# Eighth Review of Psychoactive Substances for International Control

**Geneva, 12-16 September, 1983**

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1. INTRODUCTION

Dr N. Sartorius, Director, Division of Mental Health, welcomed the participants and observers on behalf of Dr H. Mahler, Director-General of the World Health Organization. He informed the group that the World Health Organization was in constant search for the ideal procedure to implement WHO's responsibilities as specified in the 1971 Convention on Psychotropic Substances. He pointed out that in March 1983, the World Health Organization had reviewed the procedures and further, that Professor B. Rexed would be assisting in the final formulation of these procedures which would be studied by the WHO Executive Board at its Seventy-third session in January 1984. He hoped that these procedures would facilitate future work in the area of drugs being evaluated for possible international control.

The group's attention was drawn to the fact that this Review Group had been convened by the World Health Organization to respond to Resolution 4 (XXX) of the United Nations Commission on Narcotic Drugs which, through the Secretary-General of the United Nations, requested, the World Health Organization to urgently review and assess, as part of its regular function under the Convention on Psychotropic Substances, all benzodiazepines currently on the market, as of a specific date to be determined by the Organization. It further requested that the findings and recommendations be made on a substance by substance basis.

The group was briefed on historical difficulties encountered in the review process for this group of substances. Dr Sartorius emphasized that any decision reached by the participants of this review must be made exclusively on the basis of scientific, medical and health considerations. While the decisions reached by previous Review Groups for some of these substances need not necessarily be adhered to, he urged the participants to critically review the evidence and reasoning on which they had been made. He pointed out that the decisions reached at this meeting would have considerable consequences, not only for the pharmaceutical industry but more importantly, for the health of the people of the world.

The group's attention was drawn to the recent publication of a paper entitled Use and Abuse of the Benzodiazepines, which was based on the Report of the 6th Review of Psychoactive Substances2.

Dr Sankaran addressed the meeting and indicated the interest his Division had in the reports of the review meetings, particularly in respect of the needs of developing countries. This is especially important in relation to this meeting because of the widespread use of the benzodiazepines.
SCOPE OF THE MEETING

The charge given to the group was:

1. To review and make recommendations for international control where appropriate, for 39 benzodiazepine-type substances, namely

   - alprazolam
   - bromazepam
   - camazepam
   - chloridiazepoxide
   - clonazepam
   - clotiazepam
   - cloratepate
   - cloxazolam
   - delorazepam
   - diazepam
   - estazolam
   - ethyl loflazepate
   - etifoxine
   - fludiazepam
   - flunitrazepam
   - flurazepam
   - halazepam
   - haloxazolam
   - ketazolam
   - lorazepam
   - lormetazepam
   - medazepam
   - nimetazepam
   - nitrazepam
   - nordiazepam
   - oxazepam
   - oxazolam
   - pimozepam
   - pirenzepine
   - prazepam
   - propizepine
   - temazepam
   - tetrazepam
   - tofisopam
   - tibenzonium
   - triazolam
   - zopiclone

To make recommendations on:

1. Future activities of WHO including the substances that need consideration for possible international control.

2. Types of information and data that will be needed for rescheduling or descheduling of substances or drugs currently under international control.

PROCEDURES AND CRITERIA UTILIZED IN THIS REVIEW

Sources of data

The group was to review the 39 benzodiazepine substances which the Commission had requested WHO to review in its resolution 4 (XXX), and which were on the market at the end of February 1983. The substances were primarily benzodiazepine types of drugs, but in addition, other anxiolytic drugs. The data to be reviewed came from a number of sources. Data for illicit traffic was collected through Interpol, the United Nations Division of Drug Abuse, and the Ministry of State of member states as well as WHO regional offices from the countries. Information was sought from concerned industries through the International Federation of Pharmaceutical Association (IFPMA) as well as other resources available to them. In a pre-review meeting held on 11 September 1983 representatives of concerned pharmaceutical companies and the IFPMA met and presented data to the temporary working group. Participants who were assigned specific topics collected scientific information from the resources available to them.

Zopiclone

Although included on the list of substances for the review, Zopiclone was excluded from consideration because it was established that it was not marketed at the end of February and will be considered for review at a future meeting.
3.3 Scheduling criteria of 1971 Convention on Psychotropic Substances

Drugs were reviewed and reported on an individual basis. In order to establish whether a substance met the scheduling criteria of 1971 Convention on Psychotropic Substances, the group reviewed the data on the following points:

(i) chemical structure, receptor binding characteristics, sedative-hypnotic, anti-convulsant, and anxiolytic profile of central nervous system effects.

(ii) animal data on psychological and physical dependence potential.

(iii) human experimental data on both dependence and abuse potential.

(iv) clinical data on dependence and public health problems.

(v) epidemiological data on public health and social problems.

(vi) extent of abuse or likelihood of abuse and seriousness of public health and social problems resulting from such abuse.

(vii) utilization and usefulness in therapy.

Of the 38 remaining substances to be reviewed, 33 were recommended for scheduling and five were not. The decision to recommend international control of these substances was based on data relevant to the 7 points listed above. Data was available for a number of substances on these seven points. However, the group found that in the case of a number of the substances, no data other than on points (i) and (vii) of the above list was available. On these substances the group decided by a majority vote of 8 to 3, that if a substance under review fulfils point (i), the substance was adjudged to have the capacity to produce state of dependence and likelihood of abuse so as to constitute a public health and social problem warranting the placing of the substance under international control.

4. REVIEW OF INDIVIDUAL BENZODIAZEPINES

4.1 Diazepam

Diazepam has potent, well-demonstrated anxiolytic, anti-convulsive and sedative-hypnotic properties in animals and humans which are mediated by specific receptors in the brain. In regard to the dependence and abuse liability of diazepam the group concluded that:

(a) Diazepam has the capacity to produce:

1. a state of dependence as demonstrated by experimental studies in animals and humans, as well as by clinical studies showing the development of physical dependence. Further experimental studies in animals and humans have shown that diazepam does not have limited reinforcing capacity indicative of low to moderate psychological dependence potential relative to the short acting barbiturates, psycho-motor stimulants and opiates. Studies of subjective effects in humans also show that diazepam can produce euphoria. There have been clinical reports of psychological dependence;

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, as demonstrated by studies in animals and humans showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence as revealed by clinical reports and epidemiological studies, that diazepam is being abused so as to constitute a public health and social problem warranting the placing of the substance under international control.

Bearing in mind the medical usefulness of diazepam as an anxiolytic, anti-convulsive and sedative-hypnotic agent, as well as evidence of actual abuse, the group recommended that diazepam be included in Schedule IV of the Convention on Psychotropic Substances.
4.2 Alprazolam

The group reached the following conclusions

(a) Alprazolam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that alprazolam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that alprazolam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that alprazolam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies was presented demonstrating actual abuse of alprazolam.

Bearing in mind the medical usefulness of alprazolam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that alprazolam be included in Schedule IV of the Convention on Psychotropic Substances.

4.3 Bromazepam

The group reached the following conclusions

(a) Bromazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that bromazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that bromazepam does have limited reinforcing capacity indicative of low to moderate dependence potential. Clinical reports of psychological dependence were presented.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that bromazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies was presented demonstrating actual abuse of bromazepam.

Bearing in mind the medical usefulness of bromazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that bromazepam be included in Schedule IV of the Convention on Psychotropic Substances.
4.4 Camazepam

The group reached the following conclusions

(a) Camazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that camazepam can produce physical dependence.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that camazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of camazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that camazepam be included in Schedule IV of the Convention on Psychotropic Substances.

4.5 Chlordiazepoxide

The group reached the following conclusions

(a) Chlordiazepoxide has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals and humans have demonstrated that chlordiazepoxide can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that chlordiazepoxide does have limited reinforcing capacity indicative of low to moderate dependence potential. Clinical reports of psychological dependence were presented.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that chlordiazepoxide is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of chlordiazepoxide.

Bearing in mind the medical usefulness of chlordiazepoxide as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that chlordiazepoxide be included in Schedule IV of the Convention on Psychotropic Substances.
Clobazam

The group reached the following conclusions:

Clobazam has the capacity to produce:

1. A state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that clobazam can produce physical dependence. Cases of physical dependence in humans have been reported.

   Further experimental studies in animals and humans have shown that clobazam does have limited reinforcing capacity indicative of low to moderate dependence potential. Clinical reports of psychological dependence were presented.

2. Central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

   There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that clobazam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

   In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of clobazam.

Bearing in mind the medical usefulness of clobazam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that clobazam be included in Schedule IV of the Convention on Psychotropic Substances.

Clonazepam

The group reached the following conclusions:

Clonazepam has the capacity to produce:

1. A state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that clonazepam can produce physical dependence.

   Further experimental studies in animals and humans have shown that clonazepam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. Central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

   There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that clonazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

   In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of clonazepam.

Bearing in mind the medical usefulness of clonazepam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that clonazepam be included in Schedule IV of the Convention on Psychotropic Substances.
4.8 Clorazepate

The group reached the following conclusions:

(a) Clorazepate has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that clorazepate can produce physical dependence.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that clorazepate is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of clorazepate.

Bearing in mind the medical usefulness of clorazepate as an anxiolytic, anti-convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that clorazepate be included in Schedule IV of the Convention on Psychotropic Substances.

4.9 Clotiazepam

The group reached the following conclusions:

(a) Clotiazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. In addition, experimental studies in animals and humans have demonstrated that clotiazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that clotiazepam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that clotiazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of clotiazepam as an anxiolytic, anti-convulsant and sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that clotiazepam be included in Schedule IV of the Convention on Psychotropic Substances.
10 Cloxazolam

The group reached the following conclusions

1. Cloxazolam has the capacity to produce:
   1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that cloxazolam can produce physical dependence.

      Further experimental studies in animals have shown that cloxazolam does have limited reinforcing capacity indicative of low to moderate dependence potential.

   2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

2. There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that cloxazolam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

   No evidence of actual abuse was presented.

   Bearing in mind the medical usefulness of cloxazolam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that cloxazolam be included in Schedule IV of the Convention on Psychotropic Substances.

11 Delorazepam

The group reached the following conclusions

1. Delorazepam has the capacity to produce:

   1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic.

   2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

2. There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that delorazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

   No evidence of actual abuse was presented.

   Bearing in mind the medical usefulness of delorazepam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that delorazepam be included in Schedule IV of the Convention on Psychotropic Substances.

12 Estazolam

The group reached the following conclusions
Estazolam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that estazolam can produce physical dependence.

   Further experimental studies in animals have shown that estazolam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that estazolam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, presented demonstrating actual abuse of estazolam.

Bearing in mind the medical usefulness of estazolam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that estazolam be included in Schedule IV of the Convention on Psychotropic Substances.

4.13 Ethyl loflazepate

The group reached the following conclusions

(a) Ethyl loflazepate has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that ethyl loflazepate is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of ethyl loflazepate as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that loflazepate be included in Schedule IV of the Convention on Psychotropic Substances.

4.14 Etifoxine

The group concluded that since etifoxine is structurally dissimilar to diazepam and there was only limited data available on its pharmacology, that it should not be recommended for inclusion in the Convention on Psychotropic Substances, 1971 at this time. It will be reviewed at a future meeting of WHO.
Fludiazepam

The group reached the following conclusions:

Fludiazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that fludiazepam can produce physical dependence.

Further experimental studies in animals have shown that fludiazepam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that fludiazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of fludiazepam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended fludiazepam be included in Schedule IV of the Convention on Psychotropic Substances.

Flunitrazepam

The group reached the following conclusions:

Flunitrazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that flunitrazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals and humans have shown that flunitrazepam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that flunitrazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of flunitrazepam.

Bearing in mind the medical usefulness of flunitrazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that flunitrazepam be included in Schedule IV of the Convention on Psychotropic Substances.
4.17 Flurazepam

The group reached the following conclusions

(a) Flurazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that flurazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that flurazepam does have moderate reinforcing capacity indicative of moderate dependence potential. Clinical reports of psychologic dependence were presented.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that flurazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of flurazepam.

Bearing in mind the medical usefulness of flurazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that flurazepam be included in Schedule IV

4.18 Halazepam

The group reached the following conclusions

(a) Halazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that halazepam can produce physical dependence.

Further experimental studies in animals and humans have shown that halazepam does have limited reinforcing capacity indicative of low dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that halazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of halazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that halazepam be included in Schedule IV of the Convention on Psychotropic Substances.
49 Haloxazolam

The group reached the following conclusions:

1. Haloxazolam has the capacity to produce:
   1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that haloxazolam can produce physical dependence.

Further experimental studies in animals have shown that haloxazolam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

3. There is sufficient evidence of similarity in chemical structure and pharmacological action to diazepam to predict that haloxazolam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of haloxazolam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that haloxazolam be included in Schedule IV of the Convention on Psychotropic Substances.

50 Ketazolam

The group reached the following conclusions:

1. Ketazolam has the capacity to produce:
   1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that ketazolam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that ketazolam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

There is sufficient evidence of similarity in chemical structure and pharmacological action to diazepam to predict that ketazolam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of ketazolam.

Bearing in mind the medical usefulness of ketazolam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that ketazolam be included in Schedule IV of the Convention on Psychotropic Substances.
4.21 Loprazolam

The group reached the following conclusions

(a) Loprazolam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that loprazolam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of loprazolam as an anxiolytic, anti convulsant, sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that loprazolam be included in Schedule IV of the Convention on Psychotropic Substances.

4.22 Lorazepam

The group reached the following conclusions

(a) Lorazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals and humans have demonstrated that lorazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals and humans have shown that lorazepam does have limited reinforcing capacity indicative of low to moderate dependence potential. Clinical reports of psychological dependence were presented.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that lorazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of lorazepam.

Bearing in mind the medical usefulness of lorazepam as an anxiolytic, anti convulsant, and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that lorazepam be included in Schedule IV of the Convention on Psychotropic Substances.
Lormetazepam

The group reached the following conclusions:

Lormetazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that lormetazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was reported demonstrating actual abuse of lormetazepam.

Bearing in mind the medical usefulness of lormetazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that lormetazepam be included in Schedule IV of the Convention on Psychotropic Substances.

Medazepam

The group reached the following conclusions:

Medazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that medazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals and humans have shown that medazepam does have limited reinforcing capacity indicative of low to moderate dependence potential. Clinical reports of psychological dependence were presented.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that medazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was reported demonstrating actual abuse of medazepam.

Bearing in mind the medical usefulness of medazepam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that medazepam be included in Schedule IV of the Convention on Psychotropic Substances.
4.25 Nimetazepam

The group reached the following conclusions

(a) Nimetazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that nimetazepam can produce physical dependence.

Further experimental studies in animals and humans have demonstrated that nimetazepam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that nimetazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of nimetazepam.

Bearing in mind the medical usefulness of nimetazepam as an anxiolytic, anti-convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that nimetazepam be included in Schedule IV of the convention on Psychotropic Substances.

4.26 Nitrazepam

The group reached the following conclusions

(a) Nitrazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. In addition, experimental studies in animals and humans have demonstrated that nitrazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that nitrazepam does have limited reinforcing capacity indicative of low to moderate dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that nitrazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of nitrazepam.

Bearing in mind the medical usefulness of nitrazepam as an anxiolytic, anti-convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that nitrazepam be included in Schedule IV of the convention on Psychotropic Substances.
The group reached the following conclusions:

Nordiazepam has the capacity to produce:

1. A state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. Evidence of actual abuse of nordiazepam was revealed as evidenced by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

2. Central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

3. There is sufficient evidence of similarity in chemical structure and pharmacological action of oxazepam to predict that nordiazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Hearing in mind the medical usefulness of nordiazepam as an anxiolytic, anti-convulsant sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that nordiazepam be included in Schedule IV of the Convention on Psychotropic Substances.

Oxazepam has the capacity to produce:

1. A state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti-convulsant, sedative hypnotic. In addition, experimental studies in animals and humans have demonstrated that oxazepam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals and humans have shown that oxazepam does have limited reinforcing capacity indicative of low dependence potential. Clinical reports of psychological dependence were presented.

2. Central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

3. There is sufficient evidence of similarity in chemical structure and pharmacological action of diazepam to predict that oxazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of oxazepam.

Hearing in mind the medical usefulness of oxazepam as an anxiolytic, anti-convulsant sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that oxazepam be included in Schedule IV of the Convention on Psychotropic Substances.
4.29 Oxazolam

The group reached the following conclusions

(a) Oxazolam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that oxazolam can produce physical dependence. Cases of physical dependence in humans have been reported.

Further experimental studies in animals have shown that oxazolam does have limited reinforcing capacity indicative of low to moderate dependence potential;

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that oxazolam is likely to be abused so as to constitute public health and social problems warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of oxazolam.

Bearing in mind the medical usefulness of oxazolam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence predictive of actual abuse, the group recommended that oxazolam be included in Schedule IV of the Convention on Psychotropic Substances.

4.30 Pinazepam

The group reached the following conclusions

(a) Pinazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic;

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that Pinazepam is likely to be abused so as to constitute public health and social problems warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind the medical usefulness of Pinazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that pinazepam be included in Schedule IV of the Convention on Psychotropic Substances.
Pirenzipine

The group reached the following conclusion regarding pirenzipine. The group noted that pirenzipine, like diazepam, has an anxiolytic, anticonvulsant, sedative-hypnotic action. It was recommended that pirenzipine does not have the capacity to produce a state of dependence. Its spectrum action is that of an anti-muscarinic agent used in the treatment of peptic ulcer. It has central nervous system effects.

On the basis of the spectrum of action of pirenzipine, the group recommended that pirenzipine should not be brought under the control of the Convention on Psychotropic Substances, 1971.

Prazepam

The group reached the following conclusions regarding prazepam. According to its chemical structure and pharmacological spectrum of action to diazepam, prazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that prazepam can produce physical dependence.

2. central nervous system depression resulting in disturbances in motor functions, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that prazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence, as revealed by clinical reports and epidemiological studies, was presented demonstrating actual abuse of prazepam.

Bearing in mind the medical usefulness of prazepam as an anxiolytic, anti convulsant sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that prazepam be included in Schedule IV of the Convention on Psychotropic Substances.

Propazine

The group reached the following conclusions.

Although propazine is a 1,5 benzodiazepine there was insufficient evidence to conclude that it shared the spectrum of action of diazepam.

The group therefore recommended that propazine should not be reviewed for inclusion in the Convention on Psychotropic Substances at this time. It will be reviewed at a future meeting of WHO.

Temazepam

The group reached the following conclusions.
(a) Temazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic. In addition, experimental studies in animals have demonstrated that temazepam can produce physical dependence. Further experimental studies in animals and humans have shown that temazepam does have limited reinforcing capacity indicative of low dependence potential.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that temazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

In addition, evidence as revealed by clinical reports and epidemiological studies was presented demonstrating actual abuse of temazepam.

Bearing in mind the medical usefulness of temazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence of actual abuse, the group recommended that temazepam be included in Schedule IV of the Convention on Psychotropic Substances.

4.35 Tetrazepam

The group reached the following conclusions:

(a) Tetrazepam has the capacity to produce:

1. a state of dependence as predicted by its chemical similarity to diazepam with which it shares specific receptor mediated action as an anxiolytic, anti convulsant, sedative hypnotic.

2. central nervous system depression resulting in disturbances in motor function, behaviour and mood, demonstrated by animal and human studies showing sedation, ataxia, changes in behaviour and mood.

(b) There is sufficient evidence of similarity in chemical structure and pharmacological spectrum of action to diazepam to predict that tetrazepam is likely to be abused so as to constitute public health and social problem warranting the placing of the substance under international control.

No evidence of actual abuse was presented.

Bearing in mind that medical usefulness of tetrazepam as an anxiolytic, anti convulsant and sedative/hypnotic agent, as well as evidence predictive of abuse, the group recommended that tetrazepam be included in Schedule IV of the Convention on Psychotropic Substances.

4.36 Tibezonium

The group reached the following conclusions:

The group recommended that tibezonium should not be included in the Convention on Psychotropic Substances since it is not an anxiolytic or anti convulsant though it is an benzdiazepine. It is used as an anti-bacterial agent.
The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.

Tofisopam

The group reached the following conclusions.

Tofisopam is a 3,4 benzodiazepine and is marketed as an anxiolytic. Pharmacologically, it indicate that tofisopam does not share specific receptor mediated action with diazepam. Further studies in human have shown that tofisopam produces a profile of adverse and subjective effects unlike diazepam. No reports of abuse of tofisopam were produ.

Therefore, the group recommended that tofisopam should not be included in the List of Psychotropic Substances at the present time. It will be reviewed at a future session of the World Health Organization.
5. RECOMMENDATIONS

5.1 Considerations of future programmes

Reference is made to the recommendations for future review contained in the report of the Seventh Review (March 1983 MNH/83.7). At the review meeting to be held in March 1984, amphetamine-like drugs not currently under international control, will be reviewed. The subsequent reviews will consider uncontrolled barbiturates.

5.1.1 Small working group to review exempted preparation under the 1971 Convention

A pre-review meeting of a small working group may act as a clearing house before each review group considers the preparations.

5.1.2 WHO's Programme for Pain Relief in Cancer:

The WHO programme for pain relief in cancer should have close collaboration with MNH in the future. The current use of analgesics and the relation of therapeutic use to abuse of analgesics should be monitored.

5.1.3 Drugs to be considered for future review

As stated in the report of the Seventh Review of Psychoactive Substances for International Control (MNH/83.7), the following list of topics were to be considered in future review meetings:

(a) Derivatives and congeners of tetrahydrocannabinols with regard to their dependence potential, abuse liability and therapeutic usefulness.

(b) Derivatives and congeners of sedative, hypnotic, anxiolytic and stimulant substances (e.g. amphetamine derivatives, khat) already scheduled or proposed for scheduling under both the 1961 and 1971 Conventions.

(c) Analgesic drugs not subject to international control.

(d) Sedative, hypnotic and anxiolytic drugs not subject to international control, including benzodiazepine-like drugs marketed after end of February 1983, including:

   (a) midazolam
   (b) zopiclone
   (c) etifoxine
   (d) propizpine
   (e) quazipam
   (f) tofisopam

Although the above drugs were not formally considered at the 8th Review, the group discussed the results of certain pre-clinical studies which suggested that early review of their dependence potential should be carried out by WHO.

Precursors and intermediates of drugs listed in schedules of both Conventions

Synthetic and natural stimulants already scheduled under the 1971 Convention

Antipsychotic and antidepressant drugs with dependence potential and abuse liability.

The group recommended that, in collaboration with Interpol, UNODC and WHO jointly develop and implement in-depth studies to be carried out in a limited number of countries, on the relationship of the occurrence of specific substances in illicit traffic, clandestine manufacture, illicit availability, abuse as well as the implications and the impact of international control of such substances.
Types of data to be reviewed for rescheduling and descheduling:

A continuing absence and/or lack of availability of systematic data on the dependence potential, abuse liability, and likelihood of adverse social consequence of the compounds for review, being prepared for marketing, has hindered the deliberations of this group and its predecessors and made it extremely difficult to reach scheduling recommendations. Rather than wait for the unpredictable development of needed information on substances through the operation of diverse economic and social forces, the group considers that it would be wiser to ensure the production and availability of needed information. The group therefore recommends, and in turn requests, that WHO and the UN Commission on addictive Drugs recommend that in all countries the provision of a standard set of data on dependence potential, abuse liability and performance in both animals and humans be made a term requirement for initial drug registration and marketing of psychoactive drugs.

The specific type and level of data that might be required includes:

5.2.1 Measures of central nervous system effects in animals and humans including sedative-hypnotic, anti-convulsant, and anxiolytic cognitive, sensory and motor effects

(a) Speed of onset of pharmacologic actions
(b) Efficacy
(c) Relative potency

5.2.2 Animal data on psychological and physical dependence potential

(a) Reinforcing effects
(b) Discriminative stimulus effects
(c) Cross-physical dependence potential
(d) Primary physical dependence potential as indicated by abstinence or precipitated withdrawal.

5.2.3 Human experimental data on abuse potential

(a) Liking/euphoria
(b) Categorisation of subjective effects relative to prototype
(c) Reinforcing effects

5.2.4 Clinical data on dependence and public health problems

(a) Withdrawal syndrome
(b) Psychological dependence
(c) Toxicity

5.2.5 Epidemiological data on public health and social problems

(a) Data on emergency room treatment attributable to drug ingestion
(b) Prevalence of drug-related diagnoses and admissions
(c) Toxicity data from death records, both forensic and non-forensic
(d) Data on traffic and other accidents specifically related to drug administration.

5.2.6 Extent of abuse or likelihood of abuse and seriousness of public health and social problems resulting from abuse

(a) Arrest data for drug violations
(b) Seizure data
(c) Data on drug-related crime or theft among drug abusers
(d) Drug-related behaviour of drug abusers, e.g., use of other compounds, aggressive or violent behaviour
(e) Toxicity data from forensic death records
5.2.7 Utilization and usefulness

(a) Representative data on the prevalence, duration and patterns of medical use. In particular, shifts and trends in prevalence and patterns of use.

(b) Data on physician prescribing behaviour that bear on the extent, nature and appropriateness of medical practices.

(c) Data on the volume of prescribing, production and sales.

Preview WHO reports have described the methods which would be useful for obtaining this information (WHO Technical Report Series, Nos 618 and 656).

Under the provisions of the Convention on Psychotropic Substances, either party thereto or WHO may initiate a proposal for rescheduling or descheduling a substance. Such an action might be envisaged in the future if data as outlined above becomes available to warrant such a recommendation.

6. ACKNOWLEDGEMENTS

WHO acknowledges the partial financial support provided by UNFDAC for this meeting.
List of participants

J.B. Balter, Chief, Applied Therapeutics and Health Practices Program, Division of Extramural Research Programmes, National Institute of Mental Health, Rockville, Maryland, USA

Jcaro Fernandez J.C., Department of Toxicology and Forensic Chemistry, Faculty of Pharmacy and Biochemistry, University of Buenos Aires, Junín 956, Buenos Aires, Argentina

C. A. Andland Griffiths, Department of Psychiatry, The Johns Hopkins University and School of Medicine, Baltimore, Maryland, USA

Professor Joseph Knoll, M.D., Head of Department of Pharmacology, Semmelweis University of Medicine, Nagyvarad tér 4, P.O. Box 370, Budapest, Hungary

P. Legier, Département de pharmacologie clinique, Hôpital Fernand-Widal, 200 rue du Mouchoir Saint-Denis, 75010 Paris, France

P. Muya, Senior Consultant Psychiatrist, Mathari Hospital, P.O. Box 40663, Nairobi, Kenya

S. Navaratnam, Director, National Drug Dependence Research Centre, University Sains, Malaysia (Co-Rapporteur)

F. Ogunremi, Faculty of Health Sciences, University of Ilorin, P.M.B. 1515, Ilorin, Nigeria

I. Petursson, Department of Psychiatry, Borgarspitalinn, Reykjavik, Iceland

J.R. Schuster, Director, Drug Dependence Research Center, Department of Psychiatry, University of Chicago, 950 East 59th Street, Chicago, Illinois, USA (Rapporteur)

A. Shunib, Adviser, Pakistan Narcotics Control Board, Islamabad, Pakistan (Chairman)

T. Yamagita, Director, Preclinical Research Laboratories, Central Institute for Experimental Animals, Kawasaki, Japan (Chairman)

Representatives of other organizations

United Nations Division of Narcotic Drugs

D. E. Bailey, Chief, Treaty Implementation and Commission Secretariat Section, United Nations Division of Narcotic Drugs, Vienna International Centre, Vienna, Austria

J. Ramos Galino, Deputy Director, UN Division of Narcotic Drugs, Vienna International Centre, Vienna, Austria

Invited but unable to attend
International Narcotics Control Board

Professor Bror Rexed, M.D., F.R.C.P., Thomas Heftyes Gate 14C, Oslo 2, Norway

United Nations Fund for Drug Abuse Control

Mr Hans Emblad, Assistant Executive Director, UN Fund for Drug Abuse Control, Vienna, Austria

International Criminal Police Organization

Mr H. de Fine, International Criminal Police Organization, 26 rue Armengaud, Saint-Cloud, France

International Council on Alcohol Addiction

Dr P.H. Connell, Director, Drug Dependence Clinical Research and Treatment Unit, The Maudsley Hospital, Denmark Hill, London, England

Committee on Problems of Drug Dependence

Dr C.P. O'Brien, Professor and Chief, Psychiatry Service, Veterans Administration Medical Centre, University of Pennsylvania, Philadelphia, PA 19104, USA

International Union of Pharmacology

Dr J.M. Gaillard, Chief, Research Department, Psychiatric Clinic of the University of Geneva, Geneva, Switzerland

WHO COLLABORATING CENTRES

National Institute of Drug Abuse

Dr James Cooper, Assistant Director for Medical Affairs, National Institute of Drug Abuse, Department of Health, Education and Welfare, 5600 Fishers Lane, Rockville, Maryland 20857, USA

Mr Allen Duncan, Deputy Associate Commissioner for Health Affairs, Food and Drug Administration, Department of Health, Education and Welfare, 5600 Fishers Lane, Rockville, Maryland 20857, USA

Addiction Research Foundation

Dr U. Busto, Senior Researcher, Clinical Pharmacology Program, Addiction Research Foundation, 33, Russell Street, Toronto, Canada

Institute Mexicano de Psiquiatria, Mexico*

Health Research Institute, Chulangkorn University, Bangkok, Thailand*

National Drug Dependence Clinical Research Centre, University Sains, Penang, Malaysia - Dr V. Navaratnam (Temporary Adviser)

*Invited but unable to attend
SECRETARIAT

M. Arif, Senior Medical Officer in charge of Drug Dependence Programme, Division of Mental Health, WHO, Geneva

Michael C. Gerald, Consultant, Division of Mental Health, WHO, Geneva

I. Ito, Pharmacist, Division of Mental Health, WHO, Geneva

Samat Khan, Senior Medical Officer, Division of Mental Health, WHO, Geneva (Secretary)

P. Sartorius, Director, Division of Mental Health, WHO, Geneva

SERVERS

J. Holdal, Director, Pharmaceutical Division, Health Services of Norway, P.O. Box 8128, No 1, Norway

Howard McClain Jr., Chief, Drug Control Section, Drug Enforcement Administration, 1405 Eye Street, N.W., Washington D.C., 20537, USA
### Pre-review discussions between WHO temporary advisers and the pharmaceutical industry

**Sunday, 11 September 1983**

<table>
<thead>
<tr>
<th>Company</th>
<th>Represented by</th>
<th>Substances discussed</th>
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<tbody>
<tr>
<td>Hoffman-La Roche</td>
<td>Professor W. Hasfely</td>
<td>Bromazepam</td>
</tr>
<tr>
<td>P.O. Box 4002, Basel</td>
<td>Head, Pharmaceutical Dept.</td>
<td>Chlordiazepoxide</td>
</tr>
<tr>
<td></td>
<td>Dr. J. Ward</td>
<td>Clonazepam</td>
</tr>
<tr>
<td></td>
<td>Chief Medical Adviser</td>
<td>Diazepam</td>
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<td></td>
<td>Neuro- and Psychotropic drugs</td>
<td>Flunitrazepam</td>
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<tr>
<td></td>
<td>Dr. J. Witmer</td>
<td>Flurazepam</td>
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<td></td>
<td>Legal Adviser</td>
<td>Medazepam</td>
</tr>
<tr>
<td></td>
<td>Mr. R. Jones</td>
<td>Nitrazepam</td>
</tr>
<tr>
<td>Hoffman-La Roche</td>
<td>Director, Scientific &amp; Public Information</td>
<td></td>
</tr>
<tr>
<td>340 Kingsland Street</td>
<td>Dr. B. Medd</td>
<td></td>
</tr>
<tr>
<td>Nutley, New Jersey 07110,</td>
<td>Assistant Vice-President Marketing &amp;</td>
<td></td>
</tr>
<tr>
<td>USA</td>
<td>Professional Services</td>
<td></td>
</tr>
<tr>
<td>Haight-Ashbury Clinic</td>
<td>Dr. D. E. Smith</td>
<td></td>
</tr>
<tr>
<td>San Francisco, CA, USA</td>
<td>Medical Director</td>
<td></td>
</tr>
<tr>
<td>The Upjohn Company, SA</td>
<td>Dr. D. Griffiths</td>
<td>Alprazolam</td>
</tr>
<tr>
<td>10 Rue de Genève, Brussels</td>
<td>Director</td>
<td>Ketazolam</td>
</tr>
<tr>
<td></td>
<td>European Clin. Research</td>
<td>Triazolam</td>
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<tr>
<td></td>
<td>Dr. R. N. Straw</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Research Head</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Central Nervous System Research</td>
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<tr>
<td>Sanofi Recherche</td>
<td>Dr. J. Berthe</td>
<td>Clorazepate</td>
</tr>
<tr>
<td>rue du Prof. Blayac</td>
<td>Assistant Director</td>
<td>Ethyl loflazepate</td>
</tr>
<tr>
<td>34082 Montpellier, France</td>
<td>Toxicological Department</td>
<td>Loflazepate</td>
</tr>
<tr>
<td>Sanofi Recherche</td>
<td>Dr. Michel Moore</td>
<td>Tetrazepam</td>
</tr>
<tr>
<td>PARCO SA</td>
<td>Head, Neurobiology Dept.</td>
<td></td>
</tr>
<tr>
<td>195 route d'Espagne, B.P.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3005</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F-31024 Toulouse, France</td>
<td>Dr. J. M. Lwoff</td>
<td></td>
</tr>
<tr>
<td>Sanofi Recherche</td>
<td>Assistant Director</td>
<td></td>
</tr>
<tr>
<td>20 rue des Fosses St Jacques</td>
<td>Pharmaceutical Affairs</td>
<td></td>
</tr>
<tr>
<td>F-75240 Paris Cedex 05, France</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Dr. Thomas Christie  
Vice-President  
Lorazepam  
Lormetazepam  
Oxazepam  
Temazepam

Dr. David Richards  
Vice-President  
Medical Research

Dr. John H. Wood  
Director  
Legislation and Public Affairs

Dr. R. B. Dixon  
Senior Medical Director  
Halazepam

Dr. M. Briley  
Director  
Biochemical Pharmacology  
Tofisopam

Mrs. Ute Weiershausen  
Pharmacist  
Prazepam

Miss Margaret C. Cone  
Vice-President  
Scientific Affairs

I attended all day and observed all sessions.