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**Onderwerp**

Uw verzoek o.g.v. de Wet openbaarheid van bestuur

Geachte heer Baakman,

Naar aanleiding van uw verzoek om informatie op grond van de Wet Openbaarheid van Bestuur (Wob), gedateerd 31 januari 2008, waarin u verzoekt om openbaarmaking van de het onderzoeksprotocol van het COFAM onderzoek alsmede de goedkeuring van het onderzoeksprotocol door de Air Force Research Laboratory (AFRL), bericht de Raad van Bestuur u als volgt.

Het onderzoeksprotocol alsmede de correspondentie tussen AFRL en TNO waaruit de goedkeuring met zoveel woorden blijkt bevatten namen van privépersonen en zijn daarom geanonimiseerd op grond van art. 10, tweede lid, aanhef en onder e en g van de Wob. Het belang van openbaarmaking van deze gegevens weegt niet op tegen het belang van eerbiediging van de persoonlijke levenssfeer van de betrokken personen en ook niet tegen het belang van het voorkomen van onevenredige benadeling van bij deze aangelegenheid betrokken natuurlijke personen of rechtspersonen dan wel derden.

Beslissing

Op grond van vorenstaande overwegingen wijst de Raad van Bestuur uw verzoek om informatie toe. De betreffende documenten zijn bij deze brief gevoegd.

Hoogachtend

Ir. J.C. Huis in 't Veld
Voorzitter Raad van Bestuur TNO

C. van Duyvendijk
Lid Raad van Bestuur TNO

Indien u zich met dit besluit niet kunt verenigen, kunt u daartegen binnen zes weken na heden bezwaar maken door indiening van een bezwaarschrift dat u kunt richten aan TNO, Afdeling Juridische Zaken, Postbus 6008, 2600 JA, Delft.

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Op opdrachten aan TNO zijn van toepassing de Algemene Voorwaarden voor onderzoekopdrachten aan TNO, zoals gedeponeerd bij de Rechtbank Den Haag en de Kamer van Koophandel Haaglanden; de Algemene Voorwaarden zullen op verzoek worden toegezonden.

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Protocol

Project: CRF28002
TNO 015.31904

Date: August 15, 2002

Title of the study: Double blind randomized three-way crossover evaluation of general symptoms and cognitive functions with or without exposure to GSM and UMTS-like fields in subjects presenting complaints subjectively attributed to GSM fields.

Institute: TNO Fysisch en Elektronisch Laboratorium

Investigator: [REDACTED]

Project advisor: [REDACTED]

Author: [REDACTED]

Version 9.2, August 15, 2002

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3 Names, Titles and Affiliations

Title of the project: Double blind randomized three-way cross-over evaluation of general symptoms and cognitive functions with or without exposure to GSM and UMTS-like fields in subjects presenting complaints subjectively attributed to GSM fields.

Principal Investigator : [REDACTED]

Co-investigator / [REDACTED]

Co-investigator : [REDACTED]

Statistician : [REDACTED]

Project advisor : [REDACTED]

Sponsors : Ministerie van Verkeer en Waterstaat, The Netherlands
Ministerie van Volksgezondheid, Welzijn en Sport, The Netherlands
Ministerie van Volkshuisvesting, Ruimtelijke Ordening en Milieu, The Netherlands

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4 Synopsis

Study title: Double blind randomized three-way cross-over evaluation of general symptoms and cognitive functions with or without exposure to GSM and UMTS-like fields in subjects presenting complaints subjectively attributed to GSM fields.

Study code: CRF28002

Principal Investigator: [Redacted]

Co-investigators: [Redacted]

[Redacted]

Study center: TNO Fysisch en Elektronisch Laboratorium

Objectives: 1. To investigate under double-blind conditions whether or not certain complaints were reported more frequently with exposure to GSM-fields than in periods without GSM-fields, without revealing to the subject the exposure conditions at that moment. 2. To investigate under double-blind conditions the influence on cognitive functions of exposure to GSM fields. 3. To investigate under double-blind conditions the influence on cognitive functions of exposure to UMTS-like fields.

Design: Double blind complete randomized 3-way cross-over with a wash-out period of 30 minutes between each session.

Study population: Male and female subjects presenting complaints subjectively attributed to GSM fields.

Treatments [Redacted]

Test treatment 1: Controlled exposure to 900 MHz GSM fields similar to base stations

Test treatment 2: Controlled exposure to 1.800 MHz GSM fields similar to base stations

Test treatment 3: Controlled exposure to 2.100 MHz UMTS-like fields that are expected to be generated by future UMTS base stations

Reference treatment: Placebo (no exposure)

Duration of each treatment: 30 minutes

Number of subjects to be included: 72

Assessment methods:

Key parameters: Measurement of Cognitive functions through a validated computer system of TNO (Task-o-Mat).
• Simple reaction time
• Memory task
• Visual selective attention task
• Auditive selective function task
• Tracking task
Subjective symptoms as recorded in quality of life questionnaires.

Statistical evaluation methods:

Key parameters:

All key parameters will be presented individually and descriptively (mean, SD, SEM, min, max, and median) and/or as frequency tabulations. Cognitive function parameters will be analysed in nested model 2 way-ANOVA applying Dunnett's option for the appropriate contrast with the placebo session. Differences between the treatment groups will be reported as mean and 95% confidence interval of the mean.

Shifts in scores related to the answers from the questionnaires will be analysed with the Rank-sum test, while differences will be analysed as semi-quantitative data- in the Cochran/Mantel/Haenszel test. For all tests statistical significance will be assumed at $p < 0.05$.

Analysis will be performed in SAS version 6.12.

Safety/tolerability:

Subjective complaints will be recorded and coded according to the WHO-nomenclature. Applying the Fisher's Exact test will compare the coded complaints data obtained during each session.

5 List of Abbreviations.

AE	Adverse Event
ANOVA	Analysis of Variance
CDR	Cognitive Drug Research
CDROM	Compact Disc Read Only Memory
CRF	Case Report (Record) Form
CRFI	Clinical Research Facilities International B.V.
CRO	Clinical (Contract) Research Organization
EM	Electromagnetic
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GSM	Global System for Mobile Communication
ICH	International Conference on Harmonization
METC	Dutch acronym, translated into Medical Ethical Review Committee
QA	Quality Assurance
SAE	Serious Adverse Event
SD	Standard Deviation
SEM	Standard Error of the Mean
TNO	Netherlands organization for applied scientific research
W	Watt
WHO	World Health Organization
s	Second
SAS	Statistical Analysis System

6 Introduction

Worldwide, the introduction of the Global System for Mobile Communication (GSM) in the 1990's has dramatically increased the use of cellular telephones. Full-wave electromagnetic and thermal numerical models give insight into the thermal effects related to exposure to electromagnetic fields. However, very little information is available on the non-thermal influence of the electromagnetic fields caused by these telephones on human tissues and more specifically on brain tissues. Regularly reports on health effects associated with the use of mobile telephone systems are published in scientific magazines and usually taken over by the lay press. In virtual all cases the reports relate to experiments that are either studies in animals or short-term studies in human volunteers. The investigated items reported on include the incidence of brain tumors¹, influence on Electro Encephalogram², excretion of pituitary hormones³, cognitive functions^{4,5,6,7}, thermal changes in the brain⁸, DNA damage⁹, lymphocyte and mitogen stimulation¹⁰, visual functions¹¹ etc.

The user of a GSM-telephone or the resident of a building with a base station in the proximity raises primarily one question: Is the use of a GSM-telephone (or living near the base station) potentially harmful? And more specifically:

1. Can it induce cancer?
2. Does it influence brain function?

The existing data does not support the hypothesis that a relation exists between the incidence of brain tumors and the use of GSM-telephones. An extensive international epidemiological study is presently ongoing under the coordination of the International Agency on Research on Cancer (IARC). In this study the relationship between the use of a GSM-telephone and the incidence of tumors in the head and neck region is being investigated. Initial results will probably not be available until 2003.

Many studies with contradictory results on the influence of cellular phones have been published. Concerning the cognitive functions four publications^{4,5,6,7} are found that report on short-term effects on cognitive functions. Surprisingly, a slightly significant increase in reaction time as found by Preece *et al.* [4] was not supported by results obtained by Koivisto *et al.* [5]. Krause *et al.* [6] report a slight increase for some memory tasks while under exposure of a GSM-like signal. All above mentioned studies concern the acute effect on the items studied in either healthy volunteers or in animals.

Hietanen *et al.* [7] studied the hypothesis that there exist hypersensitive persons who perceive subjective symptoms from electromagnetic fields emitted by hand held mobile telephones. Double blind provocation experiments were used. From their research they conclude that no causal link was found between exposure to cellular telephones and hypersensitivity symptoms.

The present study contributes to the research on finding a causal relation between electromagnetic fields and brain functions. In contrast to Hietanen *et al.* [7] we

- focus our research to people living close to base station antennas;
- measure the cognitive functions of the volunteers during the exposure (including placebo).

There are subjects who have reported to experience physical complaints such as headaches, lack of concentration and sleeping disorders. These acute effects are associated to the presence of electromagnetic fields generated by mobile telephones of base-stations. Henceforth, these electromagnetic fields will be denoted as GSM-fields.

For regulatory purposes it is very important to know whether or not these complaints are truly an effect of the GSM-fields or that the subjects merely attribute the complaints to these fields. If the complaints are really an effect of the GSM-fields efforts must be made to reduce these fields.

6.1 Scientific goal and results

6.1.1 Volunteers

One way to find out if the complaints are really an effect of exposure is to bring these subjects into an experimental setting in which they at random undergo a period with exposure and a period without exposure, without knowing which is which. If the complaints are truly an effect of the GSM-fields the subjects should more frequently report complaints during a period of exposure than during a period without exposure.

A typical feature of the complaints reported by the study subjects is that the complaints arise shortly after exposure to GSM fields and go away once exposure is stopped. However, not all subjects report these complaints and not under all exposure conditions.

In the Netherlands, people can report complaints that they ascribe to environmental factors to Stichting Meldpuntennetwerk Gezondheid en Milieu and may be registered if they want. Those registered people form an interesting study population. Due to legal restrictions concerning privacy protection, Stichting Meldpuntennetwerk Gezondheid en Milieu will acquire the volunteers for this study from their database.

The subjects for this study are classified into two groups with similar demographic background. Group A denotes the control group, namely a group of volunteers without any complaints. Group B denotes the group whom has previously reported to experience complaints and have attributed these complaints to GSM exposure. It is noted that subjects who have an impaired health status will be excluded. Persons suffering from coronary disease and psychiatric illness will be excluded too.

6.1.2 Experimental setup

The subjects within group B do not experience complaints at any given GSM exposure and at any instance that they are exposed. Therefore it is necessary to perform the study by means of comparing the occurrence of complaints between groups and is it insufficient to perform an N=1 study. As elucidated in Chapter 16, we have calculated that with a total sample size of 72 subjects we obtain a power of 80% to find statistically significant results regarding reported complaints between the periods with exposure and without exposure. The proposed sample size of the experiment will be capable of statistically detecting a difference of 5% on the cognitive test that will be used.

If the complaints indicated by members of group B are really an effect of the GSM fields efforts must be made to reduce these fields. One way to find out if the complaints are really an effect of exposure is to bring these subjects into an experimental setting in which they randomly undergo a period with exposure and a period without exposure, without knowing which is which. If the complaints are truly an effect of the GSM fields the subjects should more frequently report complaints during a period of exposure than during a period without exposure.

Every subject (from groups A and B) is requested to undergo a period with GSM exposure and a period without GSM exposure. In this way every subject will serve as

his/her own control. Within the design of the study a sufficient washout period will be adhered to, in order to make sure that possible effects of the exposure are not carried over to the non-exposed period.

Exposure arms will be Placebo, GSM900, GSM1800 and UMTS-like signals.

6.1.3 Scientific goal

The goal of this research is to determine a causal relation between electromagnetic fields and the subjective symptoms together with cognitive performance associated with this electromagnetic stimulus. It is noted that the effects under investigation are reported as present shortly after exposure to GSM-fields.

This research goal is pursued by using a double-blind cross-over design in order to investigate the real influence of fields on the symptoms reported. Comparing the symptoms as reported by the subjects with and without the presence of GSM/UMTS-like fields, and without their knowledge of that exposure condition, would eliminate the subjectivity. At the same time cognitive functions will be evaluated.

6.1.4 Experimental design

With respect to the electromagnetic field strength used in this study it is mentioned that due to the lack on scientific data an exact prediction of reasonable exposure limits is not possible. Instead, we have chosen to generate electromagnetic field strengths in accordance to the real-life situation. It is noted that in this situation the volunteers of group B experience their subjective complaints.

Currently, there is no scientific evidence whatsoever that electromagnetic fields induce a cumulative effect that leads to any kind of saturation. Therefore, the authors assume the absence of cumulating effects and saturation.

The scientific community lacks data concerning the causal relationship between electromagnetic field strength (stimulus) and the complaints subjectively attributed to the stimulus. The number of complaints and the subject's perception is diverse.

The test system that will be used in this study is proven to be effective in the evaluation of cognition as an exponent of brain functioning, the influence of pathological processes and the effect of drugs. Thorough analysis of the collected data will contribute to answering the question whether spontaneous subjective complaints are associated with exposure to electromagnetic fields generated by GSM-telephones or base station antennas.

Finally, it is noted that the constant presence of the base-station antennas during the measurements might invite the volunteers to malingering the results. If that is the case, the design of the proposed study will lead to the conclusion that no causal relationship between electromagnetic field and the subjective symptoms from this electromagnetic stimulus are found. However, in order to have some insight whether the volunteers have a more than to be expected tendency to malingering the experimental results, we will include a personality test denoted as 'Big Five'. This test (in Dutch) is given in Appendix VII "Questionnaires".

7 Objectives

- To investigate under double-blind conditions whether or not certain complaints were reported more frequently with exposure to GSM-fields than in periods without GSM-fields, without revealing to the subject the exposure conditions at that moment.

- To investigate under double-blind conditions the influence on cognitive functions of exposure (including Placebo) to GSM fields.
- To investigate under double-blind conditions the influence on cognitive functions of exposure (including Placebo) to UMTS-like fields.

8 Study design considerations

Experience with questionnaires related to quality of life has shown that the first time such a questionnaire is filled in by a subject, the answers are given in an exaggerated way. Even a randomization as scheduled in this study and thus creating the possibility to eliminate a sequence effect cannot prevent that the discriminative power of the comparison will be affected substantially. Therefore in the present study the subjects will be evaluated during 4 sessions. During the 1st session the subjects will fill out the questionnaire and perform the cognitive function test for training reasons. It is stressed that during that first session none of the subjects will be exposed to GSM fields. The subjects will be informed on the absence of GSM/UMTS-like fields.

During the 2nd, 3rd and the 4th session the real comparison will take place under double-blind randomized conditions. The subject information sheet will state that during each session it is possible that there is exposure to GSM/UMTS-like fields. However, it is unknown by the subject during which session(s) this will take place.

To ensure reproducibility of the data, a special device will be used to create GSM fields as required on a fixed distance. An effective fixed power will be used, in accordance with the maximum effective field strength a normal GSM base station generates in public places as well as what is to be expected that UMTS base stations will generate in the near future.

TNO-FEL has carried out measurements in order to determine electromagnetic field strengths in houses and other freely accessible locations. Based on these measurements the electromagnetic field value located at a height of 1.5 m is chosen to be 1 V/m. This value is within the pertaining exposure limits¹² (less than 2.5% of the lowest reference value). The measurement setup is presented in Figure 1.

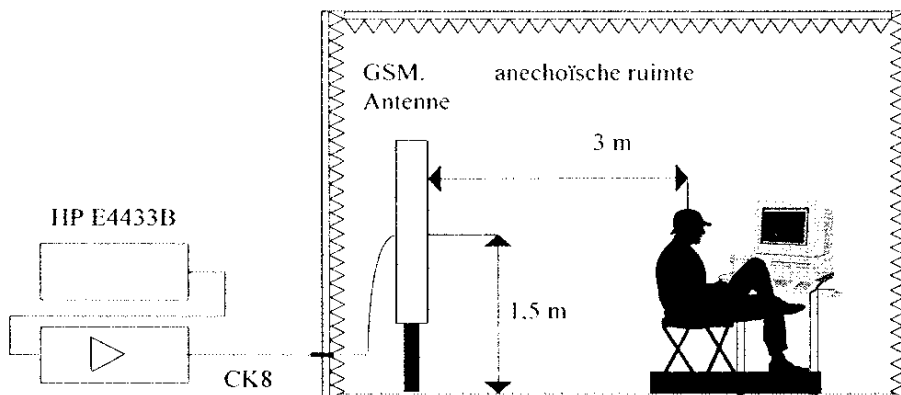


Figure 1. Measurement setup used during the proposed study.

Exposure procedure

Subjects will be exposed to GSM/UMTS-like fields in a special shielded chamber at the facilities of TNO-FEL. This room shields electromagnetic fields between 10 kHz and 20 GHz (>70 dB) and provides a conditioned environment in which exposure is limited to the in-room generated fields. Before the experiments, the exposure of 900 MHz GSM-fields, 1800 MHz GSM-fields and 2100 MHz UMTS-like fields will be defined. The field strengths will be comparable to those measured or expected in a real environment. These values are well below any health-based exposure limits. The waveform to generate a GSM-like signal is defined in the European prestandard ENV 50204¹³. Those for UMTS-like fields in ETSI TS 125 102¹⁴ and TS 125 105¹⁵.

Any restrictions in signal and waveforms will be demanded by the available equipment.

9 Measurement methods

9.1 Schedule of exposure

Subjects will be randomly allocated according to a balanced block randomization (For group A [control group] 18 blocks of 2 subjects; for group B [subjects with complaints] 18 blocks of 2 subjects.) taking into account all sequences.

Group	Block	N	Session 1	Session 2	Session 3	Session 4
A/B	1	2	Training	Placebo	2100 MHz	900 MHz
	2	2	Training	Placebo	2100 MHz	1800 MHz
	3	2	Training	Placebo	900 MHz	2100 MHz
	4	2	Training	Placebo	1800 MHz	2100 MHz
	5	2	Training	Placebo	900 MHz	1800 MHz
	6	2	Training	Placebo	1800 MHz	900 MHz
	7	2	Training	900 MHz	Placebo	2100 MHz
	8	2	Training	1800 MHz	Placebo	2100 MHz
	9	2	Training	2100 MHz	Placebo	900 MHz
	10	2	Training	2100 MHz	Placebo	1800 MHz
	11	2	Training	900 MHz	Placebo	1800 MHz
	12	2	Training	1800 MHz	Placebo	900 MHz
	13	2	Training	900 MHz	2100 MHz	Placebo
	14	2	Training	1800 MHz	2100 MHz	Placebo
	15	2	Training	2100 MHz	900 MHz	Placebo
	16	2	Training	2100 MHz	1800 MHz	Placebo
	17	2	Training	900 MHz	1800 MHz	Placebo
	18	2	Training	1800 MHz	900 MHz	Placebo

9.2 Questionnaires

Three questionnaires will be used in the study

- Questionnaire A:** General questionnaire recording demographic data and personality profile (Big Five).
- Questionnaire B:** Questionnaire recording personality profile (NeoFFI/Big Five).

- 3. Questionnaire C: Quality Of Life questionnaire** according to Bulpit¹⁷. Evaluation questionnaire to be filled out right before and after the training session and right after each exposure session.

All questionnaires will be derived from validated Quality Of Life questionnaires and are presented in Appendix VII.

9.3 TNO cognitive test

TNO Soesterberg institute "Technische Menskunde" has developed a computer program and published¹⁶ results of measurements that are very well applicable in this study. Due to the fact that each volunteer has to perform 4 times a test in a relative short period of time the number of tasks should be limited.

During the exposure to GSM fields the subjects will perform the cognitive functions test. Afterwards, these test results will be evaluated.

The experience of CRFI is that this test will take 15-25 minutes. Exposure to GSM fields will continue until the subject has finished the session.

To evaluate cognitive functions the following tests will be performed

- Simple reaction time
- Memory task
- Visual selective attention task
- Auditive selective function task
- Tracking task

From these tasks reaction ability, recognition, cognitive attention, and motoric concentration will be derived as parameters.

9.4 Session 1: Training session

Questionnaire A Demography:

A questionnaire will be filled out recording demographic data, medical history, concurrent diseases and concomitant medication.

Questionnaire B (Big Five):

Questionnaire B will be filled out recording the present situation of the subject right before the training session.

Questionnaire C QOL:

Questionnaire C will be filled out recording the present situation of the subject right before the training session and include the evaluation of subjective symptoms.

The outcome of this questionnaire will be considered as training.

Cognitive functions

Training session without exposure

Questionnaire C QOL:

Questionnaire C will be filled out recording the present situation of the subject right after the training session and include the evaluation of subjective symptoms. The outcome of this questionnaire will be considered as baseline.

9.5 Session 2: Randomized Placebo/900 MHz/1,800 MHz/UMTS-like 2,100 MHz

Cognitive functions

Exposure session

Questionnaire C QOL:

Questionnaire C will be filled out recording the present situation of the subject right after the training session and include the evaluation of subjective symptoms.

9.6 Session 3: Randomized Placebo/900 MHz/1,800 MHz/UMTS-like 2,100 MHz

Cognitive functions

Exposure session

Questionnaire C QOL:

Questionnaire C will be filled out recording the present situation of the subject right after the training session and include the evaluation of subjective symptoms.

9.7 Session 4: Randomized Placebo/900MHz/1,800 MHz/UMTS-like 2,100 MHz

Cognitive functions

Exposure session

Questionnaire C QOL:

Questionnaire C will be filled out recording the present situation of the subject right after the training session and include the evaluation of subjective symptoms.

10 Flow chart

Activity	Training	Randomized Placebo/900 MHz/1,800 MHz		
	Session 1	Session 2	Session 3	Session 4
Questionnaire A	X			
In- exclusion criteria	X			
Questionnaire B	X			
Cognitive functions	X	X	X	X
Questionnaire C	X	X	X	X

11 Hypothesis

Null-hypothesis: There is no statistically significant difference with respect to any of the subjective symptoms and the task parameters as recorded during placebo exposure, to standardized 900MHz exposure or 1,800 MHz GSM field or 2,100 UMTS-like field exposure.

Alternative hypothesis: The data analysis shows that there is a statistically significant difference between one or more subjective symptoms and/or the CDR parameters as recorded during placebo exposure, to standardized 900MHz exposure or 1,800 MHz exposure or 2,100 UMTS-like field exposure ($\alpha=0.05$, two-tailed).

12 Subject recruitment

Included will be subjects who reported spontaneously to the Stichting Meldpuntenetwerk Gezondheid en Milieu with subjective complaints they attribute to GSM-fields, and who agree to participate as volunteer. It is noted that the recruitment of the participating

control group subjects will be organized by the Netherlands Organization for Applied Scientific Research TNO-FEL located in The Hague.

13 In- and exclusion criteria

13.1.1 Inclusion criteria subjects with complaints

- Male or Female subjects that reported subjective complaints to Stichting Meldpuntennetwerk Gezondheid en Milieu
- Age between 18 and 75 years (inclusive)
- Willing to give consent for participation in the study

13.1.2 Exclusion criteria subjects with complaints

- History of brain injury
- History of epilepsy
- History of claustrophobia
- Subject under treatment for a mental disease within 6 months prior to enrolment
- Subject treated with psycho-active drugs within 2 weeks prior to enrolment
- Any other condition that may interfere with the study according to the opinion of the investigator

13.1.3 Inclusion criteria control subjects

- Male or Female subjects willing to give consent for participation in the study
- Age between 18 and 75 years (inclusive)

13.1.4 Exclusion criteria control subjects

- History of brain injury
- History of epilepsy
- History of claustrophobia
- Subject under treatment for a mental disease within 6 months prior to enrolment
- Subject treated with psycho-active drugs within 2 weeks prior to enrolment
- Any other condition that may interfere with the study according to the opinion of the investigator

All subjects will be asked to refrain from consumption of any xantine – derivative containing drinks within 6 hours prior to the test procedure.

14 Randomization

In order to create a balanced design the randomization will be performed in blocks of twelve subjects in a special program designed in MS Excel and a list containing all randomization numbers and the order of exposure will be produced in 2 copies in 2 sealed envelopes.

For each subject number the absence (as Placebo) or presence of either exposure to 900 MHz, 1,800 MHz or 2,100 MHz during all 4 sessions will be listed.

The first list will be provided to the Quality Assurance manager of Clinical Research Facilities International B.V. in a sealed envelop.

The second list will be provided to the location where the investigation will be performed where only 1 pre-assigned person will have access to the randomization list.

The list containing the randomization codes will only be provided to the statistician after the database has been officially declared to be clean and closed and a copy has been provided as a not erasable copy on a CDROM to the QA manager.

Information will be given in both oral and written form (Appendices III and IV) and the informed consent will be obtained in full compliance with section 17 C4.24 of Appendix II. The full text of the written subject information/informed consent to be given to the subject is added to this protocol as Appendices III and IV.

15 Regulatory requirements

15.1 Ethics committee

The study described in this protocol will be presented to the Independent Review Board, as independent Medical Ethical Technical Committee (METC).

15.2 Regulatory affairs

The study described in this protocol will be conducted in compliance with the current revision (Edinburgh, Scotland, October 2000 and the note of clarification Ferney-Voltaire 2001) of the Declaration of Helsinki (Appendix II), and with the current "Wet medisch-wetenschappelijk onderzoek met mensen".

All observations and findings should be verifiable. Quality control will be applied to each stage of data handling to ensure that all data are reliable and have been processed correctly.

Investigational sites, facilities and laboratories, and all data (including source data) and documentation must be available for inspection by competent authorities, should this be required.

15.3 Informed Consent

The principles of informed consent in the current revision of the Declaration of Helsinki (Appendix II) will be implemented in the study.

Information will be given in both oral and written form (Appendices III and IV) and the informed consent will be obtained in full compliance with section 4.8 of Appendix II.

The full text of the written subject information/informed consent to be given to the subject is added to this protocol as Appendices III and IV.

16 Sample size considerations

For the reaction time in the task-o-mat test¹⁶ similar values are applicable. Literature indicates^{4,16} that the intra-subject variance is approximately 40-60% of the inter-subject variance. We based ourselves therefore on a between subject standard deviation of 100 msec and a within subject standard deviation of 50 msec.

In this study an increase of 5% (37.5 msec.) in delayed picture recognition and reaction time would be considered as an important change and is therefore set as value for significance. Calculating the sample size in a cross-over setting, at $\alpha=0.05$ and $\beta=0.20$ (power 80%) gives as outcome a group sample size of 28 subjects.

Withdrawals will be replaced by new subjects exposed to the same schedule as the subject withdrawn.

However, since three different frequency exposures and a placebo exposure is planned in 3 sessions, a balanced nested cross-over model will be necessary.

In the study-design as nested model (see section 9.1 of this protocol) a minimum number of 28 measurements with exposure to 900MHz and 1800 MHz is required. This number is inflated to 36 for unexpected withdrawals and/or exclusions from the analysis.

Simulations of the data in the nested model at a standard deviation of 50 msec revealed for the comparison of 900MHz and 1,800 MHz a difference of 35 msec as statistically significant. For the comparison of 900, 1800 MHz and 2100 MHz with placebo a difference of 30 msec would be statistically significant without correction for multiple comparisons. For a completely balanced design blocks of 18 subjects are necessary. Consequently we have chosen for a sample size of 36 subjects per group i.e. 36 subjects with complaints and 36 volunteers, thus compensating for the loss of power due to multiple comparisons.

With respect to the QOL questionnaire we have estimated that at $\sigma=3.0$ between the subjects within one group an mean difference of sumscore of 2 points (minimum 0, maximum 39) would be detected as statistically significant ($\alpha=0.05$, $\beta=0.20$ i.e. power 80%) at a group sample size of 36 subjects per group. For pre-treatment corrected data (within the subjects) we assume that the standard deviation will be 50% of the standard deviation between the subjects. For such analysis a sample size of 17 subjects will be sufficient to detect a difference of 2 points as statistically significant ($\alpha=0.05$, $\beta=0.20$ i.e. power 80%).

With respect to the reaction time as measured in the Taskomat test, an Std between the subjects of approximately 80 msec has been reported at an average of 650 msec. In order to be able to detect a difference of 65 msec (~10%) between the group with complaints and the control group as statistically significant with respect to reaction time a minimal sample size of 25 subjects per group will be required ($\alpha=0.05$, $\beta=0.20$). The Std within the subjects, however, has shown to be ~ 50% of the Std between the subjects. Therefore, in order to detect a difference of 40 msec between the exposure sessions (within a group) as statistically significant a sample size of 17per group would be required.

This yields that the planned sample size as indicated in section 9.1, combined with both the sensitivity in the measurement methods of Taskomat and the QOL questionnaire, is sufficient to detect differences in an adequate way.

17 Data-management, de-blinding and Statistical Analysis

Data-entry will be performed in a double-data-entry mode according to the Standard Operation Procedure of CRFI. Corrections in the database will be appropriately trailed and reported. The test data will be downloaded as electronic data into a SAS database. De-blinding of the data will be available after closing the database and the submission of a not erasable copy of the database on a CDROM to the holder of the randomization list. Data will be collected directly from the TNO testing system, from the questionnaires and put into a SAS database.

Statistical analysis will be performed in SAS (version 6.12).

Key variable for analysis will be the subjective experience of symptoms and shift of symptoms to be analyzed with the semi-quantitative test-procedures Cochran-Mantel-Haenszel, and the categorical tests Fisher's exact probability and Chi2 test.

The analysis of cognitive parameters will be performed using two-way ANOVA (as General Linear Modeling approach) with the Dunnett option as contrast statement, thus applying a correction for multiple testing versus placebo.

The first analysis will be comparison of radiation sessions with placebo for all included subjects including as factors group, block, exposure, subjects within sequence, session, sequence and interaction group x exposure according to the following hypothesis

$H_0 \mu_{\text{placebo}} = \mu_{900\text{MHz}} = \mu_{1800\text{MHz}} = \mu_{2100\text{MHz}}$

$H_1 \mu_{\text{placebo}} \neq \mu_{900\text{MHz}} \neq \mu_{1800\text{MHz}} \neq \mu_{2100\text{MHz}}$

where μ_{placebo} , $\mu_{900\text{MHz}}$, $\mu_{1800\text{MHz}}$, $\mu_{2100\text{MHz}}$ is the mean value of the parameter evaluated. If a statistical significance occurs for sessions, data will be corrected accordingly. If a statistical significance occurs for the interaction group x exposure the groups will be analyzed further separately.

Further detailed analysis may be performed to investigate relationship with gender, background of the subject, type of complaint and other demographic factors recorded. An important element in the analysis will be the sequence (within the subjects) i.e. the order of exposure and the session number in order to analyze carry-over and periodical effects. Since a, for the subjects, known placebo session will be performed prior to the blind phase special attention will be paid to adaptation effects that may occur at the blind phase. All statistical tests will be performed applying $\alpha=0.05$ (two-tailed) as level of significance. Data will be presented as mean \pm sd for quantitative data and as frequency tabulations for categorical and semi-quantitative data. Graphical exposures will be included in the report where appropriate.

18 Amendments to the Protocol

All modifications of the study will be laid down in (an) amendment(s) to the protocol. All amendments have to be approved by the METC.

19 Reporting

The study will be reported by Clinical Research Facilities according to the FDA guidelines for reports on medical devices and the report will be available within two months after the last subject is evaluated.

20 Estimated timelines

It is expected to start the experiments at T0. Taking into account a capacity of 2 subjects per working day we expect to collect the last data before T0 + 3 months. This means that the draft report will be available by the end of T0 + 5 months.

21 Publication

The investigator has the right to publish the results of the study regardless the outcome. Scientific publications will be performed in a peer reviewed journal or magazine. Any such scientific paper, presentation, or other communication concerning the study described in this protocol will first be submitted to the sponsor for mutual consultation at least six weeks ahead of time.

In case of a difference in opinion the sponsor shall have the right to postpone publication of the results in a scientific paper, presentation or communication concerning the study with a maximum period of 1 (one) month in order to reach mutual agreement for such a publication. The sponsor cannot postpone publication in case TNO recognizes serious danger to persons or material.

In any communication concerning this study the author(s) of this protocol will be included in the list of authors and the sponsor will be acknowledged for financial support.

22 Archiving of Data

The subject records of this study will be maintained for at least 15 consecutive years by Clinical Research Facilities International.

23 References

1. Hardell L, Nasman A, Pahlson A, Hallquist A, Hasson Mild K. Use of cellular telephones and the risk for brain tumors: A case control study. *Int J Oncol* 1999 Jul; 15(1): 113-116.
2. Freude G, Ullsperger P, Eggert S, Ruppe I. Effects of microwaves emitted by cellular phones on human slow brain potentials. *Bioelectromagnetics* 1998; 19(6): 384-387.
3. De Seze R, Fabbro-Peray P, Miro L. GSM radiocellular telephones do not disturb the secretion of antepituitary hormones in humans. *Bioelectromagnetics* 1998; 19(5): 271-278.
4. Preece AW, Iwi G, Davies-Smith A, Wesnes K, Butler S, Lim E, Varey A. Effect of a 915-MHz simulated mobile phone signal on cognitive function in man. *Int J Radiat Biol* 1999; Vol 75 (4): 447-456.
5. Koivisto M, Revonsuo A, Krause CM. Effect of 902-MHz electromagnetic field emitted by cellular telephones on response times in humans. *Neuroreport* 2000; 11:413-415.
6. Krause CM, Sillamaki L, Koivisto M. Effect of electromagnetic field emitted by cellular phones on the EEG during a memory task. *Neuroreport* 2000; 11:761-764.
7. Hietanen M, Hämäläinen A, Husman T. Hypersensitivity Symptoms Associated With Exposure to Cellular Telephones: No Causal Link. *Bioelectromagnetics* 23:263-270, 2002.
8. Velizarov S, Rashmark P, Kwee S. The effect of radiofrequency fields on cell proliferation are non-thermal. *Bioelectrochem Bioenerg* 1999 Feb; 48(1): 177-180.
9. Lai H and Sing NP. Single and double-strand DNA breaks in rat brain cells after acute exposure to radiofrequency electromagnetic radiation. *Int J Radiat. Biol* 1996 69:513-521.
10. Chagnaud JL, Veyret B. In vivo exposure of rats to GSM-modulated microwaves: flow cytometry analysis of lymphocyte subpopulations and of mitogen stimulation. *Int J Radiat Biol* 1999 Jan; 75(1): 111-113.
11. Urban P, Lukas E, Roth Z. Does acute exposure to the electromagnetic field emitted by a mobile phone influence visual evoked potentials? A pilot study. *Cent Eur J Public health* 1998 Nov; 6(4): 288-290.
12. Gezondheidsraad: Commissie Radiofrequente elektromagnetische velden. Radiofrequente elektromagnetische velden (300 Hz – 300 GHz). Rijswijk: Gezondheidsraad, 1997; publicatienummer 1997/01.
13. European pre-standard ENV 50204:1995-03 "Radiated electromagnetic field from digital radio telephones – immunity test. CENELEC
14. European Technical Standardization Institute (ETSI). Universal Mobile Telecommunications System (UMTS); UTRA (UE) TDD; Radio Transmission and Reception (3GPP TS 25.102 version 3.7.0 release 1999)
15. European Technical Standardization Institute (ETSI). Universal Mobile Telecommunications System (UMTS); UTRA (BS) TDD; Radio Transmission and Reception (3GPP TS 25.105 version 3.7.0 release 1999)
16. Boer L.C.. Taskomat: Evaluation of a computerized Test battery. *International Journal of selection and assessment*. 1995 April; 3(2) 105-114.
17. Bulpitt CL, Fletcher AL. The measurement of Quality of Life in hypertensive patients: a practical approach. *Br J Clin Pharmacol* 1990, 30:353-364.

24 Appendices

24.1 Appendix I Randomization list

Balanced list below will be randomized within the blocks

Subject with complaints							Volunteers						
Block	Sequence	Subject	Session 1	Session 2	Session 3	Session 4	Block	Sequence	Subject	Session 1	Session 2	Session 3	Session 4
1	1	1	Run-in	Placebo	2100MHZ	900MHZ	3	1	37	Run-in	Placebo	2100MHZ	900MHZ
2	1	2	Run-in	Placebo	2100MHZ	900MHZ	4	1	38	Run-in	Placebo	2100MHZ	900MHZ
1	2	3	Run-in	Placebo	2100MHZ	1,800MHZ	3	2	39	Run-in	Placebo	2100MHZ	1,800MHZ
2	2	4	Run-in	Placebo	2100MHZ	1,800MHZ	4	2	40	Run-in	Placebo	2100MHZ	1,800MHZ
1	3	5	Run-in	Placebo	1,800MHZ	2100MHZ	3	3	41	Run-in	Placebo	1,800MHZ	2100MHZ
2	3	6	Run-in	Placebo	1,800MHZ	2100MHZ	4	3	42	Run-in	Placebo	1,800MHZ	2100MHZ
1	4	7	Run-in	Placebo	900MHZ	2100MHZ	3	4	43	Run-in	Placebo	900MHZ	2100MHZ
2	4	8	Run-in	Placebo	900MHZ	2100MHZ	4	4	44	Run-in	Placebo	900MHZ	2100MHZ
1	5	9	Run-in	Placebo	900MHZ	1,800MHZ	3	5	45	Run-in	Placebo	900MHZ	1,800MHZ
2	5	10	Run-in	Placebo	900MHZ	1,800MHZ	4	5	46	Run-in	Placebo	900MHZ	1,800MHZ
1	6	11	Run-in	Placebo	1,800MHZ	900MHZ	3	6	47	Run-in	Placebo	1,800MHZ	900MHZ
2	6	12	Run-in	Placebo	1,800MHZ	900MHZ	4	6	48	Run-in	Placebo	1,800MHZ	900MHZ
1	7	13	Run-in	900MHZ	Placebo	2100MHZ	3	7	49	Run-in	900MHZ	Placebo	2100MHZ
2	7	14	Run-in	900MHZ	Placebo	2100MHZ	4	7	50	Run-in	900MHZ	Placebo	2100MHZ
1	8	15	Run-in	1,800MHZ	Placebo	2100MHZ	3	8	51	Run-in	1,800MHZ	Placebo	2100MHZ
2	8	16	Run-in	1,800MHZ	Placebo	2100MHZ	4	8	52	Run-in	1,800MHZ	Placebo	2100MHZ
1	9	17	Run-in	2100MHZ	Placebo	1,800MHZ	3	9	53	Run-in	2100MHZ	Placebo	1,800MHZ
2	9	18	Run-in	2100MHZ	Placebo	1,800MHZ	4	9	54	Run-in	2100MHZ	Placebo	1,800MHZ
1	10	19	Run-in	2100MHZ	Placebo	900MHZ	3	10	55	Run-in	2100MHZ	Placebo	900MHZ
2	10	20	Run-in	2100MHZ	Placebo	900MHZ	4	10	56	Run-in	2100MHZ	Placebo	900MHZ
1	11	21	Run-in	1,800MHZ	Placebo	900MHZ	3	11	57	Run-in	1,800MHZ	Placebo	900MHZ
2	11	22	Run-in	1,800MHZ	Placebo	900MHZ	4	11	58	Run-in	1,800MHZ	Placebo	900MHZ
1	12	23	Run-in	900MHZ	Placebo	1,800MHZ	3	12	59	Run-in	900MHZ	Placebo	1,800MHZ
2	12	24	Run-in	900MHZ	Placebo	1,800MHZ	4	12	60	Run-in	900MHZ	Placebo	1,800MHZ
1	13	25	Run-in	2100MHZ	900MHZ	Placebo	3	13	61	Run-in	2100MHZ	900MHZ	Placebo
2	13	26	Run-in	2100MHZ	900MHZ	Placebo	4	13	62	Run-in	2100MHZ	900MHZ	Placebo
1	14	27	Run-in	2100MHZ	1,800MHZ	Placebo	3	14	63	Run-in	2100MHZ	1,800MHZ	Placebo
2	14	28	Run-in	2100MHZ	1,800MHZ	Placebo	4	14	64	Run-in	2100MHZ	1,800MHZ	Placebo
1	15	29	Run-in	1,800MHZ	2100MHZ	Placebo	3	15	65	Run-in	1,800MHZ	2100MHZ	Placebo
2	15	30	Run-in	1,800MHZ	2100MHZ	Placebo	4	15	66	Run-in	1,800MHZ	2100MHZ	Placebo
1	16	31	Run-in	900MHZ	2100MHZ	Placebo	3	16	67	Run-in	900MHZ	2100MHZ	Placebo
2	16	32	Run-in	900MHZ	2100MHZ	Placebo	4	16	68	Run-in	900MHZ	2100MHZ	Placebo
1	17	33	Run-in	900MHZ	1,800MHZ	Placebo	3	17	69	Run-in	900MHZ	1,800MHZ	Placebo
2	17	34	Run-in	900MHZ	1,800MHZ	Placebo	4	17	70	Run-in	900MHZ	1,800MHZ	Placebo
1	18	35	Run-in	1,800MHZ	900MHZ	Placebo	3	18	71	Run-in	1,800MHZ	900MHZ	Placebo
2	18	36	Run-in	1,800MHZ	900MHZ	Placebo	4	18	72	Run-in	1,800MHZ	900MHZ	Placebo

24.2 Appendix II: Declaration of Helsinki

WORLD MEDICAL ASSOCIATION DECLARATION OF HELSINKI

Ethical Principles

for

Medical Research Involving Human Subjects

Adopted by the 18th WMA General Assembly

Helsinki, Finland, June 1964

and amended by the

29th WMA General Assembly, Tokyo, Japan, October 1975

35th WMA General Assembly, Venice, Italy, October 1983

41st WMA General Assembly, Hong Kong, September 1989

48th WMA General Assembly, Somerset West, Republic of South Africa, October 1996

and the

52nd WMA General Assembly, Edinburgh, Scotland, October 2000

A. INTRODUCTION

1. The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to provide guidance to physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data.

2. It is the duty of the physician to promote and safeguard the health of the people. The physician's knowledge and conscience are dedicated to the fulfillment of this duty.

3. The Declaration of Geneva of the World Medical Association binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act only in the patient's interest when providing medical care which might have the effect of weakening the physical and mental condition of the patient."

4. Medical progress is based on research which ultimately must rest in part on experimentation involving human subjects.

5. In medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society.

6. The primary purpose of medical research involving human subjects is to improve prophylactic, diagnostic and therapeutic procedures and the understanding of the aetiology and pathogenesis of disease. Even the best proven prophylactic, diagnostic, and therapeutic methods must

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continuously be challenged through research for their effectiveness, efficiency, accessibility and quality.

7. In current medical practice and in medical research, most prophylactic, diagnostic and therapeutic procedures involve risks and burdens.

8. Medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection. The particular needs of the economically and medically disadvantaged must be recognized. Special attention is also required for those who cannot give or refuse consent for themselves, for those who may be subject to giving consent under duress, for those who will not benefit personally from the research and for those for whom the research is combined with care.

9. Research Investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this Declaration.

B. BASIC PRINCIPLES FOR ALL MEDICAL RESEARCH

10. It is the duty of the physician in medical research to protect the life, health, privacy, and dignity of the human subject.

11. Medical research involving human subjects must conform to generally accepted scientific principles, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and on adequate laboratory and, where appropriate, animal experimentation.

12. Appropriate caution must be exercised in the conduct of research which may affect the environment, and the welfare of animals used for research must be respected.

13. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol. This protocol should be submitted for consideration, comment, guidance, and where appropriate, approval to a specially appointed ethical review committee, which must be independent of the investigator, the sponsor or any other kind of undue influence. This independent committee should be in conformity with the laws and regulations of the country in which the research experiment is performed. The committee has the right to monitor ongoing trials. The researcher has the obligation to provide monitoring information to the committee, especially any serious adverse events. The researcher

should also submit to the committee, for review, information regarding funding, sponsors, institutional affiliations, other potential conflicts of interest and incentives for subjects.

14. The research protocol should always contain a statement of the ethical considerations involved and should indicate that there is compliance with the principles enunciated in this Declaration.

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15. Medical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given consent.

16. Every medical research project involving human subjects should be preceded by careful assessment of predictable risks and burdens in comparison with foreseeable benefits to the subject or to others. This does not preclude the participation of healthy volunteers in medical research. The design of all studies should be publicly available.

17. Physicians should abstain from engaging in research projects involving human subjects unless they are confident that the risks involved have been adequately assessed and can be satisfactorily managed. Physicians should cease any investigation if the risks are found to outweigh the potential benefits or if there is conclusive proof of positive and beneficial results.

18. Medical research involving human subjects should only be conducted if the importance of the objective outweighs the inherent risks and burdens to the subject. This is especially important when the human subjects are healthy volunteers.

19. Medical research is only justified if there is a reasonable likelihood that the populations in which the research is carried out stand to benefit from the results of the research.

20. The subjects must be volunteers and informed participants in the research project.

21. The right of research subjects to safeguard their integrity must always be respected. Every precaution should be taken to respect the privacy of the subject, the confidentiality of the patient's information and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.

22. In any research on human beings, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail. The subject should be informed of the right to abstain from participation in the study or to withdraw consent to participate at any time without reprisal. After ensuring that the subject has understood the information, the physician should then obtain the subject's freely given informed consent, preferably in writing. If the consent cannot be obtained in writing, the non-written consent must be formally documented and witnessed.

23. When obtaining informed consent for the research project the physician should be particularly cautious if the subject is in a dependent relationship with the physician or may consent under duress. In that case the informed consent should be obtained by a well-informed physician who is not engaged in the investigation and who is completely independent of this relationship.

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24. For a research subject who is legally incompetent, physically or mentally incapable of giving consent or is a legally incompetent minor, the investigator must obtain informed consent from the legally authorized representative in accordance with applicable law. These groups should not be included in research unless the research is necessary to promote the health of the population represented and this research cannot instead be performed on legally competent persons.

25. When a subject deemed legally incompetent, such as a minor child, is able to give assent to decisions about participation in research, the investigator must obtain that assent in addition to the consent of the legally authorized representative.

26. Research on individuals from whom it is not possible to obtain consent, including proxy or advance consent, should be done only if the physical/mental condition that prevents obtaining informed consent is a necessary characteristic of the research population. The specific reasons for involving research subjects with a condition that renders them unable to give informed consent should be stated in the experimental protocol for consideration and approval of the review committee. The protocol should state that consent to remain in the research should be obtained as soon as possible from the individual or a legally authorized surrogate.

27. Both authors and publishers have ethical obligations. In publication of the results of research, the investigators are obliged to preserve the accuracy of the results. Negative as well as positive results should be published or otherwise publicly available. Sources of funding, institutional affiliations and any possible conflicts of interest should be declared in the publication. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.

C. ADDITIONAL PRINCIPLES FOR MEDICAL RESEARCH COMBINED WITH MEDICAL CARE

28. The physician may combine medical research with medical care, only to the extent that the research is justified by its potential prophylactic, diagnostic or therapeutic value. When medical

research is combined with medical care, additional standards apply to protect the patients who are research subjects.

29. The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists.

30. At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study.

31. The physician should fully inform the patient which aspects of the care are related to the research. The refusal of a patient to participate in a study must never interfere with the patient/physician relationship.

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32. In the treatment of a patient, where proven prophylactic, diagnostic and therapeutic methods do not exist or have been ineffective, the physician, with informed consent from the patient, must be free to use unproven or new prophylactic, diagnostic and therapeutic measures, if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. Where possible, these measures should be made the object of research, designed to evaluate their safety and efficacy. In all cases, new information should be recorded and, where appropriate, published. The other relevant guidelines of this Declaration should be followed.

As approved by the WMA Council on 7 October 2001 at its 160th Session in Ferney-Voltaire, France.

THE WORLD MEDICAL ASSOCIATION, INC.

DOCUMENT: Par29CLAR/DoH /Oct2001

TITLE: NOTE OF CLARIFICATION

ON PARAGRAPH 29 OF THE

WMA DECLARATION OF

HELSINKI

NOTES

This note of clarification was approved by the WMA Council at its 160th Council Session on 7 October 2001 in Ferney-Voltaire, France.

Action(s) Required

For distribution to governments, regulating bodies, representatives of the pharmaceutical industry and the media

As approved by the WMA Council on 7 October 2001 at its 160th Session in Ferney-Voltaire, France.

Par29CLAR/DoH/Oct2001

THE WORLD MEDICAL ASSOCIATION, INC.

NOTE OF CLARIFICATION ON PARAGRAPH 29

of the

WMA DECLARATION OF HELSINKI

The WMA is concerned that paragraph 29 of the revised Declaration of Helsinki (October 2000) has led to diverse interpretations and possible confusion. It hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:

- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method, or
- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm.

All other provisions of the Declaration of Helsinki must be adhered to, especially the need for appropriate ethical and scientific review.

24.3 Appendix III Subject information

Informatiebriefen betreffende het onderzoek TNO 015.31904 (CRF28002) met GSM en UMTS signalen zoals die worden uitgezonden door basisstations.

24.4 Informatiebrief aan mensen met klachten

Geachte mevrouw/mijnheer,

U hebt zich bij het Meldpuntennetwerk Gezondheid en Milieu gemeld omdat u het vermoeden heeft last te ondervinden van de aanwezigheid van een signaal van een GSM-basisstation. Daarom bent u uitgenodigd om deel te nemen aan een onafhankelijk wetenschappelijk onderzoek dat erop is gericht eventuele invloeden van GSM-signalen op de mens objectief vast te stellen. Het onderzoek wordt verricht door TNO Fysisch en Elektronisch Laboratorium (TNO-FEL) in samenwerking met het onderzoeksbureau Clinical Research Facilities International (CRF) in Schaijk. TNO heeft voor dit onderzoek opdracht gekregen van het Ministerie van Volksgezondheid, Welzijn en Sport, het Ministerie van Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer en het Ministerie van Verkeer en Waterstaat.

Waarom dit onderzoek?

Hoewel al eerder wetenschappelijk onderzoek is gedaan naar de relatie tussen elektromagnetische velden en klachten van mensen, is er nog steeds geen duidelijke conclusie te trekken. Dit onderzoek zal daarom iets anders worden opgezet dan voorheen gebeurde. Wij vinden het belangrijk dat niet alleen mensen meedoen die geen klachten van elektromagnetische velden hebben, maar ook mensen die zelf vermoeden last te ondervinden van elektromagnetische velden afkomstig van GSM-antennes. Daarom wordt voor dit onderzoek uw medewerking gevraagd.

De resultaten van dit onderzoek zijn van belang om objectief eventuele verbanden tussen GSM- (en in de toekomst UMTS-) signalen en de gemelde klachten te kunnen vaststellen. Als wetenschappelijk geen beïnvloeding kan worden vastgesteld is het niet waarschijnlijk dat uw klachten in een directe en acute relatie staan met de aanwezigheid van GSM-signalen. Indien er echter wel een relatie wordt gevonden, kunnen de opdrachtgevende ministeries hierop hun beleid aanpassen.

Wat houdt het onderzoek in?

In dit onderzoek zal worden nagegaan of er een invloed is van GSM- en UMTS-signalen op de door u gemelde klachten. Tegelijkertijd doen we metingen die direct samenhangen met hersenfuncties, zoals geheugen, alertheid en reactiesnelheid. In totaal zullen ruim 70 proefpersonen aan het onderzoek deelnemen.

Het onderzoek vindt plaats in het TNO Fysisch en Elektronisch Laboratorium in Den Haag. Er is een speciale onderzoeksruimte beschikbaar, die voor GSM-signalen volledig is afgeschermd van de buitenwereld. Het onderzoek zal een halve dag in beslag nemen. Inclusief reistijd bent u maximaal een dag kwijt aan uw deelname.

Voorafgaande aan het onderzoek zal u worden gevraagd een aantal vragen te beantwoorden die betrekking hebben op uzelf, uw algemeen welzijn en de door u gemelde klachten. Deze en alle andere gegevens zullen strikt vertrouwelijk worden behandeld, en niet voor andere doeleinden dan dit onderzoek worden gebruikt.

Vervolgens zal u worden verzocht plaats te nemen aan een tafel in de onderzoeksruimte, waar twee antennes staan van een GSM- en UMTS-basisstation. U zult op een beeldscherm een aantal eenvoudige vragen, opdrachten en aanwijzingen zien verschijnen, die u met een joystick en twee knoppen kunt beantwoorden of uitvoeren. Dit duurt ongeveer 25 minuten.

In totaal zal deze procedure vier keer worden doorlopen, onderbroken door pauzes van ongeveer een half uur. De eerste keer is bestemd om u vertrouwd te maken met de procedure, overigens zonder dat er een GSM- of UMTS-signaal aanwezig is. Bovendien krijgt u een uitvoerige uitleg. Tijdens de daaropvolgende keren zal er in willekeurige volgorde een GSM-, UMTS- of géén signaal worden uitgezonden. Zowel u als de onderzoekers zullen op dat moment niet weten welke van de drie situaties op welk moment plaatsvindt.

Tijdens iedere pauze van 30 minuten wordt u gevraagd een aantal vragen te beantwoorden over hoe u zich voelt. In totaal zal de testprocedure ongeveer 3 ½ uur in beslag nemen. U wordt vriendelijk verzocht om 's ochtends voor en tijdens de metingen geen koffie, thee of andere cafeïne houdende voedingsmiddelen te nuttigen om de metingen niet te beïnvloeden.

Bijwerkingen en veiligheid

De sterkte van het signaal dat tijdens de testperiode wordt gebruikt komt overeen met dat wat een normaal GSM- of UMTS-basisstation in uw woonomgeving dat op basis van een aantal metingen is vastgesteld. Op grond van de huidige wetenschappelijke kennis verwachten wij niet dat deelname aan het onderzoek gezondheidsrisico's met zich meebrengt, maar het is natuurlijk denkbaar dat dit onderzoek juist zal uitwijzen dat er mogelijk wel effecten op uw welbevinden of de gezondheid zijn.

Bedenktijd

Wij kunnen ons voorstellen dat u voordat u beslist uw medewerking aan het onderzoek te verlenen enige bedenktijd nodig hebt. Wellicht wilt u er ook met anderen over praten. Toch verzoek ik u vriendelijk binnen twee weken het bijgaande interesseformulier in de bijgevoegde envelop ongefrankeerd terug te zenden.

Indien u vragen heeft over deelname aan dit onderzoek die u liever bespreekt met een arts die niet bij de uitvoering van het onderzoek betrokken is, kunt u contact opnemen met: Dr. E.J. van der Beek, Arbo Management Groep, Postbus 82001, 2508 EA Den Haag (Telefoon 070-3181887 Telefax 070-3181880).

Vertrouwelijkheid van de gegevens

Gegevens die in het kader van dit onderzoek over u worden verzameld, zullen vertrouwelijk worden behandeld en anoniem worden verwerkt. In rapporten en publicaties over het onderzoek zal uw naam niet voorkomen. Uw gegevens zullen uitsluitend worden verwerkt door gekwalificeerd en bevoegd personeel van het onderzoeksbureau CFR en TNO en eventueel gecontroleerd door leden van een onafhankelijke Medisch Ethische Commissie. Deze commissie heeft de opzet van dit onderzoek goedgekeurd.

Verzekering

Deelname aan wetenschappelijk onderzoek valt onder de aansprakelijkheidsverzekering van TNO. Informatie over deze verzekering vindt u in de bijlage.

Vrijwilligheid van deelname

U bent geheel vrij al dan niet aan dit onderzoek mee te werken. Verder heeft u te allen tijde het recht om zonder opgave van redenen af te zien van verdere deelname, ook als u schriftelijk heeft verklaard deel te willen nemen.

Geven van toestemming

Indien u besluit aan het onderzoek deel te nemen, zullen wij u vragen een toestemmingsformulier te ondertekenen. Hiermee bevestigt u uw voornemen om aan het onderzoek mee te werken. U blijft de vrijheid behouden om wegens voor u relevante redenen uw medewerking te stoppen. Door het plaatsen van uw handtekening bevestigt u alleen dat u bent geïnformeerd over het onderzoek en dat deze informatiebrief aan u is overhandigd.

Vervoer en vergoeding

TNO Fysisch en Elektronisch Laboratorium is per openbaar vervoer en de auto goed bereikbaar. Indien u per auto komt zijn er voldoende parkeerplaatsen beschikbaar. Uw reiskosten zullen worden vergoed op basis van openbaar vervoer 2e klasse. Indien u gebruik wenst te maken van taxivervoer van en naar het Centraal Station van Den Haag bestaat daartoe de mogelijkheid. U zult bij uw definitieve uitnodiging gedetailleerde informatie ontvangen. Voor uw deelname ontvangt u van TNO een attentie.

Resultaten van het onderzoek

De resultaten van het onderzoek worden vastgelegd in een TNO-rapport. Tevens zal een wetenschappelijke publicatie worden geschreven. Wij willen u uiteraard ook informeren over de resultaten van het onderzoek. Daarom zullen we u een verkorte versie van het TNO-rapport toesturen.

Nadere informatie

Mocht u na het lezen van deze brief, voor, tijdens, of na het onderzoek behoefte hebben aan nadere informatie dan kunt u altijd contact opnemen met ondergetekende onder telefoonnummer 070-374 0033, of met de onafhankelijk arts die hierboven genoemd staat.

Met vriendelijke groeten,

Prof. dr ir A. Peter M. Zwamborn
Onderzoeker

24.5 Informatiebrief aan mensen zonder klachten

Geachte mevrouw/mijnheer,

U bent uitgenodigd om deel te nemen aan een onafhankelijk wetenschappelijk onderzoek dat erop is gericht eventuele invloeden van GSM-signalen op de mens objectief vast te stellen. Het onderzoek wordt verricht door TNO Fysisch en Elektronisch Laboratorium (TNO-FEL) in samenwerking met het onderzoeksbureau Clinical Research Facilities International (CRF) in Schaijk. TNO heeft voor dit onderzoek opdracht gekregen van het Ministerie van Volksgezondheid, Welzijn en Sport, het Ministerie van Volkshuisvesting, Ruimtelijke Ordening en Milieubeheer en het Ministerie van Verkeer en Waterstaat.

Waarom dit onderzoek?

Hoewel al eerder wetenschappelijk onderzoek is gedaan naar de relatie tussen elektromagnetische velden en klachten van mensen, is er nog steeds geen duidelijke conclusie te trekken. Dit onderzoek zal daarom iets anders worden opgezet dan voorheen gebeurde. Wij vinden het belangrijk dat niet alleen mensen meedoen die zelf vermoeden last te ondervinden van elektromagnetische velden afkomstig van GSM-antennes maar ook mensen die geen klachten in relatie tot elektromagnetische velden hebben. Daarom wordt voor dit onderzoek uw medewerking gevraagd.

De resultaten van dit onderzoek zijn van belang om objectief eventuele verbanden tussen GSM- (en in de toekomst UMTS-) signalen en de gemelde klachten te kunnen vaststellen. Als wetenschappelijk geen beïnvloeding kan worden vastgesteld is het niet waarschijnlijk dat een directe relatie bestaat tussen de aanwezigheid van GSM-signalen en de acute beïnvloeding van geheugen functies. Indien er echter wel een relatie wordt gevonden, kunnen de opdrachtgevende ministeries hierop hun beleid aanpassen.

Wat houdt het onderzoek in?

In dit onderzoek zal worden nagegaan of er een invloed is van GSM- en UMTS-signalen op geheugen functies. Hiervoor doen we metingen die direct samenhangen met hersenfuncties, zoals geheugen, alertheid en reactiesnelheid. In totaal zullen ruim 70 proefpersonen aan het onderzoek deelnemen.

Het onderzoek vindt plaats in het TNO Fysisch en Elektronisch Laboratorium in Den Haag. Er is een speciale onderzoeksruimte beschikbaar, die voor GSM-signalen volledig is afgeschermd van de buitenwereld. Het onderzoek zal een halve dag in beslag nemen. Inclusief reistijd bent u maximaal een dag kwijt aan uw deelname.

Voorafgaande aan het onderzoek zal u worden gevraagd een aantal vragen te beantwoorden die betrekking hebben op uzelf, uw algemeen welzijn en de door u eventueel ervaren klachten tijdens het onderzoek. Deze en alle andere gegevens zullen strikt vertrouwelijk worden behandeld, en niet voor andere doeleinden dan dit onderzoek worden gebruikt.

Vervolgens zal u worden verzocht plaats te nemen aan een tafel in de onderzoeksruimte, waar twee antennes staan van een GSM- en UMTS-basisstation. U zult op een beeldscherm een aantal eenvoudige vragen, opdrachten en aanwijzingen zien verschijnen, die u met een joystick en twee knoppen kunt beantwoorden of uitvoeren. Dit duurt ongeveer 25 minuten.

In totaal zal deze procedure vier keer worden doorlopen, onderbroken door pauzes van ongeveer een half uur. De eerste keer is bestemd om u vertrouwd te maken met de procedure, overigens zonder dat er een GSM- of UMTS-signaal aanwezig is. Bovendien krijgt u een uitvoerige uitleg. Tijdens de daaropvolgende keren zal er in willekeurige volgorde een GSM-, UMTS- of géén signaal worden uitgezonden. Zowel u als de onderzoekers zullen op dat moment niet weten welke van de drie situaties op welk moment plaatsvindt.

Tijdens iedere pauze van 30 minuten wordt u gevraagd een aantal vragen te beantwoorden over hoe u zich voelt. In totaal zal de testprocedure ongeveer 3 ½ uur in beslag nemen. U wordt

vriendelijk verzocht om 's ochtends voor en tijdens de metingen geen koffie, thee of andere cafeïne houdende voedingsmiddelen te nuttigen om de metingen niet te beïnvloeden.

Bijwerkingen en veiligheid

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Vrijwilligheid van deelname

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Geven van toestemming

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Met vriendelijke groeten,

Prof. dr ir A. Peter M. Zwamborn
Onderzoeker

24.6 Aanvullende informatie inzake de verzekering

Onderstaande brief wordt als bijlage bij de informatiebrief meegestuurd.

TNO heeft als verrichter, conform het Besluit van de Minister van Justitie en de Minister van Volksgezondheid, Welzijn en Sport van 5 juli 1999, een risicoverzekering afgesloten voor proefpersonen.

De verzekering is afgesloten bij:

Winterthur Schadeverzekering Maatschappij
Postbus 83000
1080 AA Amsterdam
Tel. (020)5411754
Fax. (020) 6428428
Polis nr V00615407

Onder de polis is schade als gevolg van deelname aan het onderzoek verzekerd.

Onder schade wordt verstaan schade door letsel of overlijden.

De verzekering biedt dekking voor schade tot een bedrag van € 453.780,00 per proefpersoon, zulks tot een maximum van tot € 6.806.703,00 voor het onderzoek in zijn geheel en gelimiteerd tot € 9.075,604,00 per verzekeringsjaar. Tevens geldt een verzekerd bedrag van € 9.075,604,00 voor de uitlooptermijn van 5 jaar in geval van beëindiging van de verzekering

Uitgesloten van dekking is schade:

1. Waarvan nagenoeg zeker was dat den zich bij de proefpersoon zou voordoen;
2. Die zich bij nakomelingen openbaart als gevolg van een nadelige inwerking van het onderzoek op genetisch -materiaal van de proefpersoon;
3. Door aantasting van de gezondheid van de proefpersoon die zich ook zou hebben geopenbaard wanneer de proefpersoon niet aan dit onderzoek had deelgenomen;
4. Die het gevolg is van het niet, of foutief opvolgen van de aanwijzingen en instructies die u door TNO zijn of worden gegeven.

Bij letsel en letselschade moet(en):

1. contact worden opgenomen met de Bedrijfsarts van TNO,
2. de adviezen van de onderzoeker van TNO-FEL worden opgevolgd,
3. er zorg voor worden gedragen dat verdere schade, zo veel mogelijk wordt beperkt/voorkomen, en de huisarts wordt geïnformeerd.

Als u meent materiële schade te hebben ondervonden waarvoor TNO aansprakelijk is, neem hierover dan contact op met de Projectleider van TNO-FEL.

Schadeclaims worden na aanmelding afgehandeld door TNO.

24.7 Appendix IV Informed Consent Form

Studie: Double blind randomized three-way cross-over evaluation general symptoms and of cognitive functions with or without exposure to GSM fields in subjects presenting with complaints subjectively attributed to GSM fields.

Hiermee verklaar ik dat dit onderzoek volledig aan mij is uitgelegd, dat ik alle aspecten ervan begrijp en dat mij de mogelijkheid geboden is om vragen te stellen en dat die tot tevredenheid beantwoord zijn.

Ik begrijp dat ik een kandidaat ben om aan dit onderzoek deel te nemen omdat ik mij met klachten gemeld heb waarvan ik vermoed of zeker meent te weten dat zij voortkomen uit de blootstelling aan GSM/UMTS signalen.

Ik begrijp ook dat, aan het verlenen van mijn toestemming om aan het onderzoek deel te nemen, verbonden is dat ik een aantal keren een vragenlijst zal moeten invullen, zowel op papier als met behulp van een computerprogramma, die er o.a. op gericht is mijn algemeen welzijn te beoordelen.

Ik begrijp dat ik de vrijheid heb op ieder door mij gekozen moment mij zonder opgaaf van redenen terug te trekken en af te zien van verdere deelname aan het onderzoek. Mijn deelname is volledig vrijwillig.

Ik begrijp ook dat alle gegevens voortkomend uit het onderzoek vertrouwelijk zullen zijn en gecodeerd geanalyseerd en bewaard zullen worden op een zodanige wijze dat mijn privacy gewaarborgd is en gewaarborgd zal blijven.

Toestemming voor deelname:

Handtekening van de vrijwilliger

Datum

Voor onderzoeker

Hiermee verklaar ik dat ik aan de vrijwilliger informatie heb gegeven betreffende de studie en alle vragen heb beantwoord.

Handtekening van de onderzoeker

Datum

(naam:)

24.8 Appendix V Case Report Form

Demography, medical history, complaints pattern before enrollment are in process of design (electronic format)

24.10 Appendix VII Questionnaires

24.10.1 Big Five

In this paragraph we present the personality test. The test is in Dutch.



SCHRIJF NIET IN DIT BOEKJE

Instructies

Lees alle instructies zorgvuldig voor U begint met antwoorden.

Deze vragenlijst bevat 60 uitspraken. Lees elke uitspraak zorgvuldig.
Kruis **op het aparte antwoordformulier** aan welke uitspraak Uw mening het beste weer-
geeft. Let er op dat U geen regels overslaat.

Kruis het vakje **HO** aan als U het **helemaal oneens** bent met de uitspraak,
of als U de uitspraak absoluut onwaar vindt.

Kruis het vakje **O** aan als U het **oneens** bent met de uitspraak
of als U de uitspraak grotendeels onwaar vindt.

Kruis het vakje **N** aan als U **neutraal** bent, niet kunt beslissen,
of als U de uitspraak ongeveer even waar als onwaar vindt.

Kruis het vakje **E** aan als U het **eens** bent met de uitspraak
of als U de uitspraak grotendeels waar vindt.

Kruis het vakje **HE** aan als U het **helemaal eens** bent met de uitspraak,
of als U de uitspraak absoluut waar vindt.

Voorbeeld

Als U het bijvoorbeeld helemaal oneens bent met de uitspraak "Ik zou wel een miljoen willen win-
nen", dan kruist U op het antwoordblad als volgt aan:

~~HO~~ O N E HE

Kruis slechts één mogelijkheid aan bij elke uitspraak. Beantwoord alle uitspraken.

Als U een antwoord wilt veranderen maak dan Uw eerste keuze ongeldig door deze helemaal
zwart te maken en kruis alsnog Uw juiste keuze aan.

Wilt U eerst de gevraagde persoonsgegevens op het antwoordformulier invullen?