

# The Quinacrine Debate and Beyond

Exploring the Challenges of  
Reproductive Health Technology  
Development and Introduction

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This is a report from the meeting, "The Quinacrine Debate and Beyond: Assessing the Future of Non-surgical Female Sterilization" (April 20-22, 2001), convened by the Center for Health and Gender Equity, the National Black Women's Health Project, the National Women's Health Network, Planned Parenthood® Federation of America, and the Reproductive Health Technologies Project.

Amy Allina, Shelia Clark, Valerie DeFillipo, Jodi Jacobson, Kirsten Moore, and Shira Saperstein served as meeting organizers and editors of the report. Catalina Vallejos Bartlett prepared a painstaking transcript of the meeting as well as the initial drafts of this report. We are grateful for her intelligent and nuanced approach to this complicated issue. We would also like to thank Karen Katz, Judy Norsigian, Jael Silliman and David Sokal for taking the time to review an earlier draft of the report.

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# Contents

<b>Executive Summary</b>	<b>5</b>
<b>1. Introduction</b>	<b>9</b>
A. Background on Quinacrine Sterilization	9
B. Issues Surrounding Quinacrine Sterilization and Other Reproductive Health Technologies	10
C. Background on April 2001 Meeting	12
D. Overview of This Report	12
<b>2. Competing Paradigms of Technology Development and Cross-Cutting Themes</b>	<b>14</b>
A. Competing Paradigms of Technology Development	14
Technology-as-Neutral Paradigm	15
Technology-as-Embedded-in-Context Paradigm	15
B. Core Themes That Cut Across the Competing Paradigms	16
The Importance of Considering Reproductive Health Decisions in a Sociocultural Context	17
The Importance of Understanding the Ethical Dimensions of Contraceptive Research and Development	23
The Need to Recognize the Legacy of Social Inequities Within and Across Countries	30
The Need to Establish Accountability in Reproductive Health Research and Policy	32
<b>3. Concluding Observations</b>	<b>35</b>
Appendix A. Meeting Agenda	37
Appendix B. Meeting Participants	39
Appendix C. Letter from a Meeting Participant	42



# Executive Summary

## 1. Introduction

Female sterilization is currently the most common form of birth control worldwide. Concerns about the relative cost and risks of tubal ligation, the only form of female sterilization presently approved by the international public health community, have led to calls by some for development of non-surgical means of female sterilization. The feasibility and desirability of developing a non-surgical method of sterilization that would be safer, cheaper, easier to deliver, and more acceptable to women has become embroiled in controversy over the current use of quinacrine, a 40-year-old treatment for malaria, as a form of non-surgical sterilization.

On April 22-23, 2001, approximately 55 individuals, representing a broad cross-section of the medical, public health, and women's rights communities from both developed and developing countries, met over two days to discuss and assess the past, present and future of quinacrine sterilization (QS) as a method itself and as a reflection of parallel issues in the larger field of contraceptive research, development, and introduction.

The meeting was structured as a balanced, respectful dialogue that was not intended to reach consensus or to resolve long-standing questions or disputes about the method. As such, the agenda was organized as a series of panels that addressed

five key questions: (1) Is there a need for non-surgical methods of sterilization? (2) In a world of scarce resources, how do we set and balance priorities for development of reproductive health technologies? (3) What are the appropriate safety and risk standards for reproductive health technologies, and are they universal? (4) To what extent should the context into which new methods will be introduced limit or constrain new technologies? (5) Can a "tainted" method be reclaimed? If so, how and under what circumstances?

The meeting had a two-fold purpose. First was to discuss what is known about QS: whether existing data are sufficient to draw conclusions about its safety and efficacy; whether even a safe method of non-surgical sterilization can be effectively delivered in low-resource settings without considerable safeguards; and whether further investment in this, or other methods of non-surgical sterilization, is warranted given other pressing reproductive health needs. Second was to take a look at the larger picture of reproductive health technologies, including the safeguards and protocols needed to ensure proper introduction and sustained delivery of new technologies and better delivery of existing ones; the systemic reproductive health and rights concerns—such as client-provider communication, provider bias, and informed choice—that characterize many low-resource settings; and the importance of social and political contexts in determining the ultimate safety and efficacy of any technology outside the laboratory.

## 2. Competing Paradigms of Technology Development and Cross-Cutting Themes

The meeting revealed two paradigms of technology development and four cross-cutting themes, as reported below.

### A. Competing Paradigms of Technology Development

Meeting participants discussed two competing yet related paradigms that fuel tensions regarding research, development, introduction, and delivery of reproductive health technologies in diverse settings. The first—*the technology-as-neutral paradigm*—assumes that technology is neutral and emphasizes the benefits of reproductive technologies through expanding the array of choices for people, particularly for women. The second—*the technology-as-embedded-in-context paradigm*—views technology as embedded in the historical, sociocultural, and political structures and histories that influence research, development, introduction and delivery of reproductive technologies. Ultimately, the two paradigms are closely connected, making simplistic distinctions between them impossible. Despite the overriding concern they share with improving women's health, supporters of technology development and individuals concerned about the context in which technology is used have often found themselves at odds.

### B. Core Themes That Cut Across These Competing Paradigms

Within these competing paradigms of technology development, four cross-cutting themes emerged in discussions at the meeting.

**Theme #1: The importance of considering reproductive health decisions in a sociocultural context.** A majority of discussants emphasized the importance of embedding efforts to improve

women's overall reproductive health and well-being within a reproductive rights approach. This approach acknowledges the complex interaction between the introduction and sustained delivery of reproductive technologies, the social and institutional contexts that facilitate or hinder these efforts, and the participation of women as respected, autonomous persons who actively participate in the development of their own health agendas individually and collectively.

Throughout the meeting, participants returned again and again to the most critical principles of this rights-based approach: the promotion of informed choice and informed consent, support for the principle of voluntarism, the recognition of and response by health services to the contextual realities of women's lives, and the availability of both good counseling and of choices among methods that are as real in practice as they are in theory. Because there were divergent views on the extent to which full support for these principles is evident in many settings, participants reached differing conclusions about the use of QS in diverse settings and whether, even in the face of adequate safety and efficacy data, scarce resources should be devoted to further research and development of QS, especially in light of the growing demands for improving existing services and other reproductive health products (e.g., female condoms and microbicides).

A number of participants also argued that the role, responsibility and impact of U.S. reproductive health policy and practices must be examined critically as the United States has significant direct and indirect impact on individual country programs as well as on the overall direction of population policies, programmatic priorities, and technology development. Activists, advocates, and researchers should recognize that a U.S. Food and Drug Administration (FDA)-sanctioned technology

has pros and cons. Although FDA approval acts as an instantly credible imprimatur for use of a technology in the U.S. and elsewhere, U.S. regulatory guidelines may not be translated faithfully in diverse settings. The “FDA-approved” imprimatur on a technology may create a license for widespread distribution before assessments regarding needs and service delivery capacity in other settings have been conducted. Similarly, word of an “FDA-approved clinical trial” may be misunderstood, or even misrepresented to equate with an “FDA-approved technology.”

**Theme #2: The importance of understanding the ethical dimensions of contraceptive research and development.** Discussion regarding ethical dimensions of research, including research into QS, was distilled into two overarching questions: (1) What are the components of ethical research that can be identified with regard to what has or has not been done on the issue of QS? (2) What should be done with the data collected on research that was not conducted with those components in place?

There was wide agreement in the discussion that informed consent is one of the most important components of ethical research. However, participants differed with regard to what systems needed to be in place in order to ensure informed consent. Participants discussed the need for political participation and transparency in ethical research, development, introduction and delivery; the need to breathe life into international agreements (e.g., the Programme of Action of the 1994 International Conference on Population and Development); and whether an obligation exists on the part of the sponsoring group to provide affordable access to the intervention (if found to be effective) or appropriate treatment in the event of the method’s failure.

Some participants concluded that studies of the safety and efficacy of QS can be conducted ethically, if certain conditions are met, including respect for persons, upholding beneficence and justice through community consultation, satisfactory informed consent, and pre-clinical and clinical safety testing. While some believe such trials could resolve adequately the issues of safety and efficacy that have haunted QS, others asserted that the tainted past of QS negates any possibility of redeeming and reclaiming what they see as a flawed method.

**Theme #3: The need to recognize the legacy of social inequities—racial, ethnic, gender, and class, both within and across countries—that affect women’s reproductive health and well-being.** QS is one of many reproductive technologies that have been lightning rods for concerns related to historical and contemporary social inequities. Numerous participants stressed the fact that generations of poor, powerless women of color, from developing countries and the United States, have been targeted for contraceptive delivery, including forced or coerced sterilization, in order to meet political ends, i.e., reducing the fertility of “problem populations.” While proponents of quinacrine hold that providing a wider range of reproductive health options is in the interests of all women, and that decisions about which options are of interest should be made by individual women and not in a larger sociopolitical arena, others argue that, nevertheless, the use of QS as a method has occurred within the context of social inequities, and denial of this historical reality further reinforces the invisibility and vulnerability of poor women and women of color globally. Critical analysis of the method itself and a commitment to pursue a more in-depth understanding of the socio-political, historical abuses that poor women of color have endured would have alerted

QS proponents to its potential for abuse or at least to the intimate, often explosive politics of reproductive technology.

**Theme #4: The need to establish accountability in reproductive health research and policy.**

Discussion centered on the need to develop more stringent measures of accountability for all key stakeholders and on the types and kinds of formal structures and other mechanisms of accountability that should be considered in monitoring current and future reproductive health products and in sanctioning products involved in questionable practices in the past (e.g., QS).

Currently no international body is formally vested with the authority to investigate allegations of abuse according to any specific criteria, or to halt the inappropriate use of reproductive health technologies. A number of participants agreed there is a need for mechanisms that are based on international principles but which can be applied at country- and community-specific levels. Such mechanisms would serve to reinforce the following:

- The notion that all key stakeholders—researchers, policymakers, practitioners and others—are involved at every stage of contraceptive introduction and delivery; and
- The need for transparency in decisionmaking in policy, research and clinical practice.

However, several participants questioned whether and how a formal process could (or should) be developed that could act with authoritative legal discretion. Under whose jurisdiction would it be implemented and maintained? How would grievances be monitored, implemented, and resolved?

### **3. Concluding Observations**

The meeting “The Quinacrine Debate and Beyond: Assessing the Future of Non-Surgical Female Sterilization” was not the first attempt—nor we hope the last—to ensure that the dialogue around QS is rooted in a rights-based framework wherein the most sound, safe, and efficacious reproductive technologies are developed and marketed to consumers who need and want them. The meeting served as a reminder, however, of the challenge that remains to reinvigorate our efforts to live these principles in practice rather than halfheartedly to espouse and repeat them as rhetoric that occasionally appears in print.

# Introduction

Quinacrine and the field of reproductive technology research, development, introduction, and delivery can be viewed through microscopic and telescopic lenses respectively. These lenses enable us to grapple with the historical and contextual issues of quinacrine as a method of sterilization as well as the larger category of all reproductive health methods that seek to improve the lives and well-being of women.

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## A. Background on Quinacrine Sterilization

Female sterilization is the most common form of birth control today. Worldwide, approximately 19 percent of all female contraceptive users have undergone sterilization to end childbearing. In the United States, nearly 28 percent of current contraceptive users have been sterilized. The rate of female sterilization for birth control in any given population depends on a number of factors, including age distribution, desired family size, the acceptability of male sterilization (i.e., vasectomy), the availability of female sterilization, the availability of alternative choices of contraception, and, in some instances, the use of “targets” to ensure a specific level of sterilization.

At present, the most widely used form of female sterilization is tubal occlusion or ligation. The method requires a simple surgical procedure. The two most common approaches to tubal ligation are *minilaparotomy*, which is usually performed under local anesthesia, with light sedation, and *laparoscopy*, which requires general anesthesia. Performed correctly, with informed consent and under sterile conditions, tubal ligation is a safe procedure with a low rate of complication. Nonetheless, the procedure requires the intervention of trained medical professionals and almost always the use of general anesthesia.

Concerns about the costs and risks of tubal ligation, especially in low-resource health care settings, have driven some in the contraceptive research and development field to call for development of

non-surgical means of female sterilization. They have envisioned a method that would be safer and cheaper for, as well as easier to deliver and more acceptable to, a larger share of the female population that has reached its desired family size. Because of a legacy of abuse of sterilization in some settings in both developed and developing countries, critics have opposed the development of other forms of sterilization. For many, the discussion about whether development of such a method is feasible and desirable has become embroiled in controversy over the use of quinacrine, a 40-year-old treatment for malaria, as a form of non-surgical sterilization. That controversy, as it relates to quinacrine's rocky history as an intrauterine agent for non-surgical female sterilization, is chronicled in the timeline below [see box A].

Some studies carried out in Chile, India, and Vietnam suggest that quinacrine sterilization (QS) is an effective form of female sterilization when women are given two insertions of quinacrine tablets. Under the regimens tested in these studies, tablets inserted into the women's uterus were believed to cause scar tissue in the fallopian tubes, blocking the egress of sperm and preventing fertilization of the egg. The validity of the data collected in these studies has been called into question, however, because some of the studies had small sample sizes and did not use randomized controls. As a result, there is no single insertion protocol that has been proven to ensure the maximum effectiveness of QS. The World Health Organization (WHO), the International Planned Parenthood Federation, and numerous scientists and women's health advocates have expressed serious reservations about the safety and efficacy of QS, and about the conditions under which the method has been administered to women in low-resource health care settings. Mounting pressure has slowed further research and stymied efforts by

proponents to introduce the method into reproductive health programs on a broader scale.

## **B. Issues Surrounding Quinacrine Sterilization and Other Reproductive Health Technologies**

In many ways, issues surrounding QS illustrate the broader challenges facing the reproductive health field today. On the one hand, expanded access to reproductive health technologies has greatly improved the quality of life of millions of women worldwide. The diffusion of contraceptive technologies ranging from male latex condoms to birth control pills and intrauterine devices (IUDs) has given women and men an increasing array of choices with which to plan their families safely and effectively. These and other technologies have reduced unwanted births overall, led to improved reproductive health outcomes in many countries, and hastened a revolution in both individual and social patterns of reproduction.

On the other hand, reproductive technologies have been used by governments and institutions to achieve political ends in ways that have compromised the rights and well-being of women, particularly those who are socially and economically marginalized, and those belonging to ethnically and racially diverse groups. Over the past four decades, concerns about rapid population growth, especially in poorer countries, often led to ambitious plans for reducing birth rates. In these campaigns, little attention was paid to the social and gender inequality that supported high fertility, and left the majority of women with little choice in marriage, sex, and reproduction. Moreover, little was done to improve the poor quality of health care services through which contraceptive methods were delivered. The aggressive promotion of contraception, and use of IUDs, Norplant, and other long-acting methods targeted toward

## Box A. Non-Surgical Female Sterilization with Quinacrine A Timeline

**1920s to 1940s:** Quinacrine is first synthesized. It is widely used as an anti-malarial drug by approximately two million soldiers in the Pacific arena in WWII.

**1960s to 1970s:** Quinacrine is developed as a method of non-surgical sterilization by Jamie Zipper, M.D. Quinacrine is dissolved in a solution, and this “slurry” is inserted into the uterus. Between 1970-1979, some 1,100 women are treated mostly, though not exclusively, by Dr. Zipper. The use of intrauterine slurries is later abandoned, however, because the failure rate is high and several types of medical complications are associated with the rapid absorption of quinacrine. Although no deaths are reported in the literature, three deaths (of women who died on the operating table while undergoing quinacrine slurry sterilizations) are reported to the U.S. Food and Drug Administration (FDA).

**1977:** Family Health International (FHI) under the direction of Elton Kessel, M.D., develops solid pellets of quinacrine for transcervical insertion into the uterus. The use of quinacrine pellets does not lead to any reports of the acute toxic reaction seen with the slurry formulation.

**Early to mid-1980s:** FHI's Investigational New Drug (IND) application is approved by FDA in 1981, and FHI conducts pre-hysterectomy studies of quinacrine. FHI does not subsequently proceed with its application for FDA approval to market the drug, however, citing concerns about the drug's mutagenicity (ability to cause mutations), long-term safety, and possible carcinogenicity (ability to cause cancer).

**Late 1980s:** Dr. Kessel and Stephen Mumford, Dr.P.H., both formerly of FHI, become the sole distributors of quinacrine pellets. Research continues in a number of countries involving a variety of dose regimens, adjuvant therapies (such as Depo-Provera), and treatment protocols, often in populations too small to draw any conclusions.

A cluster of cancers is detected during long-term follow-up of 572 women who had been sterilized with quinacrine in Chile. As a result, FHI carries out a larger retrospective cohort study. The study confirms the occurrence of a cancer cluster, but again no other cases of uterine sarcoma are found, and there is no significant increase in the number of gynecologic cancers. An additional four years of follow-up data are gathered. No other cases of uterine sarcoma are observed, and there is no significant increase in the occurrence of gynecologic cancers.

**1993:** The *Lancet* publishes a field study by Hieu et al. of QS in 31,781 Vietnamese women. No increased incidence of cancer or other serious complications is detected, but the report prompts debate about the safety and effectiveness of the drug.

After receiving a letter from the World Health Organization (WHO) stating that “WHO and FDA officials would be surprised if quinacrine does not turn out to be carcinogenic,” the Government of Vietnam stops its QS program.

**1994:** QS is discussed as part of an expert meeting on new methods for female sterilization at WHO. WHO releases a statement saying that further clinical research on quinacrine is not justified until various toxicological issues have been resolved. WHO calls for completion of four pre-clinical toxicology studies.

Family Health International, with funding from the U.S. Agency for International Development (USAID), agrees to carry out the four toxicology studies recommended by WHO.

The Government of Indonesia, in response to pressure from WHO, stops its QS program.

Internationally, women's health advocates show an increasing concern over the use of quinacrine.

**1995:** FHI reports that three of the four toxicology studies show quinacrine to be mutagenic. Although mutagenicity is indicative of possible carcinogenicity, not every mutagenic compound is carcinogenic. FDA examines the results of FHI's toxicology studies and concludes that the drug's mutagenicity does not necessarily preclude FDA approval for human use.

**June 1998:** As a result of controversy generated by an article which appeared in the *Wall Street Journal* which reports on instances in which QS was performed without women's knowledge or against their will, Sipharm Sisseln AG, the Swiss manufacturer of quinacrine pellets, says it will no longer make them. In response to Sipharm's decision, Dr. Kessel and Dr. Mumford say they will seek another supplier and will continue their campaign to distribute quinacrine.

The U.S. Pharmacopeia Convention's *Drug Information*, a reference work listing drugs available worldwide, includes female sterilization as an accepted use of quinacrine.

**July 1998:** QS is banned in Chile, where the controversial method was first pioneered.

**August 1998:** Under pressure from women's-rights activists in India, the Government of India bans QS. India had been the largest market for this type of sterilization.

**October 1998:** FDA issues a “warning letter” to Dr. Kessel and Dr. Mumford to “immediately halt” all distribution of quinacrine pellets. Citing concern about the safety risks associated with the use of quinacrine for sterilization, FDA orders them to destroy their existing supply of quinacrine pellets under FDA supervision.

Dr. Mumford responds in a letter to FDA's warning letter. He claims “opponents of the method are not being required to produce any scientific evidence to support their position.”

**2000:** Long-term follow-up research sponsored by FHI finds that quinacrine appears to be reasonably effective for a protocol using two insertions in women 35 and older. Interim safety analysis finds that incidence of ectopic pregnancies does not appear to be increased, but that data on other adverse events are inconclusive.

**2001:** The University of Buffalo grants Institutional Review Board approval for a Phase I study, to be conducted by Jack Lippes, M.D. The study is to evaluate safety and efficacy of QS and to enroll up to 10 married women between ages of 25 and 45 years. This study also receives FDA approval.

specific populations both in developing countries and in the United States has also been a source of great concern.

Not surprisingly, the paradoxical potential of reproductive technologies promising increased *freedom* for, and the possibility of increased *control* of, women has informed both sides of the debate over non-surgical sterilization. Proponents of the method have tended to focus on its potential for controlling population and giving women access to cheaper and potentially safer forms of contraception. Opponents have focused on the concerns raised by questions about quality of care, informed choice, safety, and efficacy of terminal methods when introduced into resource-poor settings where women's reproductive rights and choices generally are limited.

### **C. Background on April 2001 Meeting**

In an effort to move the debate forward, approximately 55 participants, representing a broad cross-section of the medical, public health, and women's rights communities from both developed and developing countries, met over two days in April 2001 to discuss and assess the past, present and future of QS as a method itself and as a reflection of parallel issues in the larger field of contraceptive research, development, and introduction. The April 22-23, 2001 meeting, "The Quinacrine Debate and Beyond: Assessing the Future of Non-Surgical Female Sterilization," was co-sponsored by the Center for Health and Gender Equity, National Black Women's Health Project, National Women's Health Network, Planned Parenthood Federation of America, and the Reproductive Health Technologies Project.<sup>1</sup> Representatives from the sponsoring organizations shaped the meeting's contents, identified presenters and participants, and agreed

to produce any written materials associated with the meeting. The Moriah Fund, Summit Foundation, and Ford Foundation generously contributed funding for the meeting.

The meeting was structured as a balanced, respectful dialogue that, while not intended to reach consensus or to resolve long-standing questions or disputes about the method, nevertheless provided a forum to examine the complex dilemma of QS in terms of science and use across a continuum marked by differences in opinion, approach, and emphasis. The agenda was organized as a series of panels that addressed five key questions shown in the accompanying box [see Box B]. Each panel featured main presenters and a moderator, followed by commentary and discussion with the full meeting's participants.

Presenters from the research, service delivery, regulatory, and advocacy communities nationally and internationally were selected based on their familiarity and experience with debates around QS and related debates in the reproductive health field. Presenters and discussants also were chosen based on their expertise in developing and introducing other reproductive health technologies that offer some thought-provoking comparisons with quinacrine. Background materials were prepared and circulated in advance to aid participants and presenters in considering the issues and in focusing their commentary during the meeting.

### **D. Overview of This Report**

The next chapter of this report presents the essence of what was discussed at the meeting. Specifically, it focuses on two competing yet related paradigms of technology development that fuel tensions regarding research, develop-

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<sup>1</sup>The views expressed in this document do not necessarily reflect the positions of the organizations that convened or provided funding for the meeting.

ment, introduction, and delivery of reproductive technologies in diverse settings: *the technology-as-neutral paradigm and the technology-as-embedded-in-context paradigm*. The chapter also discusses four core themes that cut across these two paradigms. The final chapter of this report presents concluding observations and recommendations. A meeting agenda and list of meeting participants appear in Appendix A and B, respectively. Appendix C presents a letter from a meeting participant.

## Box B. Five Key Questions Considered in Panel Discussions

- 1. Is there a need for non-surgical methods of sterilization?** This panel reviewed the rationale for non-surgical methods largely by positioning the need for non-surgical methods within the broader context of the unmet reproductive health needs of women throughout the world.
- 2. In a world of scarce resources, how do we set and balance priorities?** Panelists presented differing viewpoints on how priorities are set, depending on economic, and political considerations, user needs, and available resources.
- 3. What are the appropriate safety and risk standards for reproductive health technologies, and are they universal?** This panel highlighted how lessons learned from other reproductive health technologies, such as medical abortifacients and microbicides, could inform a larger discussion of appropriate safety and risk standards, especially when compared with quinacrine sterilization. The importance of including user perspectives and needs also was stressed.
- 4. To what extent should the context into which new methods will be introduced limit or constrain new technologies?** The discussion centered on the critical importance of context, including, among other things, the political and social context, service delivery capacity, and women's autonomy within families and communities in determining the "safety" and "efficacy" of any particular method outside the laboratory.
- 5. Can a "tainted" method be reclaimed?** If so, how and under what circumstances? Discussants shared various perspectives, from other countries and other disciplines, to highlight the difficulties inherent in attempting to reclaim a method tainted by a history of coercion and abuse. Accountability and redress of violations was discussed.

## Competing Paradigms of Technology Development and Cross-Cutting Themes

Two statements crystallize the differences that have permeated discussions here about major themes, appropriate models, decision-making and scientific resources. First is the view that ideology is embedded in every technology. The second is that technology is neutral.

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At the April 2001 meeting “The Quinacrine Debate and Beyond: Assessing the Future of Non-Surgical Female Sterilization,” two competing paradigms of technology development frequently emerged in discussions: technology-as-neutral and technology-as-embedded-in-context. Within these competing paradigms, there arose four cross-cutting themes related to quinacrine sterilization and other reproductive health technologies. These two paradigms and four cross-cutting themes are discussed below.

### A. Competing Paradigms of Technology Development

Two competing yet related paradigms fuel tensions regarding research, development, introduction, and delivery of reproductive technologies in diverse settings. The first—*the technology-as-neutral paradigm*—assumes that technology is neutral and emphasizes the benefits of reproductive technologies through expanding the array of choices for people, particularly for women. The second—*the technology-as-embedded-in-context paradigm*—views technology as embedded in historical, sociocultural, and political structures and histories that influence research, development, introduction, and delivery of reproductive technologies. Ultimately, the two paradigms are closely connected, making simplistic distinctions between them impossible. Despite the overriding concern they share with improving women's health, supporters of technology development and individuals concerned about the context in which technology is used have often found themselves at odds.

**Technology-as-Neutral Paradigm.** The technology-as-neutral position places the greatest emphasis on the research and development phase of reproductive technology development, with a focus on scientific measures of safety and efficacy, and on the potential of an increasing array of technologies to expand the choices available to end-users.

“Technology in and of itself is not evil, moral, or immoral,” said Jack Lippes, Professor of Obstetrics and Gynecology at the State University of New York at Buffalo. “It is neutral. It is only immoral based on the application and uses to which we put it.” In the case of QS, for example, supporters argue that delaying widespread introduction of the method denies millions of women the option of non-surgical sterilization and the opportunity to reduce unintended pregnancies.<sup>2</sup> “We shouldn’t condemn the technology,” Lippes continued. “For some, this is the only option available.”

The technology-as-neutral stance is based on the contention that the benefits of technologies that have emerged from the clinical testing process outweigh the risks associated with unintended pregnancy, with labor and delivery in low-resource settings, and with surgical sterilization. The methods themselves are thought to be able to provide the solution to unwanted fertility, and thus pave the way for the wholesale introduction of new contraceptive technologies on a large scale.<sup>3</sup> Indeed, development and introduction of new reproductive technologies is one means of expanding options and addressing unmet needs. Examples include the oral contraceptive, the first reversible modern method, initially introduced in the 1960s. Shortly thereafter came the intrauterine

device (IUD), followed later by injectables (e.g., Depo-Provera) and implants (e.g., Norplant). These technologies have enabled millions of women and couples to realize their reproductive goals by avoiding unwanted pregnancies and, potentially, unsafe abortions or the morbidity and mortality incident to childbirth.

**Technology-as-Embedded-in-Context Paradigm.** Three decades of experience have shown that the introduction of new reproductive technologies, while important, does not increase choices per se unless specific constraints and other contextual factors are considered fully in both the introduction and delivery of such methods.<sup>4</sup> “Safe reproductive technology is not detrimental,” Diana Romero, at the Center for Population and Family Health and Columbia University, surmised. “What is detrimental is how it is provided or withheld and in what context.” The technology-as-embedded-in-context paradigm assumes a close relationship between the technology and the user, which requires accounting for the ways in which specific reproductive technologies may be used for political ends, and in which the interplay of gender inequities, provider bias, and poor quality of care, among other things, may limit women’s choices individually and collectively.

Individuals concerned about how technologies can be used or abused argued for approaches to technology research, development, introduction, and delivery that rely on careful assessments of the capacity of health services to deliver methods appropriately, and on in-depth consideration of user perspectives and needs within specific contexts. The introduction of the female condom in more than 70 countries offers some evidence

<sup>2</sup>A Freedman. Population bomb: Two Americans export chemical sterilization to the Third World. *The Wall Street Journal*. June 18, 1998, page A-1

<sup>3</sup>R.N. Pine and A.E. Pollack. Putting an ear to the ground: Where now with quinacrine? *International Journal of Gynecology and Obstetrics* 69:55-65, 2000.

<sup>4</sup>R. Simmons, P. Hall, J. Diaz, M. Diaz, P. Fajans, and J. Satia. The strategic approach to contraceptive introduction. *Studies in Family Planning* 28(2):79-94, June 1997.

Until 1991, the World Health Organization and Population Council had followed the latter's "put-it-in-a system" approach. There was no discussion about the method's appropriateness in the system... then, they looked at the experience of Norplant and Cyclofem and... what they learned was that adding a new method did not necessarily broaden choice unless service delivery system issues could be addressed. This gave rise to the paradigm of trying to link technology in terms of users' needs and service delivery capabilities.

Peter Hall  
Reproductive  
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that a multi-pronged approach is challenging and sometimes costly, but ultimately doable. [See Box C for more information.] Methodologies used by the World Health Organization (WHO) in several low-resource settings employing participatory assessments for contraceptive introduction have also shown that such approaches build greater credibility and sustainability for emerging technologies.<sup>5</sup>

These methodologies were developed, at least in part, on the failed introduction experience documented in numerous studies. The most influential of these were two service-delivery studies in Indonesia, one a Norplant study supported by the Population Council, the second a study of Cyclofem supported by WHO. The Norplant study, conducted during the transition from field studies to large-scale expansion within the national program, revealed important concerns about quality of care in the delivery of this method. Findings revealed, for example, that heavy promotion of Norplant by the government program undercut women's ability to make informed choice from among a range of methods, that little attention had been paid to counseling women on potential side effects, and that little or no effort had been made to ensure that women could have the implants removed should they desire to do so. Although some of these problems were later remedied, early inter-

vention would have played a significant role in identifying and ameliorating such major weaknesses.<sup>6</sup>

The provision of Cyclofem through the Indonesian family planning program focused on quality of care and quality in management of the delivery system. The results showed that, despite some broadening of women's choices, weaknesses in service delivery regarding differentiation between one, two, and three monthly injectables, compounded by poor record-keeping and counseling, played a major role in discrediting this method.<sup>7</sup>

The introduction of the IUD further underscores the problems that can arise when the social context and capacity of the health care system are ignored. In India, IUDs were introduced into a program plagued by lack of resources, poorly trained staff, poor sanitation, and with a focus on targets for the delivery of highly effective methods. Many women were "persuaded" to adopt IUDs without being provided alternatives, IUDs were delivered in the absence of appropriate levels of technical competence for sterile insertion, and those seeking removal of IUDs were discouraged or denied care. As a result, the initial favorable response to the IUD gave way to discouragement and discrediting of a method that had potential for more widespread acceptance.

## B. Core Themes That Cut Across the Competing Paradigms

Four core themes emerged at the meeting that cut across the competing paradigms of technology development. As the meeting progressed, the articulation of concerns within these thematic spheres clarified areas of agreement and divergence among participants, and established consensus on at least one objective endorsed by

<sup>5</sup>Simmons et al., op. cit.

<sup>6</sup>Simmons et al., op. cit.

<sup>7</sup>Simmons et al., op. cit.

all participants: *the promotion and protection of reproductive health and rights, while furthering advocacy for self-determination for women and men worldwide.*

## **Theme #1: The Importance of Considering Reproductive Health Decisions in a Sociocultural Context**

**Understanding the principles of a reproductive health- and rights-based framework.** A majority of meeting participants emphasized the importance of embedding women's overall reproductive health and well-being within a reproductive rights approach that acknowledges the complex interaction between the introduction and sustained delivery of reproductive technologies, and the social and institutional contexts that facilitate or hinder the success of efforts to expand contraceptive choices. Pivotal to this approach is an ethical imperative to involve women as respected, autonomous people who actively participate in the development of their own health agendas individually and collectively, particularly in the development, introduction, and delivery of new methods for which they are the intended users.

Throughout the meeting, participants returned again and again to the most critical principles of this rights-based approach: the promotion of informed choice and informed consent; support for the principle of voluntarism; the recognition of and response by health services to the contextual realities of women's lives; and the availability of both good counseling and of choices among methods that are as real in practice as they are in theory.

Of great concern to many participants was the degree to which full support for these principles is not evident in many settings throughout the world. On the one hand, economic and social conditions have restricted the availability of, and

### **Box C. The Introduction of the Female Condom: Lessons Learned**

The female condom has been introduced in over 70 countries in Africa, Asia, and Latin America over the past five years, and in more than 30 countries in the last year alone. Due in large part to a participatory, user-based introduction process, the female condom has gained considerable currency and has experienced relative success. Some overall features of its participatory, inclusive framework include the following:

- Gaining political commitment;
- Building and encouraging community advocacy and partnerships, including non-governmental organizations and community based organizations;
- Understanding the complexities of method introduction; integration into existing systems; and the commitment of one or more individuals to making it happen;
- Respecting women and providing opportunities for control and empowerment; and
- Implementing continuous feedback mechanisms to ensure that the method continues to meet their reproductive health needs.

At the program level, a variety of mechanisms and processes were implemented to ensure better success. First, a specific target audience was identified and cultivated. Next, specific training and follow-up helped to ensure that the method would meet the needs of a share of the population. Finally, outreach processes were instituted with specific locations to allow women to get answers to questions or raise concerns about the method.

Implementing a constituency-based campaign for a technology that seeks to ensure accessibility and use is often more costly than the product development itself. This situation raises issues about the financial sustainability of products. Programs must determine whether or not to proceed with the development of this or any product if no budget exists to support infrastructural concerns related to the product's use and availability. If the organizational or group will to invest in the development and marketing of the product is unclear, asking questions about where the money will come from are critical to its successful introduction.

The continued success of any contraceptive method requires ongoing surveillance and monitoring to deepen understanding and correct any mistakes made in product development and delivery. More is needed to ensure the success of these efforts, not the least of which is a profound understanding of the complexities involved in introducing a new method. This includes learning from past mistakes, soliciting and then listening to women's and men's experiences with contraceptives in the real world. From a financial standpoint, donor commitment to prevention is essential, as well as conducting advocacy at all levels and strategic planning, too.

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// This is not a debate about the need for basic research on new contraceptive methods. Rather, what are the contexts into which these methods would be introduced and what does this really mean for women?

//  
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accessibility to, reproductive technology choices that women want and need. There has been, and continues to be, tremendous unmet need for greater access to an expanded array of reproductive health technologies among much of the world's female population, and reproductive

health and rights objectives cannot be realized without such access. As Judy Norsigian of the Boston Women's Health Book Collective emphasized, however, need or more specifically, the *perception* of need, can be created, resulting in the communication of conflicting messages, the promotion of inappropriate methods, and a variety of unforeseen, and often negative outcomes. Thus, the following questions offer an informative starting point: (1) How are needs defined? (2) Who is defining them and in what context? (3) Over what period of time? A rights-based approach would incorporate careful answers to these and other questions by respecting and including women's voices and needs when individual, programmatic, and policy decisions are made on their behalf, but often not necessarily with their consent.

On the other hand, social, political, and economic disempowerment has translated generally into the lack of supportive conditions in which free, informed choices about available technologies can be made and within which good quality reproductive health care services are accessible. History, for example, shows that poor women and women of color are more likely than others to be targeted by governments with efforts to control fertility, while

they also are less likely to have access to information or quality health care services. Such difficulties extend far beyond the accessibility of services and resources. For example, "poor, often less educated, women ... don't feel entitled to reproductive health and rights," noted Monica Jasis, Centro Mujeres in La Paz, Mexico. "We are working on entitlement, to educate women about their right to complete information, time to think, and full citizenship."

Equal attention must be paid to the concerns of the individual woman herself. Of particular import are such issues as individual medical profiles, race, culture, ethnicity, gender, class, sexual orientation, and religion as central influences that affect women's decision-making and social attitudes about contraception. Other complex, interrelated issues must be considered within the overall societal context, individual women's issues, and the general delivery of health care services. These include the following:

- Women's own complex attitudes about contraception and pregnancy prevention;
- Social norms and cultural ideals and attitudes about motherhood and being female;
- The effect of gender power inequities in negotiating sex and reproduction, including the ramifications for women in violent relationships of using contraception or seeking protection from infection against their partners' will;
- Lack of social supports, such as friends, family, and community programs and activities; and
- Coercion by service providers.

The capacity of services to deliver methods in a manner consistent with the principles of this rights-based approach involves a host of factors,

not the least of which is the administration of the method itself. The critical need for infrastructure can be measured by whether and how much the proposed method conforms to the individual country's availability, accessibility, and credibility of service delivery; adequate, ongoing service provision; and respectful, ethical treatment of female clients. Economic conditions, cultural norms, political ideologies, and prevailing religions play a role in the level of human and financial resources available to existing or potential programs, which in turn has a direct bearing on quality and standards of care for women. For that reason, Tom Merrick, of the World Bank in Washington, D.C., argued that it is important to have "informed effective stakeholders who understand the lines of argument. We cannot leave it to the experts. We must be proactive, even if advocacy may not be popular, because people, especially the poor, need to know their rights and entitlements."

Fundamental efforts to rebuild the foundation of health care systems on the principles of reproductive health and rights lag behind the research and development of new products. According to some participants, therefore, the rush to production and introduction of new contraceptive products often runs counter to the principles upon which participatory approaches are founded. A critical assessment of the situation, for example, may call for postponing the introduction of a new technology—no matter how great its potential—until good faith efforts are underway to address these principles.

No perfect reproductive health technology—completely accessible to everyone, completely free of any side effects—has ever been or is likely ever to be created. Yet even a perfect product delivered in a system incapable of assuring basic rights of choice and information can undermine those

broader goals. As has been shown with Norplant and the IUD, when problems arise that are primarily rooted in social constraints and the health care system, the product, rather than the system, often becomes the focus of repudiation, limiting its future usefulness and availability to women everywhere.

**Applying the principles of a rights-based approach to QS.** The multifaceted, complex milieu—where society, culture, and the individual converge and often clash—brings into bold relief the paradox of the potential demand for non-reversible methods of contraception and of their potential for misuse. Many factors contribute to women's need for non-surgical sterilization methods. Although millions of women of reproductive age worldwide are at or near their desired completed family size, some may yet decide to use reversible methods while others may opt to undergo non-reversible sterilization. Of these, an unknown number may in fact prefer non-surgical sterilization to surgical, were an approved method available. Given accurate current information about a method like quinacrine, women might opt to either try it or forgo the risks associated with its yet unstudied side effects.

The majority of these women live in societies in transition, where many are caught between social and familial pressures to have numerous children, and government and political pressure to limit births. They may be unable to exercise their own choices, or compelled to do so clandestinely. They may want access to reversible contraception to limit births, but find themselves pressured into undergoing non-reversible sterilization under government or programmatic policies. Or they may have received incorrect, incomplete, or inadequate information while making contraceptive decisions. As a result, women may often use a

method of contraception, such as non-surgical sterilization, not as an exercise in choice, but rather as an endpoint in contraceptive use that has been circumscribed by intense poverty, gender inequity, and poor health.

Given this backdrop, the use of QS in diverse settings to date has elicited divergent views. Some participants advocated strongly for expanded access to QS as a necessary, safe method of non-surgical sterilization for women who want to end childbearing. “Quinacrine is another health care option for a woman who has all the children she wants. Clearly, it offers the knowledge that she is safe from unintended pregnancy and provides the tools to make plans for her life and family,” asserted Mildred Hanson, a private practice physician in Edina, Minnesota. Supporters of QS contended that quinacrine can help achieve the primary goal of improving the lives and protecting the health of women in developing countries—more than 500,000 of whom die from pregnancy-related complications each year.<sup>8</sup>

Supporters of QS argue that QS was developed in response to a worldwide, latent demand that is impossible to meet through surgical sterilization alone and that over 100,000 women in more than 20 countries have undergone QS without serious injury or death. This method of sterilization, they contend, may provide the only available option to many of the world's poor women and can be performed by trained paramedics in basic clinical settings for less than one U.S. dollar—an inexpensive option compared with surgical sterilization.<sup>9</sup> Despite any past transgressions, supporters of QS argued that the method still appeals to a vast majority of women as an option that could increase their ability to control their fertility and

attend to the needs of an already established family, free from the fear of unwanted future pregnancy. To deny that option to women, according to some panelists, would limit severely their overall reproductive health options and limit their rights to choose.

Opponents of QS—a method principally introduced to poor, uneducated women within developing countries—argue that QS provides a textbook example of how a marriage of ideology and technology resulted in the introduction of a method into settings in which both the method and the environment were (and are) fraught with deep concerns about choice, consent, and safety.

Foremost among the concerns articulated by this group was the widespread use of QS in several countries despite the apparent lack of sufficient safety testing, standardized protocols, and lingering questions about the quality and legitimacy of existing data on the method. Drug product development in the United States, for example, follows an FDA model that begins with initial toxicology studies among animals. These are followed by a three-phased clinical trial process among human subjects, approval by the FDA for general use, and post-marketing surveillance after introduction. Scientific and ethical reviews are repeated consistently throughout the process. While proponents of QS argue that prior FDA approval of quinacrine for other indications exempted it from portions of this research protocol, others hold that omissions in QS research do not conform to the standardized design for and accepted stages of clinical research. Additionally, strong concerns were raised about the lack of evidence of informed consent of patients. Equally strong concerns were expressed about the

<sup>8</sup>Hill, Kenneth, Carla AbouZahr, and Tessa Wardlaw. World Health Organization (WHO). “Estimates of maternal mortality for 1995,” *Bulletin of the World Health Organization*, 2001, 79(3), p 182.

<sup>9</sup>Quinacrine sterilization: Introduction and overview. Available at [www.quinacrine.com](http://www.quinacrine.com); accessed Apr. 9, 2002.

apparent inability of investigators to ensure adequate follow-up of women receiving QS in countries where health services are not widely accessible, and women often have to put aside work and travel long distances for care.

Critics of the handling of QS to date further expressed concern that the method's potential benefits may be outweighed by the potential for abuse in family planning programs where demographic goals or poor service delivery override individual needs and interests. Moreover, they argued that much greater consideration must be given to the introduction of provider-controlled contraceptive technologies into existing service delivery systems. For example, the procedure requires at least two, and often three, insertions to be fully effective. Given these requirements, it is often difficult to ensure adequate follow-up in low resource settings where women may not have the time or the financial resources to return for a second, never mind a third, visit to a distant clinic. The intimate nature of the method's administration, especially the need for the provider's presence, emphasizes the importance of the client-provider relationship and adequate follow-up.

The client-provider relationship cannot be overlooked, as it often is the first and only point of contact for prospective end-users. However, as Kate Bourne, at Pathfinder International in Watertown, Massachusetts, noted, "the real work has been put on frontline providers with no emphasis on how to do that. Although it is important to integrate research and women's perspectives, we also need to include frontline providers as they will be the weakest, though most crucial, link." She continued:

*When a method is approved, the providers will make the final decisions, will decide how to use it, and whether to inform women or not. We are a little careless in speaking about the*

*unethical behavior or abuse of health care providers as though they were a monolithic group, when they have far more in common with the women served than researchers or people in this room. To not involve them is part of the problem and then to ask them to implement the methods perfectly is unrealistic. It's not about whether it is a good idea to develop an easy method. Who wouldn't want an easy method? Make sure that the person who has patient or client contact is able to follow through with enough information.*

Thus, although the potential for non-surgical sterilization may appear to be advantageous to women seeking to end childbearing, questions about the quality of service delivery also are in play and must be addressed openly and transparently. What procedures for informed consent were used in studies carried out in India and Vietnam? How well did women understand the need to return for several insertions of quinacrine pellets, and given travel and economic restrictions, how many actually did so? What types of side effects were experienced? Did these adversely affect women's daily lives and work? Were they addressed, and if so, how and by whom? Why was consumer input in the introduction of QS not sought in each setting?

Undoubtedly, QS should not be made to bear the burden of ameliorating all the social ills that continue to plague women or incur the blame for not having done so already. Nevertheless there is currently a broad consensus among advocates and scientists that, at the very least, additional research is an essential prerequisite to determining whether quinacrine can be recommended as a safe and effective method of non-surgical sterilization. In addition, there seems to be growing agreement with the need for more methodical approaches to assess the capacity of health systems to deliver such a method in a manner consistent with health and rights objectives.

There was widespread disagreement among participants, however, as to whether, even in the face of adequate safety and efficacy data, scarce resources should be devoted to further research and development of QS, especially in light of the growing demands for improving existing services. Furthermore, even if need were established for

delivery are such needs identified? Is there sufficient evidence of a need for non-surgical sterilization methods among women to warrant further investments in these technologies? If so, how is that balanced against other needs, and against what criteria? Whose needs get met in an era of scarce resources? Who decides?

**Until I was invited to speak, I had never heard of quinacrine. As a woman living with HIV in Africa, the women I work with need dual purpose contraception that includes HIV/AIDS prevention so they can have healthy babies, safe and legal abortion, and good, free postnatal care. We have 2,500 clients, and 70% are women. About 60% are under 30 and they want to have babies without putting their partners and themselves at risk. The concept of sterilization in the face of high husband mortality is a very low priority.**

Through a research project that worked with HIV-positive women in rural areas in Zimbabwe, women designed and conducted their own research and did advocacy training. Very, very few of their results and answers included sterilization as one of the priorities. Sterilization is something that is available to those in urban areas with private means. In the longer term, we need microbicides and we also need basic health priorities.

Put the money for quinacrine into microbicides.

**Lynde Francis**  
The Centre  
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non-surgical sterilization, should scarce resources for reproductive health technologies be allocated to the development of QS and take precedence over the widespread distribution of female condoms, more concerted efforts to integrate sexually transmitted infection and family planning services, or the development of microbicidal products? "Disease prevention, contraception, and women's overall health and well-being are the giant unmet needs," asserted Judy Norsigian, at Boston Women's Health Book Collective.

Different levels of need might result in the development of different objectives. If so, what would they be? How and at what stages in the continuum of research, development, introduction, and

In making such decisions, the rocky marriage between science and realities on the ground must ultimately be sustained, especially as the development and implementation of rights-based approaches continue. "Although we constantly have parallel discussions about the scientific and the contextual, in reality they are married," Jodi Jacobson, of the Center for Gender and Health Equity, noted. "We can ill afford to sell technology in words, language, and emotion without understanding our responsibility to both the technology and the profound context into which it potentially would be introduced. Microbicides offer one example of an iterative process." [See Box D for more details.]

The importance of understanding how reproductive health decisions are made and who makes them extends to financial and policymaking spheres. With the present dearth of resources and technologies, questions about how best to allocate existing resources take on added dimensions of importance. Organizations and policymakers have choices and set the priorities. Ideology plays a central role in determining, for example, whose voices are heard. Those who make critical policy decisions should consider hearing the voices of all key stakeholders in the process. Otherwise, decision-making remains an extremely privileged and exclusive enterprise. Allowing women's voices to be heard and incorporated can expand respectfully the set of choices and the technologies that could be made available. Decision makers who

proceed without the benefit of more voices will ultimately be limited in what they know about the technologies and how people make choices regarding new or existing technologies.

A number of participants strongly believed that the role, responsibility, and impact of U.S. reproductive health policy and practices vis-à-vis the international community, as well as at the individual country level, must also be examined critically and understood within the larger geopolitical context. Activists, advocates, and researchers need to be politically cognizant that an FDA-sanctioned method has pros and cons. Although FDA approval represents the “gold standard” in the United States and acts as an instantly credible imprimatur for use elsewhere, U.S. FDA regulatory guidelines may not be translated faithfully in diverse settings throughout the world. The imprimatur of “FDA-approved” may in fact create a license for widespread distribution before assessments have been carried out regarding specific needs and service delivery capacity in other settings. Similarly, word of an “FDA-approved clinical trial” may be misunderstood, or even misrepresented to equate with an “FDA-approved method.”

## **Theme #2: The Importance of Understanding the Ethical Dimensions of Contraceptive Research and Development**

Difficulties in coming to consensus over the ethical dimensions related to QS may or may not auger well for its future but nevertheless provide insight into concerns related to development and delivery of other methods that affect women in untold ways. An iterative, self-correcting, and transparent research and policy-making process that values community input from a variety of key stakeholders, from end-users to scientists to women's health advocates, is of utmost importance to the success-

### **Box D. Lessons Learned from the Ongoing Development and Introduction of Microbicides**

Microbicides are chemical entities that can prevent or reduce transmission of sexually transmitted infections when applied to the vagina or rectum. The similarities between microbicides and quinacrine are many. Both microbicides and quinacrine are reproductive health methods for use by women; both technologies compete for scarce resources for development and introduction; and both have had the majority of their clinical testing conducted in developing countries. Additionally, participants in clinical trials often have had limited or no access to education and health care, which has led to concerns about issues of informed consent. Much like quinacrine, the efficacy of nonoxynol-9 (a spermicide recently tested for use as a possible microbicide) had been assumed in the absence of clinical testing. Finally, both can be used during pregnancy and have been used in healthy women for prevention, which raises issues that pit effectiveness against the risks for healthy women.

The differences between microbicide development and quinacrine, however, are just as prolific and notable. First, whereas the potential for abuse has been linked with quinacrine, nonoxynol-9 has enjoyed a long history of use as a vaginal product. Moreover, QS is not the only alternative for contraception, whereas currently abstinence and the use of condoms are the only alternatives for HIV/sexually transmitted disease prevention. Finally, adherence issues would be a moot point for QS, provided it is administered correctly, whereas efficacy of a microbicide product is user-controlled.

Finally, unlike QS, the approaches taken to ensure efficacy, accessibility, and user satisfaction and adherence with microbicides have been more participatory, inclusive, and context- and user-friendly. Women's advocates have played a central role in the microbicide research arena, community consultation occurs at all stages of the research process, and the informed consent process is crucial.

Running clinical trials that yield reliable answers to questions about safety and efficacy of new methods, particularly as they compare to the safety and efficacy of existing methods, is complicated, and there are few clear-cut answers. Nevertheless, clinical testing is a necessary first step to generating information and to developing first generation products that can be improved upon in subsequent efforts.

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ful development of reproductive technologies. How and to what extent that has occurred, or is occurring, has been and continues to be fraught with confusion, resistance and an overall lack of rigor in ensuring that necessary and appropriate safeguards are met.

I am struck by domestic and international differences over key reproductive health issues. In the United States, we often confront anti-choice forces who misleadingly allege that abortion and even some forms of contraception are unsafe, when the alternatives they propose, such as restrictions on abortion or abstinence-only sexuality education, are clearly much more dangerous for women than legal abortion and wide access to contraception and comprehensive sexuality education. An example relates to mifepristone. Those seeking to block it always alleged how unsafe it was, when what they were really doing was trying to restrict women's options.

Another example is a ruling that we won in *Stenberg v. Carhart* that said government cannot ban so-called "partial-birth" abortion so long as the method used is the safest for that particular woman, even if the method as a whole isn't proven to be safer than existing alternatives. Regarding the safety issues, how might international language purporting to protect women from new and not fully proven technologies play out in the U.S. domestic context? Rigorous demands to prove that a new technology be safer than existing alternatives could be misused to restrict women's options and insert the government into the doctor-patient relationship.

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The meeting's discussions around ethical concerns were distilled into two overarching questions: (1) What are the components of ethical research that can be identified with regard to what has or hasn't been done on QS? (2) What should be done with the data collected through research protocols in which the necessary ethical components were not in place?

**Question #1: What are the components of ethical research that can be identified with regard to what has or hasn't been done on the issue of QS?** The components of ethical research are complicated by a number of factors, not the least of which is cost, and in impoverished areas, lack of data collection and technology. Under the best of conditions, research requires a leap of faith, as there is virtually no sure way to guarantee a product's complete safety and efficacy. Clinical trials are conducted in controlled settings where potential problems of safety and efficacy are expected to be monitored thoroughly and carefully.

However, safety and efficacy as a laboratory finding, while necessary, is by its very nature different, unpredictable and incomplete when translated into widescale introduction. Even so, argues Zeda Rosenberg of Family Health International, there is still the need for "some scientific data to make decisions, and even if it doesn't work, we can build on it before next-generation methods arrive. There will always be imperfect technologies, but with good scientific knowledge, we can work to perfect them and get new-generation technologies out there."

Over the past several decades, frameworks and accompanying documents have been instituted for the conduct of human experimentation and adapted for use in the research design and implementation process. These documents, which have been the basis for integrating more fully the concepts of equity, respect, and integrity into research, are meant to emphasize for researchers not only the importance of conducting ethical research but also the avoidance of engaging in unethical research practices. There exists a "pattern where researchers rely on unethical or bad methods and use new research to fix the problem," commented LaTonya Slack of the California Black Women's Health Project in Inglewood, California. "They use third world countries to provide fodder or data for clinical trials, which presents a larger, philosophical problem—depending on developing countries and then leaving them without improving the health care there."

Historically, efforts to establish ethical protocols and processes are rooted in three major codes developed since the end of World War II. Using the codes to "question the appropriateness of human experimentation," Judith Scully, Associate Professor at West Virginia University, offered a bioethical analytical model through which to critically view,

analyze and measure the extent to which reproductive health technologies, specifically QS, have adhered to a principled ethical standard.<sup>10</sup>

Developed in response to war crimes committed by Nazi scientists and physicians, the Nuremberg Code was the first internationally acceptable set of legal guidelines for research on human beings. Most importantly, it established the importance of informed consent as a prerequisite for subjects to participate in experimental research. Investigators were obligated to ensure that subjects were provided with full information needed to give informed consent for participation, and subjects also were able to give consent, i.e., that they were able to understand and process the information provided to them. The Code's most critical component, therefore, is the interplay by which the subject *gives consent* on the part of the subject and the researcher *obtains* full consent from the subject [p. 117, emphasis added].

Subsequent codes—the Helsinki Declaration in 1964 and its 1975 revision, and the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Guidelines) in 1982—sought to improve upon the notion of informed consent. The Helsinki Declaration added two critical “checks and balances” that set the stage for monitoring compliance to ethical principles [pp. 120-121]. First was the requirement that those researchers who failed to fulfill their ethical obligations be penalized by being denied publication of research results, and, second was the establishment of an independent ethics committee to advise, guide and comment upon research protocols. The Guidelines' most significant contributions were: (1) that subjects who suffered

injury as the result of participation in an experiment were entitled to financial compensation; and (2) that the document was the first attempt to internationalize scientific research.<sup>11</sup>

Within these ethical frameworks, numerous components necessary to the conduct of ethical research have been enumerated, yet attention remains focused largely on informed consent. Most researchers, advocates, policymakers, and scientists agree equally on the necessity of implementing full informed consent in clinical trial settings and the disappointing lack of rigorous application in the field. “Informed consent is too often viewed as a kind of paperwork you have to sign. Our view of the concept is completely different: it is the process of empowering users,” observed Monica Jasis. One reason for that concern is symbolic: if we cannot agree on how to protect participants adequately in a trial, then we have every reason to worry when the trial is over.

**QS: a bioethical analysis.** Scully articulated the ethical principles shared by all three codes: (1) beneficence (obligation to benefit others) and non-maleficence (obligation not to do harm), (2) autonomy (respect for persons), and (3) distributive justice (obligation to distribute benefit and harm fairly)—as they applied to QS.

Beneficence and non-maleficence, the first of the three commonly accepted principles, specifically highlights the ethical obligation to maximize benefits and minimize harm to human subjects involved in research. Benefits must outweigh risks, the research design be well thought out and sound, and the competence of the researchers ensure the welfare of the subjects [p. 127].

<sup>10</sup>J.A.M. Scully. Maternal mortality, population control, and the war in women's wombs: A bioethical analysis of quinacrine sterilizations. *Wisconsin International Law Journal* 19(2):104-151, Spring 2001.

<sup>11</sup>This explication of J.A.M. Scully's bioethical analysis of QS is culled from her presentation and her publication on the same topic. See previous note for a full citation.

**Even if it is argued that QS will reduce the numbers of pregnancies, and hence the number of maternal deaths, the prevention of pregnancy as a way to solve the problem of the high level of maternal deaths is to argue that never getting out on the road is the best way to prevent deaths from traffic accidents. It doesn't address the issue of making wanted pregnancies and delivery safer for women.**

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The argument against quinacrine, according to Scully, is that its chief proponents, Mumford and Kessel, did not consider it to be a new drug. Quinacrine had been administered orally as an anti-malarial drug during World War II with a well-established track record for efficacy and safety. They concluded that the same would be true of intrauterine application. This effectively freed

them from considering quinacrine as an experimental drug and allowed for widespread dissemination without attention to quality of care issues, follow-up studies, or monitoring for short- and long-term effects in women.

According to Scully, this was combined with the

ideological viewpoint that a decrease in the world's population would be of greatest benefit to the world. Simply put, their argument was that, because women in developing countries are at high risk for dying in childbirth, more sterilization would prolong life by reducing maternal mortality. They also connected population control in developing countries to the maintenance of peace

and security globally. Scully contended that the fatal flaw in their argument was its assumption that all women at risk for maternal death in developing countries do not want to be pregnant and want sterilization. An ethical perspective demands consideration of other effective ways to address the problem of maternal mortality. Because QS does not address maternal mortality caused by unhealthy lifestyles and lack of health care, Scully contends its use for this purpose calls into question whether the principle of beneficence can be fulfilled.

The second principle, distributive justice, refers to the need for treating each person fairly or according to moral rightness [p. 137]. This specifically includes the equitable distribution of the "burdens and benefits" of participation in research. No one group—racial, socio-economic, gender, or geographic—should be the recipient of those burdens and benefits, nor should those deemed "undesirable" or "disadvantaged" be subjected to risky research.

Clearly, almost all the women who underwent QS were low-income, rural women who lived in developing countries and had very little education. The justification for targeting poor women in developing countries for QS was that women's lives are at risk not just in pregnancy but generally as well [p. 139]. The rationale appeared to be that, given high mortality rates from diseases such as malaria, diarrhea or some form of cancer among women generally, any long-term consequences from quinacrine would be negated. Furthermore, the justification that higher risk of pregnancy justifies higher risk in contraceptive method promoted a social theory in which some are more important and worthy than others. If that equation were to be accepted, those with access to wealth and health care would be deemed worthy of the goodness of life and those without such access

**In a clinical situation, where there are women who are willing and well informed, offering a non-surgical option is less dangerous than surgery. Some women might prefer it and if they understand the failure rate is higher, it would be ethical. Other women have contraindications to surgery but I don't think that factor alone is sufficient to warrant including them in a clinical trial.**

David Sokal  
Family Health International  
Research Triangle Park  
North Carolina

would not be and thus are more available for risky research. Such a theoretical approach would ensure prolonged and exacerbated tensions related to race, religion, gender, and class in the debate around reproductive technologies.

Autonomy—respecting the individual's capacity for self-determination—is the third principle. Human subjects can be respected by (1) being informed about possible risks associated with the nature of the research; (2) receiving detailed information about all unknown risks associated with the process; (3) knowing about all known risks of injury; and (4) being informed about alternative treatments [p. 142]. Only after clients are informed in language they understand can they grant full consent to become involved in the experimental process. Without the principles of informed consent in place and strictly being observed, subjects cannot freely decide, according to their own values, whether or not to participate.

One mechanism for ensuring informed consent is to obligate the sponsors of large clinical trials to administer a simple questionnaire to a subset of women, asking questions related to their ability to leave the trial freely or be notified about the use of placebos. Current microbicide trials offer evidence of an informed consent process involving testing what women understand about information provided, and whether that understanding changes over the course of the trial itself. In the case of QS, anecdotal evidence from several settings indicates that women did not receive adequate information about the experimental nature of the method or the known risks involved, and that information about alternative methods of fertility regulation and sterilization was not made fully available. Reports of involuntary sterilizations with quinacrine were collected from Vietnam, Pakistan, and India between roughly 1989 and

1995 and some women have reported lack of informed consent, inadequate follow-up, and often misinformation that led to acceptance of a permanent method when it was presented as a temporary one. In some of these settings, neither providers nor clients were aware that quinacrine was still considered an experimental method.<sup>12</sup> As a result of these and other concerns, women's advocacy groups have questioned the ethical propriety of the use of quinacrine anywhere until well-regulated trials can be undertaken.

The bioethical analytical model represents one tool with which to evaluate methods like QS. The panel and discussion revealed additional components of political participation and transparency of

The recent debate over AZT and the conduct of other clinical trials has refocused attention to the need to develop better ethical codes and standards of care. A series of studies on the prevention of mother-to-infant HIV in developing countries was conducted in which HIV-positive pregnant women were randomized to receive drugs not proven to be effective, including placebo. In a study in the United States and France—conducted before any developing country study was underway—there was a 22% transmission rate in the placebo group, 8% in the other group. A total of 18 studies were subsequently proposed, two in the United States.

All the women in both U.S. studies received some antiretroviral drug. In 15 of the 16 proposed developing country studies, however, some women received either placebos or drugs not proven to be effective in preventing mother-to-infant transmission. This situation raised concerns about the ethics of conducting such studies in the developing world, where the drug might be unobtainable for many, if not all, groups of women. Another issue was whether a shorter regimen could be developed without sacrificing the efficacy of the regimen that proved effective in the United States and France.

Peter Lurie  
Public Citizen's Health Research Group  
Washington, D.C.

<sup>12</sup> AVSC International. Insights into reproductive health: Quinacrine for female sterilization. *AVSC International* 1-4, 1999.

process as also integral to ethical research, development, introduction, and delivery. For example, international agreements, such as the Programme of Action of the 1994 International Conference on Population and Development, stress the need for transparent processes in setting priorities, and in developing and introducing reproductive health technologies. Of paramount concern to all participants in the meeting was the need to breathe life into these principles through the

creation of specific processes and action steps that would be considered obligatory and would be systematically followed, rather than being acknowledged rhetorically and ignored in practice.

A final point, now addressed in the Helsinki Declaration, is related to whether an obligation exists on the part of the sponsoring group to provide an intervention if it is found to be effective. The tentative answer appears to be that it should be made reasonably available to the community. Thus, one component of ethical trials can be to make this understanding more forceful or binding by clarifying what post-trial availability will be.

## **Question #2: What should be done with the data collected on the research that was not conducted with all those ethical components in place?**

The report of the 30,000+ insertions among women in Vietnam led to an uproar in the international community, especially regarding concerns about the safety and efficacy of the QS method. Other considerations transcend safety issues; to many, quinacrine was considered an experiment in abuse on poor women, who were sterilized without their own knowledge or consent. Moreover, because women already had been administered QS as a method, how were they to be treated in the follow-up process? Without clear answers to these concerns, a consensus view emerged that discouraged further clinical trials until toxicological and retrospective studies had been completed.

For some participants, the conduct of appropriate clinical trials could resolve adequately the issues of safety and efficacy that have haunted QS. While past abuses cannot be erased, many contend they can be somewhat ameliorated by satisfying the nagging questions surrounding QS today and preventing future abuses. Others assert that the tainted past of QS negates any possibility of redeeming and reclaiming what they see as a flawed method. The more than 100,000 women who were sterilized by quinacrine have yet to be fully followed up and tested for long-term health problems, and the current procedures for administering QS appear not to have changed from those used in previous trials.

Family Health International (FHI) has been conducting retrospective studies and following women from clinical trials in Chile and Vietnam, with results expected in the fall of 2002. As part of its decision to carry quinacrine through the U.S.

**I am worried about the definition of ethical and unethical. Who decides the standard of this definition? What are the standards to judge what an adequately tested drug is? There is a question as to whether this group can set up the definition of what is adequate in all these categories.**

Jack Lippos  
State University of New York  
Buffalo, New York

**How do you monitor ethical conduct with a show of transparency in clinical trials? Those who want the method to be accepted widely and who continue to promote it as if it is an accepted method are doing a disservice. There would be a better chance [for acceptance] if it had gone through proper channels and processes including safety and efficacy testing in animals before testing in humans.**

Shree Mulay  
McGill Centre for Research  
and Teaching on Women  
Montreal, Quebec  
Canada

Food and Drug Administration (FDA) marketing approval process, FHI is conducting new animal toxicology studies and clinical studies to conform to FDA requirements. This is a crucial step toward seeking FDA's approval to market quinacrine as a drug in the United States and also serves as a conscientious attempt to fill the gaps in knowledge about the use of quinacrine as a method of non-surgical sterilization.

Why study quinacrine? First, according to FHI, is the need to answer the ethical and scientific questions about its side effects, safety, and efficacy. Second is the possibility that the method is worth pursuing. Regardless of the controversy surrounding it, FHI and others have argued, QS is the only non-surgical method that has been used for the past 20 years and the current data suggest it is a desirable option for some women. Some participants offered that quinacrine permits access to safe sterilization for a large population that would otherwise be denied sterilizations.

In agreement with the concept that it is worth pursuing, and after extensive debate, the Board of Planned Parenthood® Federation of America passed a resolution in 1999 stating that research studies on the safety and efficacy of QS should be methodologically rigorous, designed for FDA approval, and sensitive to the social and ethical issues surrounding the introduction of a new method of sterilization. The board also resolved "the participation of affiliates in clinical trials for QS may be considered if and only when the FDA signals that the toxicological studies permit the initiation of Phase II and/or Phase III clinical trials."

FHI is also researching the possibility of developing a new method of non-surgical sterilization using erythromycin. Work is being done on the formulation to take into account its stability,

**How do we deliver a technology ethically?** The history of contraceptive technology shows that the first approved class of a totally new technology always has more problems than anticipated, and sometimes paves the way for the introduction of a second generation of similar technology. It took a new product like Norplant, which is service delivery intensive, to make us look at quality of care and the readiness of systems to offer a particular new method. The provision of Norplant resulted in an overall improvement of quality of care. Every penny spent on Norplant development and introduction was well worth it because it forced programs to look at the influence of products on quality of care.

Regarding long-term safety issues for any new product, the fact is that we don't know how safe a product actually is without post-marketing surveillance studies; rare adverse events cannot be identified until thousands of people are using a product. We do our best to ensure from clinical trials that a new product is safe. In this regard, we are sometimes accused of following an FDA or medical model in product development that severely slows down progress and registration of new products that are desperately needed in developing countries while on the other hand that model provides a certain degree of protection.

Jeff Spieler  
U.S. Agency for International Development  
Washington, D.C.

sterility, and ease of use. It is hoped that a low-tech method will be developed, but it is too soon to know what the method of administration will be.

This research will not be conducted in isolation, but rather with awareness of the larger economic, political and legal context. As part of its efforts to maintain open communication with advocates, formative research is being planned across the spectrum to determine actual needs, methods and overriding issues. In addition, FHI has convened a committee of women's health advocates to help inform this research process.

### Theme #3: The Need to Recognize the Legacy of Social Inequities Within and Across Countries

QS, and the controversy that has swirled around it, can be added to the lengthy list of other reproductive technologies that have served historically as lightning rods for concerns related to social inequities. Numerous participants stressed the fact that poor, powerless women of color, from developing countries and the United States, have been targeted for generations for contraceptive delivery and sterilization abuse in order to meet

political ends, i.e., reducing the fertility of “problem populations.”

Therefore, QS has crystallized for many participants lingering concerns about methods introduced as improvements in women's reproductive health, but which have devolved into thinly disguised agendas to promote population control ideologies reminiscent of the eugenics movement in the United States during the 1930s. QS, they assert, has followed (and continues to follow) a trajectory fraught with both inertia and controversy, and has accentuated the need to constantly examine

critically the role of race, ethnicity and gender in the development and distribution of reproductive health methods.

Issues surrounding social inequities merited a separate, thoughtful focus that did not marginalize the subject, but that underscored the centrality of gender, race, and class to the intimate, inseparable, often explosive politics of reproductive technology. As Shelia Clark, at the Washington, D.C.-based National Black Women's Health Project observed, “discussions around race are always perceived as provocative and polarized. Rather than being incumbent upon certain people or panels to bring up the issue, it really should be institutionalized, incorporated and thought about in every discussion.”

Social inequities are at the center of much of the international contraceptive research industry. For example, developing countries, such as India, China, Chile, Mexico, and Brazil hosted at least one fifth of contraceptive research and development and safety evaluation projects between 1980 and 1983.<sup>13</sup> QS represents but one of a long line of methods that historically have had severe, if nearly invisible, consequences within those communities. Other examples of the unethical targeting of women of color for the purpose of advancing reproductive health objectives abound in several international and domestic contexts—particularly within communities of color and those of low income.<sup>14</sup>

The first example concentrates on two studies conducted in San Juan, Puerto Rico as part of the introduction of the pill, a then new hormonal drug called Enovid, in order to determine its safety and effectiveness. Puerto Rico was chosen as the site

... it is important to place QS within a historical, political, and social context. There's a history of exploiting poor and powerless women... and the main targets of QS are primarily women in developing countries who are poor and politically powerless. The introduction of QS has been divorced from these issues, but we cannot erase the history of reproductive health technology nor can we divorce it from the history of sterilization abuse, attempts to control or reduce the population in developing countries, and the reduction of immigration into the U.S. Should we promote QS as a method that is easy and cheap, given the history and political context in which it has arisen?

Judith Scully  
West Virginia University  
College of Law  
Morgantown, West Virginia

<sup>13</sup> B. Hartmann. *Reproductive Rights and Wrongs: The Global Politics of Population Control*. Revised edition. Boston: South End Press, 1995.

<sup>14</sup> Scully, op. cit.

for the clinical trials precisely because fears about its potentially explosive population growth were considered a public health problem.<sup>15</sup>

The first study, conducted in 1956, tested a group of approximately 132 women, followed by a second study a year later. Those tested were Puerto Rican women, who were among the most poverty-stricken in the territory, which resulted in a high dropout rate from the study—556 of 811 in one group alone.<sup>16</sup> Although one woman succumbed to congestive heart failure and another developed pulmonary tuberculosis, researchers nevertheless asserted the pill's safety. One study went so far as to dismiss such side effects as nausea, vomiting, and dizziness as psychosomatic. Despite these troubling signs, Searle received FDA approval to market Enovid in 1960. Two years later over 100 cases of thrombosis and embolism had been reported and 11 deaths were attributed to Enovid.

The use of reproductive technologies as tools for social engineering among poor women and women of color is not limited to developing countries or to history itself. Within two days of FDA approval of Norplant, for example, the *Philadelphia Inquirer* suggested that Norplant be used as an antidote to black poverty.<sup>17</sup> Regarding counseling and screening procedures, Native American health advocates alleged that the Indian Health Service in South Dakota neglected to implement informed consent procedures and gave Norplant to women medically at risk.<sup>18</sup> Further, legislators in 13 states introduced nearly two dozen bills to make the use of Norplant a condition for receiving welfare or using financial incentives to entice women to use it.<sup>19</sup>

As with these reproductive technologies, proponents of quina-craine have argued that its introduction was intended to provide a wider range of reproductive health options to all women, not just to specific, targeted communities. Nevertheless, the use of QS as a method has occurred within the context of these social inequities, and denial of this historical reality further reinforces the invisibility and vulnerability of poor women and women of color globally. "There is a difference between pattern and incident. In reality, with women of color, regardless of the technology, there has been a pattern of abuse and that difference needs to be acknowledged," asserted Shelia Clark.

"We think about those things as perceptions and emotion and yet they have happened historically and socially." Critical analysis of the method itself and the commitment to pursue a more in-depth understanding of the socio-political, historical

**I see polarization and hostility developing in this group. We are all interested in women's health domestically and globally. With so many knowledgeable people, we can make it a positive meeting and come to common ground to help resolve the global and domestic problems in women's health. We should avoid emotive terminology.**

Mildred Hanson  
Private Practice Physician  
Edina, Minnesota

**In terms of common ground, I agree, but I think if you preface this with things like, "Do not emote," you are automatically limiting the dialogue. Some issues raised are emotional and involve racial and class issues. We have to be brave enough to state our honest opinions even if it offends someone else and others must be clear to receive the message. I feel the need to state the case as it relates to women of color. All I can say is that that is a level of tension we need to grapple with and not fall apart at the seams about.**

Judith Scully  
West Virginia University  
College of Law  
Morgantown, West Virginia

<sup>15</sup> Hartmann, op. cit.

<sup>16</sup> Hartmann, op. cit.

<sup>17</sup> Issues and answers—Norplant: Reality Check. *Public Health Magazine* 4(1):Spring 1996. Available at <http://cpmcnet.columbia.edu/news/chronicle/archives>; accessed Jan. 22, 2002.

<sup>18</sup> Hartmann, Op. cit. See also Lara V. Marks. *Sexual Chemistry: A History of the Contraceptive Pill*. New Haven, CT: Yale University Press, 2001.

<sup>19</sup> Hartmann, Op. cit. See also Lara V. Marks. *Sexual Chemistry: A History of the Contraceptive Pill*. New Haven, CT: Yale University Press, 2001.

abuses that poor women of color have endured would have alerted QS adherents to its potential for abuse.

In response to these concerns, some participants stressed the importance of taking a broader view of methods chosen even by marginalized women. In fact, they pointed out, in the context of marginalization, access to birth control, including forms of non-surgical sterilization, may provide options for regulating fertility that were not previously present. The decisions about the best interests of women and their connection to the larger global sociopolitical arena played a major role in proponents' arguments for making QS an option. As Jack Lippes of the State University of New York in Buffalo further explained:

*The goal of what is in the best interest of women in terms of health and provision of services and the goal of world peace are not mutually exclusive. Racism exists, abuse of women exists in many forms and sins must be gotten rid of to make human progress. However, when it comes to clinical trials, does denying a well-informed woman the choice of QS get rid of racism? Of abuse? Does stopping that woman promote informed choice? ... we believe in a contraceptive cafeteria that can provide every birth control method and where each one is described, not just listed.*

Scrupulously attending to and respecting the realities and contexts in which women make such decisions is the central challenge of reproductive technology introduction and delivery.

#### **Theme #4: The Need to Establish Accountability in Reproductive Health Research and Policy**

The controversy surrounding QS has stressed the need to develop more stringent measures to hold accountable researchers, policymakers, practitio-

ners and other key stakeholders for transgressions related not only to QS specifically, but to other existing reproductive health technologies generally. Ensuring accountability regarding potential product development also merited similar attention. Discussion centered on the type and kinds of formal structures and other mechanisms of accountability that should be considered in monitoring current and future products and censuring those involved in questionable practices in the past, such as QS.

At this juncture, no formal legal mechanisms for accountability exist regarding reproductive technologies. The three codes mentioned earlier regarding the oversight of human experimentation, while representative of advances in the arena of bioethics, are problematic for one major reason. All are predicated on moral, ethical values and standards and as such offer no authoritative legal mandates for the global medical community. Peter Lurie of the Washington, D.C.-based Public Citizen's Health Research Group put it another way: "the Declaration of Helsinki is toothless; there are no regulatory conditions attached to it. It is focused on physicians' concerns rather than on clients' needs. The real fight will take place on the ground where people are facing potential exploitation daily." While these codes can and often do influence the conduct of researchers, they are not intended to be, nor are they enforced as, legally binding statutes. Further, not until national legislatures voluntarily enact them as laws are these codes considered enforceable. Most importantly, each country can determine its own standards; this unevenness in implementation leaves human subjects vulnerable to unethical research practices with little or no protection.

Despite this lack of enforceability, the codes offer an ethical framework and attest to the convergence of international agreement on medical

experimentation. Discussion at the meeting, therefore, focused primarily on underscoring the need for developing formal mechanisms of accountability that would and could be put to practical use. Participants put forward several criteria as points of discussion, including:

- The need for mechanisms based on international principles that can be applied at country- and community-specific levels;
- The notion that all key stake holders—researchers, policymakers, practitioners and other key stakeholders—are involved at every stage of contraceptive introduction and delivery; and
- An examination into what body, if any, could regulate and administer sanctions. Currently no international body is formally vested with the authority to investigate allegations of abuse according to any specific criteria, or to halt the inappropriate use of reproductive health technologies.

Perhaps the most persistent call to action regarding accountability was the need for transparency in decision making in policy, research and clinical practice. The ability to hold researchers accountable rests largely on this transparency. “Another strategy,” according to Peter Lurie, “is to show up and testify when there are public meetings. The press is really important—researchers understand bad press.” Another critical tool, he continued, “is to use prevention—consulting broadly and helping many communities. In the end, however, there are other, more punitive, ways that sometimes need to be used.”

Other questions surfaced regarding accountability, such as whether and how a formal process could (or should) be developed that could act with authoritative, legal discretion. Under whose

jurisdiction would it be implemented? How would grievances be monitored, implemented, resolved and maintained? FHI, as mentioned earlier in this report, has taken strides to model how such a process might look, taking some cues from similar progress in other reproductive health arenas—e.g., drugs for HIV/STI treatment and prevention.

The levels of accountability that can and should be brought to bear in situations like QS must be discussed broadly and be determined within a reasonable timeframe, although some participants would argue that the time for action and acknowledgment is long overdue. “Several times we have made the point of QS in past tense,” challenged Rajani Bhatia of the Committee on Women, Population and the Environment in Baltimore, Maryland. “Human trials are still going on and animal toxicological studies are not complete. What happens to all those women who were exposed and are now being exposed? Where is the accountability?” No consensus has been reached regarding its safety and efficacy, yet calls to discontinue use have been made by institutional actors, such as WHO and other international organizations, and by health advocates throughout the world. At the same time, supporters of QS continue to advance their cause.

The rectification of previous violations in the context of continuing use of quinacrine was a topic of great concern for some participants in the

**Should this field or technology be held hostage to the individuals or historical trajectories from which it has emerged? In any event... what hasn't happened enough around quinacrine is self-policing. Even if the introduction of quinacrine was motivated out of a desire to increase choices for women, we need to stop and hold those accountable for behaviors that came before.**

Lori Heise  
Global Campaign for  
Microbicides, PATH  
Washington, DC

**The issue of informed consent brings out the difficulties of conducting clinical trials in developing countries, given the political climate and multiple methods for conducting them. For example, Zipper found a way to keep doing trials even though quinacrine is banned in Chile. This does not occur independently of our cultures, and yet there are those who continue doing things behind women's backs. There is a big need to discuss how the informed choice process includes women as participatory agents in that process. We need to demand accountability from our governments.**

Monica Jasis  
Centro Mujeres  
La Paz, Mexico

meeting. How would such a process be agreed upon and implemented? For some, the data from previous trials can be reviewed, studies can be implemented in an ethical manner, and the correct information can be presented. Although unable to reverse the damage already done, it can provide some measure of restitution at least at the level of clinical trials. There may always be, however, collateral damage as a result of quinacrine's tainted past.

Following up on unethically conducted studies may provide useful data, but separating it from the unethical data of the past may prove more difficult

than anticipated, according to other participants. Lurie drew analogies between information generated by the Nazis during World War II and from the Tuskegee Syphilis Study. The general views regarding these past studies would argue against using such data, but it also so thoroughly infiltrates the current body of knowledge that it is difficult to ignore. The same may be true for quinacrine. Thus, the question of whether or not to expose additional women to quinacrine, given the safety concerns and the lack of FDA-quality Phase II and III trials, persists.

Finally, correcting for problems within the context of trials to test safety and efficacy is but one aspect of the broader challenge ahead, and is in itself insufficient to address fully fundamental rights and health issues presented by provider-dependent reversible and non-reversible methods. For it is in the context of how clinical safety and efficacy, and informed choice play out in the real world—in effect it is how the social safety and efficacy of such a method is ensured and through what processes that ultimately determines whether rights and health objectives are being promoted.

## Concluding Observations

...women's bodies are not testing grounds for potentially hazardous technologies; the priority of meeting the basic needs of women extends far beyond contraceptives.

N.B. Sarojini  
SAMA  
New Delhi, India  
(from written presentation)

The main goal of the meeting "The Quinacrine Debate and Beyond: Exploring the Issues of Non-Surgical Female Sterilization" was to create a forum for discussion and to develop shared themes by which to examine at a microscopic level the controversial issue of quinacrine sterilization (QS) and to view telescopically the larger context of intricate issues that envelop the field of contraceptive research, development, introduction and delivery. Although it was not structured as a consensus-building process, the meeting identified four cross-cutting themes and recommendations that the majority of participants determined were essential when seeking to protect and encourage self-determination among the users of such technologies.

1. Consider the context(s) in which reproductive health decisions are made.
2. Explore the ethical dimensions of contraceptive research and development.
3. Examine social inequities of race, ethnicity, gender and class within and across countries that affect women's reproductive health and well-being.
4. Develop mechanisms and processes to ensure accountability in research and service delivery.

Arguments for and against QS as a continuing practice and as a method to be researched more thoroughly were well articulated at the April 2001 meeting. Concerns related to sociocultural context, ethical dimensions, social inequities, and accountability also dominated the two-day discussion. The complexities of effectively joining the need for an array of reproductive technologies

with the importance of considering sociocultural context, particularly end-users' wants and needs, were detailed more fully. These dovetailed with questions of safety, accessibility, and efficacy, which also played an important role in the discussion.

The ethical dimensions of QS research, development, introduction, and delivery emerged as another major theme of the meeting. Exploring how and to what extent principles of a rights-based approach have been implemented with regard to QS—and other reproductive technologies by extension—brought to the fore the gaps, difficulties, and thorny issues that have haunted QS since its inception. One of the major gaps—social inequities—has exacerbated concerns related to the abuse of QS and its association historically with campaigns to impose coercive sterilization practices on women of color domestically and globally. These obstacles and difficulties have led most observers to agree that mechanisms of accountability must be in place to address those concerns—past, present, and future—in order to ameliorate past abuses and prevent future ones. The lack of authoritative, enforceable international accountability mechanisms for the development and delivery of reproductive health technologies makes it difficult to ensure needed changes are made.

Finally, correcting for problems within the context of clinical trials is just one aspect of the broader challenge ahead. Such efforts, in and of themselves, are insufficient to address the fundamental rights and health issues presented by provider-dependent reversible and non-reversible methods. For it is in the context of how clinical safety, efficacy, and informed choice play out in the real world—in effect, how the social safety and efficacy of such a method is ensured and through what processes—that ultimately determines whether rights and health objectives are being promoted.

The April 2001 meeting provided a forum for spirited dialogue and debate in an environment that sought a balanced inclusion of disparate approaches to the issues of QS and to the entire field of contraceptive research and development itself. The meeting highlighted the importance of engaging in thoughtful debate, while showing respect for the complicated political, sociocultural, and scientific arguments that framed the discussion. Participants used the meeting, as was intended, as an opportunity to articulate past and current issues to move the field forward as new technologies and old ones continue to live uneasily in the present. Throughout the meeting, participants acknowledged and respected differences and sought to articulate carefully and thoughtfully the lessons learned from past efforts and concerns that can be addressed to avoid future difficulties.

Meetings such as “The Quinacrine Debate and Beyond: Exploring the Issues of Non-Surgical Female Sterilization,” have historical antecedents in similar gatherings held over the past few decades to discuss and debate not only QS, but a montage of entangled concerns surrounding reproductive technologies in general. Thus, the April 2001 meeting was neither the first attempt—nor we hope the last—to ensure that the dialogue around QS is rooted in a rights-based framework wherein research, development, introduction, and delivery processes ensure that the most sound, safe and efficacious reproductive technologies reach consumers who need and want them. The recommendations that emerged from this meeting are probably not new. The meeting served as a reminder, however, of the challenge that remains to reinvigorate our efforts to live these principles in practice rather than halfheartedly to espouse and repeat them as rhetoric that occasionally appears in print.

## Appendix A

# Meeting Agenda

### THE QUINACRINE DEBATE AND BEYOND:

#### *Assessing the Future of Female Non-Surgical Sterilization*

Lansdowne Resort  
Lansdowne, VA  
April 22-23, 2001

### Sunday, April 22, 2001

- 8:30-9:00      **Opening Remarks**  
*Kirsten Moore*
- 9:00-11:00    **I. Is there a need for non-surgical methods of sterilization?**  
*Moderator: Kirsten Moore*  
  
Presenter:    Sundari Ravindran, Rural Women's Social Education Centre (India)  
  
Discussants: Judy Norsigian, Boston Women's Health Book Collective (US)  
                 Mildred Hanson, Private Practice Physician (US)
- 11:00-12:15   **II. Update on science, technology, and research design**  
*Moderator: Valerie De Filippo*  
  
Presenters:   Karen Katz, Family Health International (US)  
                 Jack Lippes, University of Buffalo (US)
- 12:30-1:30    **Lunch**
- 1:30- 3:30     **III. How do we set and balance priorities in a world of competing needs and scarce resources?**  
*Moderator: Amy Allina*  
  
Presenter:    Tom Merrick, World Bank (US)  
  
Discussants: Mitchell Warren, Female Health Company (US)  
                 Lynde Francis, The Centre (Zimbabwe)
- 3:30-3:45     **Break**

3:30- 5:30 **IV. What are the appropriate safety and risk standards for reproductive health technologies, and are they universal?**  
**Moderator: Valerie DeFillipo**

Discussants: Monica Jasis, Centro Mujeres (Mexico)  
Peter Lurie, Public Citizen's Health Research Group (US)  
Zeda Rosenberg, Family Health International (US)

6:30 **Dinner**

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**Monday, April 23, 2001**

8:00-9:00 **Breakfast**

9:00-12:00 **V. To what extent should the context into which new methods will be introduced limit or constrain the development of new technologies?**  
**Moderator: Jodi Jacobson**

Presenter: Peter Hall, Reproductive Health Alliance Europe (UK)

Discussants: N.B. Sarojini, SAMA (India)  
Judith Scully, University of West Virginia (US)

12:30-1:30 **Lunch**

1:30-3:30 **VI. Can a "tainted" method be reclaimed? If so, how and under what circumstances?**  
**Moderator: Shelia Clark**

Presenter: Leslie Watson, Campaign for Access and Reproductive Equity (US)

Discussants: María Rosa Garate, Cayetano Heredia Peruvian University (Peru)  
Diana Romero, Columbia University Center for Population and Family Health (US)

3:30-3:45 **Break**

3:45-5:00 **Open Discussion and Closing Remarks**  
**Moderator: Jodi Jacobson**

5:00 **Adjourn**

## Appendix B

# Meeting Participants

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Anna Benton	Center for Health and Gender Equity Washington, D.C.
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\* Paper submitted in absentia

## Appendix C

# Letter from a Meeting Participant

Editor's Note: Every effort was made by the organizing committee to create a balanced and respectful dialogue at the meeting and an accurate description of the meeting's content and outcomes in this report. We invited participants from a wide variety of viewpoints to attend the meeting and sought review of this report from several individuals of diverse perspectives. Some invitees from both sides of the debate declined to participate, while the vast majority accepted. We would like to thank Mildred Hanson, Karen Katz, Judy Norsigian, Jael Silliman, and David Sokal for their careful review of an earlier draft of this report. One participant who was asked to review the manuscript, Jack Lippes, declined to do so and asked that we instead publish the following letter.

A Dissenting Opinion to:

Executive Report  
The Quinacrine Debate and Beyond:  
Exploring the Issues of Nonsurgical Female Sterilization

There are three major deficiencies of the Report: a) failure to state the position of proponents of quinacrine sterilization (QS), b) erroneously assumed abuses and claims of unethical procedures in use of QS, and c) inadequate description of institutional deterrents to development of QS.

### **The position for QS**

Proponents of QS claim the method is safer than surgical sterilization, easier and less expensive to deliver, preferred by well informed women with access to both QS and surgical sterilization, and reasonably effective with the currently accepted protocol, although not as effective as surgical sterilization.

The argument for safety of QS is as follows. Quinacrine as an oral medication has been widely used and remains Food and Drug Administration (FDA) approved for prevention and treatment of malaria and treatment of giardiasis, using much higher doses over longer periods of time than the dose required for QS. This essentially relieves concerns for systemic effects. For both oral and intrauterine administration, quinacrine is rapidly absorbed into the circulation and redistributed to other tissues of the body (1-3). A rapid decline in plasma levels over a 4-hour period indicates high intrauterine levels persist for a relatively brief period (4). Only 2 doses are needed in a woman's life. Such brief exposure to any drug at therapeutic level has never been reported to cause cancer. Tice (5) notes the extensive medicinal use without reports of cancer suggests risk of cancer, if any, may be quite small. After 18 years follow-up of 1492 cases in Chile, no evidence of increased cancer risk has been detected (6). The experience of over 100,000 QS cases in over 20 countries without a reported death is reassuring (7).

Paramedics in the largest QS field trial in Vietnam (8) did as well as physicians in terms of efficacy of the method. Women in Nam Ha Province of this trial preferred QS over surgical sterilization on an 11 to 1 basis. A similar preference for QS was found in Croatia (9).

Efficacy of QS is thought to be 99% at 2 years of use (4) and might be improved by monitoring spread of the lake of dissolved quinacrine by ultrasound (10) or progression of the intratubal scar by ultrasound as seen in the current FDA approved trial.

There is now a growing consensus that QS be available for women requesting sterilization and for whom existing methods are not available or present unacceptable risks (11). This would include many women in developing countries like India where anemia is so prevalent (12).

### **Claimed abuses and unethical procedures**

Although there has been wide publicity to alleged abuses of QS, including that in a rubber plantation in Vietnam as reported in the Wall Street Journal (13), where the reporter did not actually interview concerned subjects at the plantation. When a careful investigation was conducted, no abuse was found (14). Every subject had clearly signed a consent form. Another false report appeared in a video produced by students in New Delhi where they interviewed a woman in a phase I trial at a New Delhi medical school. This literate woman had signed a consent form in clear English script. She had not told her husband she had been sterilized and denied she knew she was sterilized in the video. To date there has been no documented case of QS abuse. The good record is possibly due to lack of incentives. In all known cases the family either paid a fee for the procedure or incentives for surgical sterilization was considerably higher than for QS.

There were 3 general kinds of QS experience, namely a) government sponsored trials, b) trials in medical schools, and c) experience in service centers of NGOs who had conducted their own risk/benefit assessment and decided QS was appropriate technology for their local circumstances. Two government trials were in Vietnam (8) and Indonesia (15). A third government trial was started in India but not completed. Such trials were obviously reviewed by appropriate authorities. The Vietnam field trial was remarkable in that all 31,000 subjects were followed. It was lessons of this trial that led to the current protocol with standard insertion technique (16), which has improved efficacy of the method (17). Several medical school trials have been reported (9,12, 18-20). They required institutional approvals at government hospitals. One of these trials (18) also had Institutional Review Board (IRB) approval of the International Fertility Research Program (now called Family Health International — FHI). FHI had approved a second trial in Vietnam which was not initiated as Vietnam QS experience was terminated after receipt of a World Health Organization letter (21) stating they would be surprised if quinacrine was not carcinogenic. Other investigators have reported valuable QS experience (22-24). NGOs both conducted QS trials (17, 25-26) and monitored QS experience in their service programs. Such experience was not considered as research. The largest of this service experience was with the Indian Rural Medical Association (IRMA) in West Bengal, India including approximately 10,000 cases.

### **Institutional deterrents to development of QS**

There have been two major deterrents to development of QS: a) one organizational defect in the WHO Department of Reproductive Health and Research, and b) funding strategies of major donors supporting contraceptive research.

Although most regulatory agencies, such as the FDA, follow the Helsinki Declaration in requiring a risk/benefit assessment before approval of any clinical trial, this is, de facto, not done for contraceptive research of WHO. It is definitely done in the WHO Special Programme for Research and Training in Tropical Diseases, as outlined by its director, Dr. Tore Godal (27). In the case of WHO's Special Programme for Research and Training in Human Reproduction, approval by its Toxicology Panel is required. This panel has in effect veto power over the Programme's director. As the Panel is made up of toxicologists and not program administrators or clinicians, risk/benefit assessment cannot be made. The Toxicology Panel desires standard toxicology studies to be concluded before the first cases in a clinical trial. At this time such toxicology studies cannot be conducted concurrently with a phase I trial. Why would we want to do animal toxicology studies when we have 20+ years of QS experience with people?

The position of WHO makes it difficult for other agencies to consider encouraging QS development. The International Planned Parenthood Federation (IPF) is now closely related to WHO and of course the UNFPA and World Bank are UN related agencies. Organizations receiving funds from WHO, such as the State Family Planning Commission of China, are reluctant to sponsor QS trials, although they had expressed interest in a trial.

The largest contraceptive research support is from the US Agency for International Development (USAID). As part of the State Department and receiving its funds from Congress, its contraceptive research interests are influenced by opinions of members of Congress. Some members oppose all artificial contraception. When a method like QS is made controversial by media reports it becomes institutionally risky for USAID to fund QS development in the form of clinical trials — even with FDA approval of the trials. Grantees of USAID funds generally follows USAID support patterns. FHI supports toxicology studies only, even though they could support phase II FDA approved clinical trials.

USAID supported service programs require FDA approval for all supplies used. The two most promising developments in sterilization are QS and a method of reversible vas occlusion (RVO) developed in China (28).

### **Conclusion**

Science is all on the side of QS. The Executive Report describes concerns of several feminist organizations. This dissenting opinion attempts to describe science favoring QS and some organizational limits for its support.

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 February 23, 2002

**Executive Report of a meeting  
convened by the:**

**Center for Health and Gender Equity**

[www.genderhealth.org](http://www.genderhealth.org)

**National Women's Health Network**

[www.womenshealthnetwork.org](http://www.womenshealthnetwork.org)

**Reproductive Health Technologies Project**

[www.rhttp.org](http://www.rhttp.org)

**National Black Women's Health Project**

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