DRUGS, SCIENCE, AND ETHICS: LESSONS FROM THE DEPO-PROVERA STORY

CLAIRE D. F. PARSONS
Centre for Research in Public Health and Nursing, School of Health Sciences, La Trobe University, St. Helliers Street, Abbotsford, Victoria 3067, Australia

Synopsis—In the light of a decade-old controversy surrounding the use of Depo-Provera in family planning, the situation of Depo-Provera use in developing countries raises important ethical and scientific questions for health professionals and for those involved in family planning in other developing countries. Despite reports in the major family-planning journals that Indonesia and Jamaica are the highest users of injectables, Tongan health professionals appear to administer the world's highest rates of Depo-Provera per capita. The high level of use in the developing countries continues, yet conclusive findings from clinical trials are not available. There seems sufficient evidence to show that in many countries women are administered the drug in varying states of health and are given little information upon which to make an informed choice; surveillance of consumers is inadequate on both scientific and ethical grounds. The comparative data raise the question of whether there is a legitimate reason why health providers in the developing countries should not be observing the recommendations for Depo-Provera use. Questions are also raised about the administration of any new drugs where (a) clinical trials are not completed or are inconclusive, and (b) recommendations on the controlled administration of the drug are ignored in practice. The discussion of issues has implications for both the developing and developed countries.

INTRODUCTION

For more than a decade there has been constant debate over the drug Depo-Provera (depot medroxyprogesterone acetate (DMPA).[1] The debate has centred around issues such as the length and type of clinical trials required before marketing and widespread testing of the drug in humans, the relevance of side effects found in animal studies for human populations, the ethical issues surrounding the informed choice of consumers, and the relationship between multinational drug companies and developing countries. Evaluations of the relative merits and hazards of the widespread use of this drug have been summed up under the rubric *risk-benefit.* Risk-benefit assessments involve both scientific and ethical questions.

A review of the literature shows the current weight of evidence, issuing mainly from the World Health Organization (WHO) case-control studies in nine countries and the Save the Children Fund studies in Thailand, supports the continued widespread use of Depo-Provera as a long-term contraceptive for the following reasons:

- DMPA is quick and easy to use, requiring one injection every three months.
- DMPA is a highly effective contraceptive, at least equal to the oral contraceptive effectiveness rate.
- DMPA has few proven side effects.[2] Most are associated with irregular bleeding. Side effects may include amenorrhoea, break through bleeding, and (rarely) serious haemorrhage.
- There is no evidence that DMPA reduces lactation, or that DMPA in breast milk harms the breast-fed infant.
- Carcinogenic effects demonstrated in animal studies have not been found in women users, though the long-term effects are as yet unknown and some questions remain.

Despite this rather positive picture of DMPA, other complaints have been reported. They include headaches, abdominal discomfort, anxiety and nervousness, adrenal suppression, weight gain, hair loss, decreased libido, mood swings, dizziness,

fatigue, allergic reactions and severe mental depression. Such effects cannot be reversed quickly *(Citations in Population Reports,* 1983; Gold & Willson, 1981; Gold, 1983; Stephen & Chamratrithirong, 1988). Dissatisfaction with injectable contraceptives is associated mainly with the disruption to the menstrual pattern. Such irregularities were seen as the cause of 20–25 % of women turning away from DMPA (*Population Reports,* Series K-35, 1983). Breakthrough bleeding, though not considered life threatening (Archer, 1986), nevertheless may be incapacitating while it lasts. One research group (*Population Reports,* Series K-36, 1983) found several women bled for a total of more than 30 days in a three-month interval. While this may not be dysfunctional for women in the West, it can be socially incapacitating for women in cultures where strict custom and taboo are associated with menstruation. For example, there are often prohibitions on menstruating women attending certain rituals, cooking, or visiting friends and family (John, 1982; Whelan, 1975; WHO, 1981), from attending prayer, for example, Muslims (Whelan, 1975), or, from engaging in sexual intercourse (WHO, 1981). In Sub-Saharan Africa, lack of signs of fertility may be interpreted as divine disapproval of a couple, and Islamic law shuns contraception and abortion (Caldwell & Caldwell, 1988). Furthermore, in some cultures menstruation is regarded as necessary to rid the body of "bad blood" and other impurities. In several African, Asian, and Middle-Eastern countries, menstruation is thought to be necessary to prevent the blood accumulating in the body, which may otherwise cause headaches, lethargy, insanity, and debilitation. Thus, amenorrhoea and bleeding may cause considerable concern for women in cultures where failure to menstruate raises social and moral questions, and where menstruating women must observe social restrictions (*Population Reports*, Series K-36, 1983).

Where DMPA has been approved for long-term contraception, recommendations as to its proper use have been made by such research bodies as the Johns Hopkins University, which publishes its recommendations in the *Population Reports,* and by others.[3] The recommendations are as follows:

- The primary users should be healthy women.
- DMPA is not to be recommended as a first-choice contraceptive.
- Family planning personnel should be given thorough training.
- An accurate and simple record-keeping system should be maintained.
- The consumers should be fully informed of the action of DMPA, including any side effects, so informed consent can be assured and individuals can assume responsibility for any risks they take.
- Provision should be made for medical back-up for heavy bleeding, a rare but potentially serious side effect.
- The consumers require surveillance, that is, monitoring while taking the drug and follow-up after cessation of use of DMPA.

It is by following such recommendations, and thereby controlling the conditions under which a drug is used, that accurate scientific data can be collected and ethical questions be addressed. While the FDA refused approval of DMPA for widespread use in the United States because of medical evidence from the initial clinical trials, the U.S. Agency for International Development (AID) decided not to restrict DMPA distribution in developing countries which requested it, though its current policy is not to supply DMPA via this agency (Gold & Willson, 1981; Gold, 1983). The AID panel argued that the recommendations governing its use be followed wherever DMPA was distributed. The manufacturer of DMPA, Upjohn, which first sought approval for DMPA use for contraception in 1967, has since widely distributed the drug. DMPA has been approved for contraception in at least 90 countries, yet the scientific and ethical controls have not been rigorously met. This is especially so at the levels of selection of appropriate subjects for the administration of this drug and surveillance of its effects. Added to the question of ethical use of DMPA are reports that impoverished women have been offered inducements (such as chicken and fish oil) to persuade them to use DMPA (Prakash, 1984).

COMPARING RATES OF DEPO-PROVERA USE

DMPA use in the West varies considerably. In the United States, the drug Depo-Provera is not approved for contraception, as the FDA evaluating

committee chose to wait for evidence as to its safety after carcinogenic, and other side effects of high-dose progesterones, had been found in tests on dogs and rhesus monkeys (Gold & Willson, 1981; Richard & Lasagna, 1987). The United Kingdom uses the drug widely because of the evaluating committee's decision to await proof of its harm, rather than suspend approval of the drug until its safety was demonstrated. In New Zealand, West Germany, and Sweden, DMPA has also been approved for long-term use in women (Potts & Paxman, 1984; Richard & Lasagna, 1987; *Populations Reports,* Series K, 1987). In Australia, the use of DMPA is reserved for those who are "unwilling or unable to use other contraceptives," as it was phrased in 1974 by the FDA for the U.S. market. This usually means those women who the medical profession determines have a questionable record of compliance, such as the mentally incompetent in psychiatric institutions who might be sexually active, but represent instances where reproduction is considered undesirable.

In 1983, the FDA was pressured to review its decision on DMPA. The Acting Director of the FDA's Office of New Drug Evaluation, Robert J. Temple, reiterated the FDA stance by stating that approval should not be given to DMPA as the possibility of cancer is "alarming enough for us to think it should not be approved since the drug would be given mostly to healthy young women" (Gold, 1983, p. 80). He did not ask whether people should be concerned about susceptibility to cancer and other long-term complications when the majority of DMPA recipients are in less than optimum health, such as those women in the developing world.

Even though some countries were balancing the risk—benefit ratio in favour of making DMPA available for use in spite of possible risks (i.e., they focussed on the benefits, while the United States focussed on the risks) they retained the recommendations for the selection, informing, and monitoring of recipients, as previously described. It is here that the use of DMPA in the developing world departs from Western practices.

While there are many countries where it is difficult to access information on the rates of DMPA use (and this is especially so of the Pacific Islands), the *Population Reports* show New Zealand to be the highest user of DMPA in the developed countries (4% of married women of reproductive age in 1984). While some developing countries have rates less than 0.5%, in Indonesia the rate was 10% in 1984. The rates of users of injectables, compared to other forms of contraceptives, is as follows: Mexico, 11% in 1982; Thailand, 12% in 1984; Jamaica, 15% in 1983. The 1985 *Population Report* for September—October contraceptive rates states that "Jamaica has the highest percentage of women using injectables" (Mauldin & Segal, 1988). This was correct only for the countries named in that report. In 1988, a summation of the international use of contraceptives reported the highest use of injectables was to be found in Jamaica (8%) and Indonesia (10%). In all these reports, such countries as the Kingdom of Tonga are omitted. Yet in Tonga, the level of DMPA use was 46% in 1986. These numbers may seem low when presented this way. However, going by Up-john's own records (Gold, 1983) this constitutes (in predominantly developing countries) in excess of two million women overall.

A comparison between the use of this drug in the West and in the developing countries shows that its use is markedly higher in the developing world. This was intended from the outset (*Population Reports,* Series K, 1983, Series K-33, 1985, 1987; *Citations in Population Reports,* 1983; Gold & Willson, 1981; Gold, 1983). While concerns about overpopulation and high maternal mortality rates may be legitimate concerns, a question is raised about whether there is a legitimate reason why health providers in the developing world should have to use such high rates of drugs where the results from clinical trials are incomplete. A related question is whether there is a legitimate reason why health providers in the developing countries should not be observing the recommendations for DMPA use followed in the West? The developing world is precisely where women are the least likely to be healthy, have the least opportunity to freely make choices about their own bodies, and have the least education by which to understand chemically induced changes to their bodies.

The actual question of the magnitude of potential risk to these women is difficult to address in the absence of definitive findings on the safety of DMPA. Nevertheless, they must be asked. For example, there is no research which demonstrates the altered effects of such long-acting drugs in the

malnourished. One can only speculate that any adverse reactions would be amplified in a body with impaired physiology, yet it is in the developing countries (where women are usually the least healthy) that the highest levels of DMPA are being used. Family-planning agents in developing countries may argue that the women are carefully screened and monitored, but this is not so in Tonga, it is not so in Indonesia,[4] and it is not too fanciful to speculate that these are not the only two countries with questionable practices. Therefore, in a number of developing countries a profile of mismanagement may well exist, as will be discussed in relation to Tonga.

THE PACIFIC KINGDOM OF TONGA

In 1979 and 1980, I was conducting field work in the Kingdom of Tonga, researching indigenous sickness beliefs and healing practices. During the course of that research I was able to accompany Public Health nurses visiting villages around the main island of Tongatapu, where the main agenda was family planning. At the time I was surprised by the limited amount of detail provided by the nurses who were engaged in family-planning education and monitoring contraceptive users. I was aware that a controversy was brewing over the use of the drug DMPA, although the nurses promoting family planning were not. Logically, if the nurses were unaware of the debate over DMPA then the women using this method of contraception were also unaware. I was interested to follow-up the impact of this debate on the use of the drug in Tonga over the next few years. I have found the pattern of DMPA distribution and administration both interesting and disconcerting.

Compared to its use in other developing countries, the level of use of DMPA by health professionals who have assumed responsibility for controlling female fertility in Tonga is exceptionally high. During the year of my first visit to Tonga, 1979, the Tongan Department of Health Report showed new users of contraceptive as follows: 286 contraceptive pill, 113 IUD (loop), 73 rhythm, and 580 new users of Depo-Provera. The statistics for the previous four years show 600–800 women who were users of DMPA per annum, compared to 100–300 new users of the contraceptive pill, and 150–250 new IUD (loop) users. That is, DMPA, a chemical compound which during the 1970s began to be surrounded by controversy, was used to control female fertility at double the rate of any other form of contraceptive, and in some areas, it was five times higher. This was clearly against the recommendations for its use. In Tonga, DMPA was being promoted as a first-choice method, a quick and easy method of contraception.

In 1979 alone, 1,009 women were administered DMPA (*Report of Minister of Health,* 1979). By 1986, in spite of the serious debate in scientific circles, the administration of DMPA to Tongan women had not been reduced and was still being given at twice the rate of any other form of birth control (*Report of Minister of Health,* 1986). Investigation of the Department of Health records in Tonga gives no indication that the medical profession discouraged the high use of this drug (*Report of Minister of Health,* 1979, 1985, 1986). The Minister of Health reports, "Depo-Provera is still the leading method and 46% of the *new* acceptors use this method" (emphasis added) (RMOH 1986:31). He reports that this high level of DMPA usage in comparison with other contraceptive methods has existed for the past 12 years.

The women in the group I was observing were being given no information about the contraindications or adverse reactions to such drugs, and lacking such information could not be said to have made an informed choice. Indeed, informed consent was not possible, for as I found during my time in Tonga, the nursing staff had only limited information themselves. Nor were the women given detailed education on the use of the contraceptive pill as a preferable option to DMPA. Health professionals found it easier to give limited information, emphasising the benefits of DMPA. The women concerned were simply advised that the long-acting DMPA injection was the quickest and easiest method, and, lacking further information, they consented to be injected. The women were not given an extensive physical examination to assess their state of health, an observation noted in other countries (Prakash, 1984; Robinson, 1988). As for the careful monitoring of these women for adverse reactions, there appeared to be none. The nurses said they would visit the villages every few months, but otherwise there was no further contact until the next injection. This breached three more of the

recommendations for DMPA use, namely, that only healthy women were to be administered the drug, that informed consent was required, and that careful medical surveillance and medical back-up should be provided.

REASONS FOR THE TONGAN SITUATION

While a conspiracy theory (in terms of an intentional deception of the nurses and the women, by the state and medical profession in Tonga) is not being suggested, the situation does raise important questions about the nature of science and drug trials. DMPA arrived on the market at a time when concerns were being expressed, mainly in the West, about overpopulation of the world. "Zero population growth" became the slogan. Later, Western health professionals came to focus on the high maternal mortality rates in the developing countries. Furthermore, the literature on DMPA promoted the drug as being most appropriate for women in developing countries, especially in rural, or remote, areas. Therefore, it is easy to understand why in a country such as Tonga, where the population is dispersed throughout numerous small islands and the birth rate in the 1970s was high, the government and medical decision makers would favour a contraceptive with the features of DMPA.

While there is no official explanation for the high use of DMPA in Tonga, it could be surmised that remoteness was a major reason for the promotion of DMPA. Interviews with the nurses suggest another reason. They referred to the unreliability of users of the contraceptive pill. Yet neither of these reasons seem to justify its use at two to five times the rate of other contraceptives. First, the Kingdom of Tonga has numerous dispensaries and MCH clinics scattered throughout the island group. The 1985 report by the Minister of Health in Tonga states that 86.3% of the population were within an hour's access to some health facility. While such facilities could dispense a range of contraceptive devices, my encounter with the health providers at such facilities gave reasons to doubt whether they had the knowledge and skills to monitor and interpret any signs and symptoms the women might report that might be due to DMPA. Thus, access to supplies of other forms of contraception is not a problem, though the detailed knowledge and expertise of staff at these centres to evaluate patients and side effects may be.

Second, I found there is no questioning the reasons for noncompliance or unreliability in Tongan women who do not use the contraceptive pill as prescribed, or indeed, in women in other developing countries where I have worked.[5] The assumption that it is a matter of ignorance on the part of women, that they do not understand and follow instructions on oral contraceptive use, means serious ethical questions can be avoided. That is, to ask such questions as these is to question the adequacy of the training of health providers as educators, and to question the medicating of compliant, ill-informed, subordinate populations who are prevented from making informed choices. It is simply easier and cheaper to use drugs like Depo-Provera, and maintain control of fertility. Questions of gender politics and the power and collaboration between state and medicine do need to be asked in such instances. Figures, such as those above, show that despite the recommendations for the appropriate administration of DMPA, an extraordinarily high usage of this drug is both tolerated and encouraged in Tonga. It compares most unfavourably with the pattern of DMPA usage in the West.

INFORMED CHOICE

It has sometimes been pointed out that women in Tonga enjoy high status and therefore are key decision-makers capable of choosing which family-planning method they want. This high status is true for the position of a sister who carries authority over her brother's family, but is not true for the position of wife and mother. It is in these latter positions that the issue of contraception emerges, and while decision-making may appear to be freely made by the woman concerned, there may be very real coercion from the husband, his family, or by older female relatives of her own kin network. Indeed, while on the Tongan island of Kapa in the Vava'u group of islands, my interviews with the women in the village revealed the sexual politics associated with condom use. Reportedly, some of the men would puncture the condoms. The women believed the acceptance of condoms in Tonga did not result from a high level of concern by men over the number of pregnancies their wives endured, or the possibility of maternal mortality. Rather, it meant the men could retain procreative control.[6] Hence, women may readily

consent to the administration of long-acting drugs to their bodies as a result of (a) a lack of knowledge of contraindications and reactions to the injectables; (b) a lack of knowledge of how to compare available contraceptive methods; (c) as an escape from the hazards of condom politics, while inadvertently surrendering to government and medical control over their fertility; and (d) as a result of coercion from husband or relatives.

To some, this may seem an irrational evaluation of DMPA use and that there are no politics involved. Some may wish to argue that the women do have free choice. However, the evidence I gathered in Tonga indicates this is not the case.

In addition, the Johns Hopkins University *Population Reports* show that when women are given balanced information and a genuine choice of contraceptive methods, their preferences differ country by country. A study of countries where strict methods were used to control the advice given to women, without coercion to use one method over another, showed the women made quite different choices to those they made before such rigour was introduced *{Population Reports,* Series K, 1986). Unfortunately, the reader of these reports is not told what constitutes balanced information and there may still be an assumption that where health providers give full and unbiased information prior to the woman making her choice, that informed choice is somehow independent of social pressures or cultural ideology. While no choices are ever made outside a social and cultural framework, communication between provider and client will remain distorted where the provider is oblivious of salient social and cultural constraints. Health education is inadequate where the provider does not consciously address such issues. The *Population Reports* do not appear to address these issues.

THE POPULARITY OF INJECTABLES

Why do women favour injectable contraceptives? In many developing countries women would rather take medicines by injection than orally. It has been suggested that the reason for this is the success of antibiotics, which have been commonly given by injection throughout the world (*Population Reports,* Series K, 1986). However, from my own research I have found there is a resistance to injections by Tongans and other Polynesians (Parsons, 1981; Parsons, in press). More plausibly, injections allow privacy where exposure of genitals and examination by male doctors (such as is required for IUDs) contradicts customs and taboos. I have certainly found this to be so throughout Polynesia. It is also possible to contracept this way without a husband, or relatives, knowing.

Thus, the popularity of DMPA, especially in the face of little or no information about side effects, is based on sociocultural, rather than health, reasons. Are these the right reasons? They can only be so when a woman is given full information of possible health risks, including realistic information on the availability of back-up services if complications arise, especially as there are still a number of unanswered questions about the long-term safety of using DMPA, and where she is given an realistic opportunity to discuss the pressures influencing her decision and the concerns she has about its use. Only then can she choose to take the associated risks.

WHAT HAPPENS WHEN THINGS GO WRONG

Reporting side-effects

Statistics on reported drug side effects have always been problematic. Most of us know from experience that very few drug side effects are ever reported, whether by upper-middle-class Europeans or by villagers in developing societies. So the question must be asked, how can the Tongan women monitor themselves for possible side effects? The illiterate are not able to return to their village and write down the instructions given, in order that they not forget. Memory of any instructions by a health professional must be relied upon. So, how is a woman to remember the range of possible signs or symptoms which she may experience (if she were told), or know that the pain, discomfort, dizziness, collapse, rash, discharge, and so on, is somehow related to an injection she was given at a hospital weeks or months ago? In cultures where biophysiological processes are not understood, at least not in biomedical terms, the relationship between an injection given a week or more ago and what one is experiencing today seems obscure at best. For many, it will be incomprehensible. Indeed, how many literate people can do these things? From my own experience in the community health arena,

few working-class or middle-class people in western societies (a) read the pamphlets or other written information (occasionally) given to them by their doctor, (b) write down instructions when they get home from a visit to a doctor, or (c) would think of associating signs and symptoms which may be side effects of drugs after several days have passed.

In Tonga, side effects would be unlikely to come to the attention of health professionals because (a) health providers do not always have the skills to recognise them; (b) they are often not available at the time; (c) such signs and symptoms would be managed within the household, within a kinship network (a family therapy management group), or by an indigenous healer; (d) the signs and symptoms would most likely be interpreted emically (applying an indigenous meaning) because such side effects could be interpreted as signs and symptoms of an indigenous disorder (especially in cultures where people are treated symptomatically); and (e) it is unlikely that the side effects would be related to some injection the woman had a month or so ago. So, if something goes wrong, who gets to interpret the situation? It is unlikely that the side effects of drugs will ever come to the attention of a health provider, or that it will be interpreted, unequivocally, as a side effect which should be reported.

This begs the question of what medical science means when it records and constructs the statistics of side effects associated with clinical trials or general prescribing practices.

Monitoring and provider-patient communication

The relationship between monitoring populations and the effects of drugs and provider-patient communication also requires investigation. In Tonga, provider-patient communication is usually unidirectional and limited. Observations in Tonga revealed that the health provider usually gives directives. Open confrontation, disagreement, or direct questioning by patients is culturally inappropriate. Consideration of a problem over a few days or weeks, or circumlocution, is the culturally appropriate way to deal with sensitive topics to avoid social tensions or conflict. Clinical and community health contexts are not usually conducive to this mode of communication. I have noted Tongan appraisals of the Western health care system and doctor-patient communication elsewhere (Parsons, in press). Thus, Tongans may listen to the directives and may leave the clinical encounter with little or no understanding of the biomedical explanation of their bodily processes, or of the impact of drugs on physical or mental processes.

The monitoring and provision of medical back-up for the remote dweller

The *Population Reports* show that DMPA is emphasized as being a particularly "good method for a woman who lives in a remote area" (*Population Reports*, Series K, 1983). Yet there is a paradox here between the convenience for women and health professionals and that of the problems of surveillance of women in remote areas and their access to health providers who know and recognise the signs and symptoms of drug side effects.

If the clinical trials on new drugs are completed and the drug has been proven safe, then the problem of close monitoring and careful, ongoing follow-up may not be an issue. However, with DMPA, the statistics on side effects are yet to be collected. They are based on those reported by users, yet the odds are against reporting.

Tongan records show that DMPA is given mostly to women in the remote areas. Here, it is used up to four times more often than any other contraceptive. Monitoring effects and attending to the rare but possible emergency (severe haemorrhage) is a problem. For the northern islands of Tonga there is only one hospital and that is in the main town of Vava'u. This is the only site where medical practitioners are located. The Public Health nurses occasionally make visits to the rural villages, or give services at the MCH clinics, and visit the outer islands perhaps once or twice a year. Throughout Vava'u in the north, DMPA more than doubles any other method of contraception used. Throughout the Ha'apai group of islands, women are given DMPA not only as first choice (the choice being that of the health professionals) but at a rate five and one half (5.5) times greater than any other method (other than sterilization, which is still less than the DMPA rate). In 1985, on the northernmost island of Niuafo'ou, the number of women using DMPA in this small community was four times greater than any other method of contraceptive. In sum, the questions raised relate to the fact that while women in remote areas are a

particular target population for DMPA (*Population Reports,* Series K, 1983, Series K-33, 1985, 1987, Series K-36, 1983), a contradiction exists whereby they may not be the most suitable population for DMPA due to the following:

- They usually receive the least supervision (if any).
- They often have the lowest level of literacy.
- They usually have the least comprehension of health professionals' instructions regarding such matters as self- monitoring and reporting of drug side effects (not because of ignorance or unreliability, but principally due to the conceptual differences between biomedical and indigenous explanations of physical and mental functioning).
- They operate from verbal instructions and are not able to return to their village and write down possible side effects, if indeed they were told at all. As any reported side effect may be explained and managed in several ways, it is doubtful that accurate records are maintained.
- They manage the majority of signs and symptoms (side effects) whether mild or serious, by ignoring them, self-management, management by a kinship therapy group, or by an indigenous healer.
- They are usually the most restricted by traditional female roles and learn that pain, discomfort, and other health problems are simply part of everyday life and a normal part of being a woman.
- They have little, if any, opportunity to compare their experiences with other women (e.g., urban dwellers experiencing a pluralism of ideas and values) who may not be so willing to accept ailments, such as those arising as drug side effects.
- They are often the least healthy. For example, Ha'apai and the more remote islands often experience hurricanes and droughts which deplete food resources, leaving them with a largely carbohydrate and fat diet.

How do researchers know that "no one has died from injectable progestagens", as has been argued? How do researchers know that "few cases of serious haemorrhage have occurred as a result of using Depo-Provera" (Archer, 1986)? Facts regarding such drugs as DMPA are gained from those projects closely monitored, such as the WHO centres (e.g., the McCormack Hospital Family Planning Programme in Thailand). However, these are the centres where the recommendations governing the use of DMPA are most strictly adhered to and the findings are not representative of what is happening elsewhere.

Remoteness amplifies the problems of reporting and documenting drug side effects. It amplifies the ambiguities of science in the real world. Yet in the end, it will probably be argued that sound (empirically valid) judgements about DMPA's side effects have been made.

Most health professionals would agree that on both ethical and scientific grounds the administering of drugs, before long-term clinical trials have been completed and have demonstrated their safety, should occur only where the providers closely adhere to the guidelines (recommendations) for its controlled distribution. This is not the case for DMPA. Furthermore, researchers may well get a distorted picture from statistics on the reported side effects of DMPA for the reasons given above and these may be applicable to other therapeutic interventions, their complications and other outcomes.

SCIENTIFIC AND ETHICAL IMPLICATIONS FOR CLINICAL DRUG TRIALS

The politics of drug testing in the manner described above strongly favours the drug companies and does little to protect the well-being and rights of consumers. The political and ideological questions about state and medical control of women and women's bodies have been addressed elsewhere (Turner, 1987; Ehrenreich & English, 1976), but are applicable here. The focus in this article is on the scientific and ethical issues.

The comparison of DMPA administration throughout the developed and developing world showed that not only is the rate of DMPA usage much lower in the developed countries, but those developing countries which are most closely monitored (such as those in the WHO study) administer DMPA at far lower rates than those unlikely to face scrutiny, such as Indonesia and Tonga. Not only does Tonga appear to have the highest rate of usage in the world, it may also monitor its consumers least adequately. It would therefore seem that the more a country's government and medical profession comes under scrutiny, the less they are likely to deviate from the

intended usage of drugs and the greater the accuracy of statistics on drug side effects.

Those government and medical officials who sit on committees evaluating the risk—benefit of distributing new drugs based on limited clinical trials have a responsibility to ensure that recommendations for control of that drug are a reality and not rhetoric. Those committee members who focussed on the benefits of DMPA in the risk—benefit assessment have the ethical obligation and the scientific responsibility to ensure that those new drugs, which have undergone only limited short-term clinical trials, are administered where the health providers are properly trained to recognize and consistently report complications, that the recipients can realistically seek help when necessary, and are capable of interpreting and reporting any abnormal signs and symptoms so they can be fully evaluated as to their possible association with the drug. Such side effects can then be recorded with greater accuracy. As has been shown, women living in remote villages and where communication and transport is limited would not seem to be the appropriate population.

CONCLUSION

While there is evidence of the advantages of using DMPA as a contraceptive, the evidence is not yet complete and therefore caution is still required. It seems a paradox exists in the management of DMPA usage: the highest usage of DMPA amongst the least well-selected, the least well-informed, and the least well-monitored. The likelihood that the consumers in the developing countries are, in Western terms, healthy, informed, and freely consenting is even more questionable than among Western consumers. The notion of acceptable risk is accompanied by the question, "Acceptable to whom?" In the case of Tonga, it would seem it is the government officials and health providers who find the risks acceptable. This is no consolation for the women who are the ones to suffer any complications. As was made clear from the histories of other contraceptives, such as the (Robins) Dalcon shield and the (Searles) Copper 7, risk-assessment based on clinical trials by drug companies and by (some) medical professionals may be tenuous.

The paradox of the Depo-Provera story carries important scientific and ethical implications for all drug trials and therapeutic management. On both moral and scientific grounds, it must be argued that if risk—benefit assessments do favour the distribution of a new drug because of the perceived advantages, then drugs with limited clinical trial should at least be distributed to populations where subjects are selected according to recommendations, where informed choice is not compromised, and where monitoring and long-term follow-up are not mere Drugs, Science, and Ethics 113rhetoric. The administering of DMPA, at least in some parts of the world, appears to be failing to meet the basic tenets of scientific and ethical medical practice.

ENDNOTES

1. United States Food and Drug Administration (FDA). (1987). FDA denies approval of Depo-Provera in United States for contraception—risks outweigh benefits. *Family Planning Perspectives*, 10, 304–314; Kasper, A. (1979). Depo Provera—a political and legal issue. *Women and Health*, **4**, 407–410; McDaniel, E. (1980). Depo Provera—a critical analysis. *Women and Health,* **5**(4), 85–88; Bahemuka, M. (1981). Benign intracranial hypertension associated with the use of Depo-Provera; a case report. *East African Medical Journal,* **58**, 140–141; Gold, R., & Wilson, P. (1981). Depo-Provera—new developments in a decade old controversy. *Family Planning Perspectives,* **13**, 35–39; Gold, R. (1983). Depo Provera—the jury still out. *Family Planning Perspectives,* **15**, 78–81; Prakash, P. (1984). Retreat on Depo-Provera. *Economic and Political Weekly,* **19**, 2072–2073; Potts, M., & Paxman, J. (1984). Depo-Provera—ethical issues in its testing and distribution. *Journal of Medical Ethics,* **10**, 9–20; Public Board of Inquiry. (1985). Public Board of Inquiry advises that Depo-Provera not be approved for use as contraceptive in the United States. *Family Planning Perspectives,* **17**, 38–39; Nair, S. (1986). Injectable contraceptives in developing countries. *The Lancet,* **June 21**, 1440; Richard, B., & Lasagna, L. (1987). Drug regulation in the United States and the United Kingdom: the Depo-Provera story. *Annals of Internal Medicine,* **106**, 886–891; *Population Reports,* Series K. (1980-1987). Baltimore, MD: The Johns Hopkins

University; Weiss, J., Ross, G., & Stolley, P. (1984). Food and Drug Administration, Rockville, MD: Report of the Public Board of Inquiry on Depo-Provera.

2. *Population Reports,* Series K. (1983). Series K-33. (1985). (1987). Baltimore, MD: The Johns Hopkins University.

3. *Population Reports,* Series K. (1984). Series K-36. (1983). Baltimore, MD: The Johns Hopkins University.

4. Robinson, K. (1988, August). Family planning in Indonesia. A paper delivered at the AAS Conference, University of Newcastle. Robinson suggested there might be problems associated with injecting women with DMPA before the return of a normal menses postpartum. I conclude from her remarks that while Upjohn recommends "injecting either during the first five days of a normal menstrual period, or, before the fourth week postpartum" (Gold, 1983, p. 81), the dilemma becomes injecting before the woman can become pregnant, thereby ensuring no harm to a foetus, yet not knowing the state of health of the woman concerned. That is, if she has no normal menses following childbirth, how can the health provider know she has returned to normal, healthy body functioning?

5. The author has a biomedical background in both nursing and medical studies.

6. The KAP surveys are not designed to elicit the sexual politics of contraceptive use.

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