Reflections on Strategy for Psychedelic Research in Light of the Medical Marijuana Struggle

By Rick Doblin, MAPS President

HOWARD LOTSOF'S STRATEGY (see previous article) of following normal guidelines for pharmaceutical development and not seeking special accommodations from regulatory agencies is fundamentally the same as MAP's strategy. Choosing to work within the guidelines of the FDA means that the requirements that apply to large multinational pharmaceutical companies must also be met even by much smaller organizations. The cost of required pre-clinical and clinical studies in time and money is a significant hurdle, even for large pharmaceutical companies developing non-controversial drugs. Such obstacles are particularly vexing for advocates of the medical use of psychedelic drugs.

After participating in and observing the struggle surrounding the medical use of marijuana, I've come to believe that working with the FDA is the path of least resistance for the development of the medical use of any Schedule 1 drug. The strategy employed by most advocates of the medical use of marijuana was to seek to provide marijuana to patients through FDA's "compassionate use" program. A major drawback of this approach was that the "compassionate use" program was designed to supply experimental drugs to relatively few patients while full-scale clinical trials are in progress. The program involves a patient-by-patient review by the FDA and does not generate data in support of the prescription availability of marijuana as a regularly approved pharmaceutical drug. Most importantly the ad hoc nature of the "compassionate use" program makes it subject to the vicissitudes of political manipulation.

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As long as the compassionate use program for marijuana remained very small, it was grudgingly tolerated. Unfortunately, there has been a bureaucratic backlash against the program as physicians in 1990 and 1991 increasingly sought legal marijuana for their AIDS patients to reduce nausea, stimulate appetite, and promote weight gain and a more positive attitude. Though the FDA approved about thirty new patients to receive government-supplied marijuana, Dr. James Mason, the director of the Public Health Service (of which the FDA is only a part), grew very worried at the thought of the "compassionate use" program growing from a small handful of patients to hundreds or even thousands. In June 1991, ideologically yoked to the position that marijuana has no medical benefits, Dr. Mason prevented the newly FDA-approved patients from receiving their marijuana by claiming among other things that smoking marijuana might induce them to practice unsafe sex.

In January 1992, advocates of the medical use of marijuana succeeded in winning some support from the White House Office of Drug Control Policy. Its support was limited, however, to requesting that Mason allow the 30-odd newly FDA-approved patients to receive marijuana, and that he move forward with studies designed to find alternatives to marijuana.

On March 10, 1992, Mason responded by announcing that he is shutting down compassionate access to medical marijuana permanently to all 13 patients already receiving it. To explain his decision to deny marijuana to all additional glaucoma, cancer, spasticity and AIDS patients, Mason claimed that marijuana might harm the immune systems of AIDS patients. Though no scientific evidence proves this to be the case (and much government money has been spent trying to find such problems), neither have any studies specifically in AIDS patients shown it not to be a problem. Mason also claimed that no studies showed marijuana was better than the currently available medicines, a blatantly false claim concerning cancer patients but true about AIDS patients. There is now no chance that the "compassionate use" program will become a

vehicle to provide medical marijuana to more than the tiniest fraction of the patients who could benefit from it.

In the same period of time that most advocates of the medical use of marijuana have been unsuccessfully trying to enlarge the "compassionate use" program for AIDS patients, UNIMED - the pharmaceutical company that markets oral THC (Marinol) - has made remarkable progress in securing permission to market oral THC to AIDS patients to increase appetite and reduce weight loss. A small Phase 1 pilot study at a hospital in San Francisco involving around ten AIDS patients showed that oral THC did indeed promote weight gain. UNIMED was able to get oral THC classified by the FDA as an "Orphan Drug" in the treatment of AIDS patients, giving UNIMED tax incentives, protocol assistance and patent protection. A larger Phase 2 trial was also conducted successfully . On January 8, 1992 UNIMED announced that it had reached its enrollment target for its Phase 3 studies. In UNIMED's quarterly report mailed to stockholders in late February 1992, it indicated that it plans to file an FDA Supplemental New Drug Application (SNDA) by July 1992. In addition, clinical trials will be conducted throughout Europe, including at The Pasteur Institute in Paris where Professor Luc Montagnier discovered the AIDS virus.

When evaluating the progress of UNIMED, it is essential to note that oral THC does not carry with it all the political liabilities of smoked marijuana. Indeed, the Bush Administration is willing to approve oral THC so that it can claim that an alternative to smoked marijuana does exist and that shutting down the "compassionate use" program would cause no real hardships to patients.

Despite smoked marijuana's political connotations, the Bush Administration would be hard- pressed to keep denying smoked marijuana to AIDS patients if FDA-approved studies showed that smoked marijuana worked better than oral THC and had no harmful effect on patient's immune systems. Indeed, if a study comparing oral THC to smoked marijuana were conducted, it is highly likely that smoked marijuana would prove the better medicine. This is partly due to the fact that smoking THC has been proven to be a more efficient and effective route of administration than oral consumption. In addition, some researchers speculate that the variety of ingredients in the natural marijuana plant offers pharmacological synergisms not present in refined THC. MAPS has long advocated scientific studies to arrive at conclusive answers to these questions.

One lesson from the struggle concerning the medical use of marijuana is that special FDA procedures such as the "compassionate use" program can be capriciously shut down by political pressure from outside the FDA. It is much harder to imagine the administration shutting down the conventional drug development process just to block the approval of smoked marijuana, ibogaine, MDMA, or any other Schedule 1 drug. Another lesson is that the FDA is more willing than other government agencies to permit the medical use of Schedule 1 drugs.

The strategy of following normal guidelines for pharmaceutical development and not seeking special accommodations is designed to minimize the political pressure that can be placed on the FDA by generating objective scientific data that must be reviewed on its merits. This is the strategy that MAPS has advocated in its struggle to open the door to medical research with MDMA. While predicting what the FDA will do is impossible, there is evidence that the strategy may work. First, the MDMA protocol has been endorsed by several of the main MDMA neurotoxicity researchers. Normally opponents of human studies, these scientists have been won over primarily because the risk of significant harmful consequences to the subjects is minimized by the choice of end-stage cancer patients. They have been persuaded that such risks are outweighed by the potential benefits to the patients and the gain in scientific knowledge. Second, the doses involved in the experiment (a maximum of four doses of up to 2.3 mg/kg of MDMA administered at least two weeks apart) are less than half the lowest level at which neurotoxicity has been found in the primate. Third, animal researchers have failed to find significant functional consequences of even massive MDMA-related neurotoxicity.

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