial. The mean age was 50.2 years, 48.7 years in the Placebo Plaster Arm, and 51.7 years in the Lidocaine Plaster Arm. Most subjects were Caucasian/White (90.4%), 3.8% of subjects each were African/Black or Asian, and 1.9% had a Mahgrebi/North African origin. The majority of all subjects (78.8%) was >18 years and <65 years old; 21.2% were at least 65 years old (26.9% in the Lidocaine Plaster Arm and 15.4% in the Placebo Plaster Arm). The body mass index for all subjects ranged from 15.9 kg/m^2 to 47.3 kg/m^2 which indicates that several subjects in this trial were below or above normal or were obese. Mean (28.62 kg/m^2) and third quartile (32.30 kg/m^2) body mass indices were numerically higher in the Lidocaine Plaster Arm than in the Placebo Plaster Arm (mean 25.93 kg/m^2, third quartile 28.41 kg/m^2).

Efficacy and quality of life

This trial was terminated early when only 50% of the planned subjects were allocated to treatment. Given the low number of subjects in this trial, data have to be interpreted carefully. Additionally, the trial was designed as a proof-of-concept trial with a treatment period of only 4 weeks.

The application of lidocaine 5% medicated plaster and of placebo plaster led to a reduction of pain in subjects with chronic localized PoNP. The analysis of covariance for the change in pain intensity compared to baseline indicated no statistically significant difference between the treatment arms (LSmean for placebo plaster -1.27, LS mean for lidocaine 5% medicated plaster -0.89). In the Placebo Plaster Arm, more subjects (N = 25) than in the Lidocaine Plaster Arm (N = 21) completed 4 weeks of treatment indicating a protective device effect of the plaster even in the absence of lidocaine.

In the FAS, the baseline pain intensity (NRS-A_enroll) was numerically higher in the Placebo Plaster Arm (mean NRS of 7.03) than in the Lidocaine Plaster Arm (mean NRS of 6.42). Both treatment arms may not have been completely balanced in this proof-of-concept trial. Pain right now before plaster application (NRS-N_0) was the only value among all assessed pain values (NRS-A, NRS-W, NRS-N_0, NRS-$N_{\geq 12}$) that based on the mean weekly pain intensity in the fourth week, showed a numerically higher decrease in the Lidocaine Plaster Arm (-1.30) compared to the Placebo Plaster Arm (-1.02).

The change in NPSI in the overall score from Visit 2 to Visit 4 was similar in both treatment groups. A separation in favor of lidocaine 5% medicated plaster was observed for the single items Q2 (squeezing), Q3 (pressure), Q5 (electric shocks), and Q6 (stabbing).

Allodynia severity testing pointed towards a numerically more pronounced response in the Lidocaine Plaster Arm compared to the Placebo Plaster Arm.

The HADS questionnaire showed more pronounced anxiety and depression score reduction in subjects applying the placebo plaster than in subjects who used lidocaine 5% medicated plaster but these changes have to be interpreted with caution because mean baseline values were close to the threshold for potentially clinically relevant anxiety or depression.

For pain, allodynia severity testing, HADS, and NPSI, the baseline values were numerically higher in the Placebo Plaster Arm than in the Lidocaine Plaster Arm. Both treatment arms may not have been completely balanced in this proof-of-concept trial potentially due to a limited number of subjects.

The PGIC and CGIC assessments indicate an improvement in both treatment groups to a similar extent. At Visit 4, 8 of 25 subjects (32.0%) applying lidocaine 5% medicated plaster and 8 of 25 subjects (32.0%) applying placebo plaster rated their overall impression of change as “very much improved and much improved” (cumulative response). In both treatment arms, no subject reported that their overall status was worse since they began trial treatment. At Visit 4, clinicians stated that the overall impression of change was “very much improved and much improved” for 8 of 25 of their subjects (32.0%) applying lidocaine 5% medicated plaster and for 10 of 25 subjects (40.0%) applying placebo.

The TSQM showed slightly better overall treatment satisfaction in subjects who applied lidocaine 5% medicated plaster. “Taking all things into account” (Question 14 of the TSQM), a numerically greater proportion of subjects who completed 4 weeks of treatment and applied lidocaine 5% medicated plaster were satisfied with the medication they received (16 of 21 subjects, 76.2%) when compared to treatment completers who applied placebo plaster (17 of 25 subjects, 68.0%).

The Weighted EQ–5D Health Status Index increased from baseline (Visit 2) to Visit 4. The mean changes from baseline to Visit 4 were numerically higher for a treatment with placebo plaster than for a treatment with lidocaine 5% medicated plaster (0.1985 for placebo, 0.1624 for lidocaine 5% medicated plaster). Mean changes from baseline in the General Health State on the visual analogue scale were small and similar in subjects treated with lidocaine 5% medicated plaster (5.4) and with placebo plaster (3.1).

Rescue medication was used as allowed and is characterized by a wide dose range. The mean intake of paracetamol per subject and per week decreased during the trial in both treatment arms. Changes over time in the Lidocaine Plaster Arm were smaller than in the Placebo Plaster Arm.

Safety

- In total, 23 subjects in this trial reported 43 TEAEs: 11 subjects (42.3%) reported 19 TEAEs while they applied lidocaine 5% medicated plaster, and 12 subjects (46.2%) reported 24 TEAEs under placebo plaster treatment.
- There were no deaths, other serious adverse events, or TEAEs leading to a premature discontinuation from the trial during the Double-blind Treatment Period.

- The most frequently reported TEAEs (frequency of at least 5% in any treatment arm) had PTs belonging to the primary SOC "general disorders and application site conditions" (3 subjects with 3 events in the Lidocaine Plaster Arm and 6 subjects with 8 events in the Placebo Plaster Arm), "infections and infestations" (2 subjects with 2 events in the Lidocaine Plaster Arm and 6 subjects with 6 events in the Placebo Plaster Arm), and "gastrointestinal disorders" (3 subjects with 4 events in the Lidocaine Plaster Arm and 2 subjects with 2 events in the Placebo Plaster Arm).
- Three of 26 subjects (11.5%) in the Lidocaine Plaster Arm and 5 of 26 subjects (19.2%) in the Placebo Plaster Arm experienced TEAEs of the SOC "general disorders and application site conditions" that were considered by the investigator to be at least possibly related to the IMP application. All of them were skin-related. Under lidocaine 5% medicated plaster treatment, application site erythema (1), application site pain (1), and application site warmth (1) were reported, under placebo plaster, application site cold feeling (1 subject), application site pain (1), application site pruritus (2), and application site ulcer (1). In the Placebo Plaster Arm, 1 further subject experienced application site pruritus not judged as related to IMP application. Skin related TEAEs were observed with a similar frequency as in previous trials with lidocaine 5% medicated plaster.
- Three of 19 TEAEs (15.8%) in the Lidocaine Plaster Arm and 7 of 24 TEAEs in the Placebo Plaster Arm (29.2%) were expected and comprised application site disorders like cold feeling, erythema, pain, pruritus, ulcer, and warmth. Nine subjects (34.6%) in each treatment arm had unexpected TEAEs. In the Lidocaine Plaster Arm, 16 of 19 TEAEs (84.2%) were unexpected, in the Placebo Plaster Arm 17 of 24 TEAEs (70.8%).
- Based on the available data, no safety concern has been identified.
- Data from this trial do not change the benefit to risk ratio of lidocaine 5% medicated plaster.

Conclusion

- The application of lidocaine 5% medicated plaster over a 4-week treatment period and of placebo plaster both led to a clinically relevant reduction of pain in subjects with localized chronic PoNP. No differentiation between treatment arms was observed.
- The NPSI results indicate a treatment effect in favor of lidocaine 5% medicated plaster for specific neuropathic pain components (squeezing, pressure, electric shocks, and stabbing).
- Skin-related TEAEs were observed in both treatment arms with a similar frequency as in previous trials.
- Based on the available data, no safety concern for lidocaine 5% medicated plaster was identified.

Publications based on this trial

No data from this trial were published prior to the issue of this report.

ICTR SYNOPSIS SUPPLEMENT

KF10004/08

Original ICTR issue date:	01 Oct 2013	**DMS version:**	2.0
ICTR synopsis supplement date:	11 Mar 2015	**DMS version:**	1.0

1 SUPPLEMENT CONTENT

This document contains information about the trial that is not already covered in the synopsis of the corresponding clinical trial report.

2 INFORMATION ABOUT PROTOCOL AMENDMENTS

There were 3 amendments to the original protocol dated 05 Feb 2010.

Amendment 01 of 24 Mar 2010

This amendment was prepared to document the change in the responsible trial biostatistician, the decision to use ePen technology to complete paper-based questionnaires, to clarify when data were collected using an electronic Diary (eDiary) rather than other systems (e.g., electronic case report form [eCRF]), to mention that 0.5, 1, 1.5, 2, 2.5 or 3 plasters could be used, and to indicate that used investigational medicinal product (IMP) was not collected for drug accountability.

Amendment 02 of 18 Mar 2011

Amendment 02 changed the scheduled time point for the recruitment of the last subject, implemented new signature rules at the sponsor, and changed the address of the coordinating investigator.

Amendment 03 of 13 Apr 2011

This amendment was prepared to reflect the following changes:

- The scheduled time point for the recruitment of the last subject was updated.
- The enrollment failure rate was adapted in accordance with observations made during the trial.
- Subjects with additional types of surgeries leading to postoperative neuropathic pain (PoNP) were allowed for inclusion into the trial. The title of the trial was adapted accordingly.
- The analysis of the secondary endpoints by location of neuropathic pain (knee replacement or thoracotomy) was deleted.
- The procedure for collection of medical/surgical history at the Enrollment Visit was adapted.
- The sponsor’s Medically Qualified Person was changed.
- Definitions of the Safety Set and the Full Analysis Set (FAS) were corrected to reflect the possible use of only half of 1 plaster per application.
- The definition of non-treatment emergent adverse events (non-TEAEs) and TEAEs was adapted and shifted to Section 15.3.4.1 of the protocol as this differentiation was only required for the statistical analysis. Additionally, the analysis of the expectedness of adverse events by subject was corrected to be performed by event.
- The term of center was deleted in all statistical analysis models (primary and secondary) as the number of subjects per site was expected to be very small and thus centers were not expected to have any influence on the primary or secondary variables because they were unlikely to represent influences of clinical importance.

3 INFORMATION REGARDING CLINICAL HOLD OR EARLY TERMINATION

This proof-of-concept trial was prematurely terminated by the sponsor on 15 Oct 2012 due to slow enrollment. The coordinating investigator and all investigators were informed by mail/e-mail on the planned discontinuation of the trial. No subjects were enrolled thereafter. The last subject completed the last visit on 27 Nov 2012.

4 NAMES AND ADDRESSES OF PRINCIPAL INVESTIGATORS

The names of principal investigators for all sites are not included in the list below because consent for public disclosure was not obtained.

Site number	Investigator	Site address
11	(Name not given, since no consent given)	75019 Paris, France
12	(Name not given, since no consent given)	92100 Boulogne-Billancourt, France
14	(Name not given, since no consent given)	06003 Nice Cedex 1, France
15	(Name not given, since no consent given)	36000 Chateauroux, France
17	(Name not given, since no consent given)	87000 Limoges, France
18	(Name not given, since no consent given)	45032 Orleans, France
19	(Name not given, since no consent given)	69230 Saint Genis Laval, France
20	(Name not given, since no consent given)	42055 Saint-Etienne Cedex 2, France
21	(Name not given, since no consent given)	13285 Marseille, France
22	(Name not given, since no consent given)	35043 Rennes Cedex, France
23	(Name not given, since no consent given)	59037 Lille Cedex, France
24	(Name not given, since no consent given)	29609 Brest, France
26	(Name not given, since no consent given)	64109 Bayonne, France
27	(Name not given, since no consent given)	75012 Paris, France
28	(Name not given, since no consent given)	38500 Voiron, France
30	(Name not given, since no consent given)	91100 Corbeil Essonnes, France
31	(Name not given, since no consent given)	80100 Abbeville, France
33	(Name not given, since no consent given)	82013 Montauban, France
34	(Name not given, since no consent given)	93000 Bobigny, France
35	(Name not given, since no consent given)	33076 Bordeaux, France
36	(Name not given, since no consent given)	75475 Paris Cedex 1, France
38	(Name not given, since no consent given)	37000 Tours, France
39	(Name not given, since no consent given)	85925 La Roche Sur Yon, France