

Ministry of Health, Welfare and Sport

United Nations International Narcotics Control Board  
Mr Herbert Schaepe, Secretary of the Board  
Vienna International Centre  
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AUSTRIA

|  |                           |                  |                |
|--|---------------------------|------------------|----------------|
| Our reference  | Information               | Telephone no.    | The Hague      |
| CIBG/BMC 2413726   | Ms N.V. Celebi-Barkmeijer | + 31 70 340 5863 | 22 July 2004   |
| Subject  |                           | Enclosure(s)     | Your reference |
| Update research on medical use of cannabis<br>in The Netherlands |                           | 1                | INCB-NAR 56/04 |

Dear Mr Schaepe,

Thank you for your fax of 18 June 2004, ref. INCB-NAR-56/04, requesting information on the update on the specific areas of research on the medical use of cannabis in the Netherlands, which was forwarded by the Dutch Health Care Inspectorate to the Office of Medicinal Cannabis.

Enclosed you will find an annex with an overview of research related to medicinal cannabis in which the Netherlands is or was involved through the Office of Medicinal Cannabis.

I hope the information in this letter complies with your request.

Sincerely yours,

Deputy Secretary-General,

P.H.A.M. Huijts

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## 1. Study programming

### **ZonMw ([www.zonmw.nl](http://www.zonmw.nl)):**

Programme study entitled *Verkenning medicinale cannabis, complex simplex*. It is a survey made for the policy department of the Ministry of Health, on what research is needed and what the government policy on medicinal cannabis research could be.

Status: finished; report published (in Dutch)

## 2. Clinical trials

### **Free University Medical Centre, Amsterdam:**

Killestein et al. did a clinical trial (placebo controlled, double blinded and cross-over) some years ago, comparing placebo, dronabinol (Marinol) and standardized cannabis extract capsules (Cannador). The outcome was that there was no difference between the three branches. However, it is generally accepted now that the dosages were too low.

Status: This study has ended and there were several publications.

Killestein J, Hoogervorst EJM, Reif M, et al. Safety, tolerability and efficacy of orally administered cannabinoids in multiple sclerosis. *Neurology* 2002; 58: 1404–07.

Killestein J, et al., Immunomodulatory effects of orally administered cannabinoids in multiple sclerosis, *Journal of Neuroimmunology* 4741 (2003) 1 –4

### **Free University Medical Centre, Amsterdam:**

Killestein intended to do a trial of a similar design for smoked cannabis on the request of the Dutch parliament. The branches would be placebo cannabis, high dronabinol cannabis and cannabis with equal dronabinol and cannabidiol. However, there were problems in the production of the study medication and the study was cancelled before it even started.

Status: cancelled

### **University Hospital Groningen, Groningen**

Dr M.P. Neeleman, study entitled: Correlates a cannabis induced decrease in allodynia, measured with monofilaments, with an increased subjective well-being in patients with a neuropathic pain syndrome.

Status: in progress

### **Centre for Human Drug Research (CHDR), Leiden:**

Is performing a clinical trial (phase 1) on delivery of dronabinol by inhalation, using a vaporizer device. dronabinol is used as a marker to develop a method for future studies with agonists and antagonists of dronabinol. Subjects have to perform a variety of tests and pharmacokinetic and pharmacodynamic studies are done.

Status: in progress

## 3. Hybrid programmes

### **CRAFT-consortium**

European consortium existing of 9 contributors in 7 EU-countries, among whom the Dutch Office of Medicinal Cannabis and TNO Voeding, Leiden. Programme entitled: *Cannabis Standardised extracts of Cannabis for use in the treatment of migraine and rheumatoid arthritis*.

Status: EU-subsidy granted, starting up the cultivation of the plant varieties in autumn 2004.

#### **4. Laboratory research**

***Leiden University, Dept. of Pharmacognosy, Prof. Dr. Robert Verpoorte and Dr. Arno Hazenkamp***

Has developed methods for the preparative isolation of cannabinoids from cannabis plant materials and their quantification by nuclear magnetic resonance (NMR) techniques. Can produce several important cannabinoids as reference compounds. Leiden University also studies the composition of cannabis smoke and the use of a vaporizer device for the delivery of THC.

Status: in progress

***TNO Voeding, Leiden, Dr. Mei Wang en Dr. Henrie Korthout:***

Synergy of dronabinol with other (known and unknown) compounds present in cannabis, which may be an important factor in the specificity of a typical variety for a typical medication. Current cannabis research activities are focused on finding correlations between the presence and concentration of certain compounds (not only cannabinoids) in a cannabis extract and its biological effects. TNO hopes to find these correlations by linking the transcriptomes, metabolomes en biological effects (in vitro screening and animal models) from a vast variety of cultivars that are grown, processed and harvested under various standardized conditions, by means of Multivariate Data Analysis.

Status: in progress

***Chemic Labs, Massachusetts USA***

Composition of vapour produced by the Volcano vaporising device with Cannabis flos SIMM 18. Sponsored by Multidisciplinary Association for Psychedelic Studies, Sarasota, Florida, USA

Status: under review for approval by the US' Department of Health and Human Services

#### **5. Industrial development**

***Farmalyse, Zaandam***

Has developed the preparative isolation of cannabinoids under GMP conditions suitable for clinical purposes. The cannabinoids are extracted by supercritical carbondioxide (CO<sub>2</sub>) from GAP cultivated plants grown under supervision of the Dutch Office of Medicinal Cannabis. Has developed validated methods for analysis and quantification of cannabinoids in different types of samples. Production of high purity analytical standards of cannabinoids (dronabinol to a unique purity of 99,5%!).

Status: developed methods are operational

#### **6. Addiction care research**

***National Institute for Health and the Environment, Bilthoven, the Netherlands***

Study to determine the relation between health effects and the strength of smoked cannabis, part I: Double blinded placebo controlled study with as branches: placebo cigarettes (NIDA) and cigarettes with 5% (NIDA), 13% (OMC) and 18% (OMC) cannabis.

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(all cannabis combined with tobacco, as usual in the Netherlands). In this study the relation between dosage, strength and blood level will be established.

Status: study is designed now. Start planned for second half of 2004.

***University of Maastricht, Maastricht,***

Study to determine cognitive function after the use of strong cannabis.

Status: study design approved. Start planned for September 2004.