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• *ABSTRACT*

Studies of laboratory work have rarely focused on the role of intermediary organizations in developing R&D activities. Most studies focus on a single university-based research laboratory or an industrial R&D unit. Moreover, the rejection by social constructivist scholars of universalistic, deterministic explanations of the development of science and technology has led to an overemphasis on the local features of scientific and technological work. Based on a case study of the role of the World Health Organization (WHO) in contraceptive R&D, this paper suggests that an analysis of the role of intermediary organizations enables us to go beyond a too-narrow focus on the micro-sociological dynamics of laboratory work, to include the macro- and meso-sociological dimensions of science and technology. First, a focus on intermediary organizations enables us to learn more about the manner in which locally specific laboratory cultures are transformed into translocal research practices. This paper shows how literary technologies, and to an even greater extent material technologies, are important tools in accomplishing standardization of local laboratory cultures. Second, a focus on intermediary organizations enables us to study how concerns that go beyond the laboratory — in this case, population control policies and the agenda of the WHO — help to shape laboratory practices.

From Population Control Politics to Chemicals: The WHO as an Intermediary Organization in Contraceptive Development

Nelly Oudshoorn

The late 1970s witnessed the emergence of new types of R&D organizations. In Europe, science policy stimulated the creation of intermediary organizations to promote or to organize cooperative research between industry and the public sector.[1] In a broader context, public sector international agencies, such as UNESCO and the World Health Organization (WHO), launched research programmes in the agricultural and health sectors. Despite the growing importance of these intermediary organizations in scientific and technological developments, such research networks have generally

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been overlooked by STS scholars.[2] Most studies of laboratory work focus on a single university-based research laboratory or an industrial R&D unit. This choice tends to restrict the scope of analysis to the micro-sociological dynamics of laboratory work.[3] The world outside the laboratory comes into the picture only if it presents itself in the form of a well-defined actor 'enrolled' by the scientists in the laboratory. In this approach the dynamics begin within the laboratory, and scientists are thus portrayed as the pivot on which everything hinges. Similarly, the rejection by social contructivist scholars of universalistic, deterministic explanations of the development of science and technology has led to an overemphasis on the local features of scientific and technological work. The study of intermediary organizations provides a useful opportunity to broaden the scope of analysis to include the macro- and meso-sociological dimensions of science and technology. Working across these levels simultaneously is important if we want to understand science and technology as the product of local laboratory practices, organizational dynamics and macro-structures of the wider world. In this manner, we can avoid the pitfall of isolating scientific and technological developments from the larger social and political currents in society.[4]

In this respect, contraceptive technologies are an interesting field to study. Over the last decades, the development of new contraceptives has been shaped by the agendas of governments, non-governmental organizations (such as women's health organizations), industry and reproductive scientists. Taking as a case study the role of the WHO in promoting and coordinating R&D in the area of contraceptive technologies, I analyze how concerns which go beyond the laboratory help to shape laboratory practices. In the late 1970s, the WHO launched an R&D programme to develop new long-acting contraceptives for women and men. This was an intriguing programme because it required the organization of a research network with locations all over the world.[5] I will describe how the macro-sociological concerns of population control (that is, the politics of enhancing fertility control in developing countries) became linked to local laboratory programmes for the synthesis of specific chemical compounds. The study of this 'world-wide laboratory' also enables us to learn more about the manner in which the standardization and synchronization of local laboratory cultures may be accomplished. What needs to be the same, and what can be

different, when scientists try to implement translocal research practices?

I begin by briefly discussing the macro-sociological changes in contraceptive politics which resulted in demands for new contraceptive technologies. I then proceed to examine the work that was needed to accomplish translocal laboratory practices. I conclude by arguing that we can understand the standardization of local laboratory cultures in terms of literary and material technologies.

The Changing Politics of Contraceptive Technologies

Over the last three decades, the heterogeneous worlds of family planning and population control organizations, national governments, contraceptive researchers and industry have witnessed drastic changes in what is deemed the most adequate solution to 'the population problem'. The earlier reproductive paradigm of the 1950s through the 1970s can best be characterized as the 'One Size Fits All' approach. The inventors of the pill were very explicit about the type of contraceptive they were seeking to develop: it had to be a 'universal' contraceptive that could be used by all women, regardless of colour, class, age, location or educational background.[6] This dream of an ideal contraceptive for any woman, regardless of her specific background, was not realized. In the 1970s, population control organizations and scientists concluded that the strategy to develop a universal contraceptive had failed.[7] The pill had been accepted mainly by middle- and upper-class women in the western industrialized world, with one exception: China. Most women in Southern countries used sterilization and intra-uterine devices as their means of contraception.[8] In *Reproduction and Human Welfare*, a review of the reproductive sciences and contraceptive development published in 1976, the authors evaluated their experiences with birth control methods as follows:

> Thus, current technology cannot be regarded as adequate to meet individual or societal needs in either industrial or developing nations . . . . The heterogeneity of personal, cultural, religious, and economic circumstances of human life, as well as the varying needs of individuals at different stages in the life cycle, impose diverse demands upon the technology. It is thus likely that there will never be an 'ideal' contraceptive for all circumstances.[9]

The previous twenty years of experience with the pill had made it clear that this method had significant limitations, not only with

respect to acceptability but also to safety and continuity of use.[10] In the 1970s, the safety issue became of central concern because feminist health advocates and physicians reported serious side-effects from both oral contraception and intra-uterine devices.[11] During this era a different type of contraceptive discourse emerged. In *Birth Control Technologies: Prospects by the Year 2000*, the author aptly described the new contraception paradigm:

> Family planning programmes need to have available for consumers a variety of safe and effective methods, so that in a 'cafeteria' style, self-selection by consumers will lead to greater individual motivation to use any particular method and ensure continued widespread use of birth control methods.[12]

This drastic shift in the reproductive paradigm coincided with broader cultural changes in the 1970s: the collapse of the dreams of modernity. The declining belief in grand theories and ideologies to understand and control the world led to a situation in which locality and individuality became of central concern in Western culture. This crisis in modernity eroded the belief in a single technological fix to improve the human condition.[13]

Most remarkably, the acknowledgement of the need to 'modify technology to fit fit people, rather than modifying people to fit technology',[14] broadened the demand for contraceptive R&D to include a new group of consumers: men. Since the introduction of the condom and vasectomy (both methods that date from the nineteenth century), no new means of contraception for men had been developed. The request for developing new male contraceptives came from outside the scientific community: from feminists in the Western industrialized world and governments in Southern countries, most notably in China and India. Feminists demanded that men share the responsibilities and health hazards of contraception, whereas governmental agencies urged the inclusion of 'the forgotten 50% of family planning' as targets for contraceptive development.[15]

Family planning and population control organizations articulated the need to design long-acting contraceptives as one of the products required in the envisaged supermarket of contraceptives, in order to enhance effectiveness in preventing pregnancy.[16] Long-acting contraceptives were expected to provide better tools for population control programmes. This type of contraceptive is a good example of a 'technical delegate' — an artefact that is designed to compensate for the perceived deficiences of its users (in this case, the

users' tendencies to 'forget' to use contraceptives).[17] These voiced needs for new contraceptives called for a new effort in R&D activities in contraceptive development.

However, during the 1970s, the contraceptive R&D climate had also changed drastically. In the 1970s in the United States, encouraged by the success of the pill, at least thirteen major pharmaceutical firms were actively involved in contraceptive research.[18] The first clouds in the apparently blue sky appeared when reports began to circulate about the health risks of oral contraceptives, most notably increased risks for cancer and diseases of the circulatory system.[19] Both consumer advocates and the women's health movement questioned the adequacy of laboratory testing and clinical trialling of the pill, and suggested that the reproductive sciences and industry had shown inadequate concern for the health of women.[20] Similar criticism was raised with respect to the introduction of the Dalkon Shield, a new intra-uterine device (IUD).[21] Harm, including death, caused by the pills and IUDs had resulted in an increase in liability suits and insurance costs, and in stricter regulatory procedures. The demand was for safer means of contraception. This eventually led to a decline in industrial involvement in contraceptive R&D, particularly in the United States.[22] Currently only Ortho maintains a significant R&D programme in this area.[23] Contraceptive R&D has largely shifted to Europe, where three major drug companies, Organon, Schering AG and Roussel-Uclaf, maintain sizeable R&D programmes.[24]

Building an Alternative R&D Network

In the early 1970s, the WHO became very much aware that industry was failing to meet the need for new contraceptives, particularly for developing countries. In 1972, this international health organization established a new branch specifically devoted to reproductive R&D: the Special Programme for Research and Development and Research Training in Human Reproduction (abbreviated to Human Reproduction Programme: HRP). Besides contraceptive R&D, HRP was given a number of tasks, including 'the development of scientific institutions and manpower in Third World countries; the setting of scientific and technical standards; the provision of supplies and equipment needed for research; and establishment of information about the performance of existing methods of birth planning'. Since

its founding, the HRP has established several task forces, each devoted to a specific contraceptive technology.[25] In 1975, HRP decided to initiate a specific task force for the development of long-acting contraceptives outside the traditional pharmaceutical industry channels. This decision was a response to the appeals of population control organizations and several governments in developing countries, who stressed the need for alternative contraceptives with an effective duration of up to six months.[26]

The development of long-acting contraceptives had initially been taken up by industry. In the 1960s, the American pharmaceutical company Upjohn had developed a long-acting injectable contraceptive (medroxy-progesterone acetate, MDPA, commonly known by its trade name, Depo Provera), which was prevented from being approved by the US FDA because of feminist lobbying in the United States. Feminist health advocates took the view that this new contraceptive conflicted with women's rights, since injections might easily be abused in certain societies. The 'ban the jab' political lobby was an important factor in discouraging industry from further research of this kind.[27] According to Stephen Matlin, a professor of biological chemistry at Warwick University in Coventry, UK, and one of the central investigators in HRP's programme for the development of long-acting contraceptives,[28] it was the vacuum created by the absence of a long-acting injectable that brought the WHO into the field:

> By the mid 1970s it was clear that many developing countries saw this [long-acting injectables] as a very desirable approach to contraception. There was a demand for this product. The only other product available was Schering's oily solution of Norethisterone enanthate, which is only a two-month injectable. It was less advantageous to use in a variety of ways and so [there] was perceived to be a need for long-acting methods of contraception that would be suitable for a mass-market in developing countries, easy to apply and with infrequent contacts [with health-care workers]. And the pharmaceutical industry was absolutely unwilling to touch it, because they had seen what had happened to Upjohn and the feminist movement. So that was the gap in the market that the WHO was trying to fill.[29]

The WHO launched its programme for the development of long-acting contraceptives with the following rhetoric:

> The development of new injectable contraceptives requires that a concerted effort be made to synthesize novel steroid compounds and subject them to thorough biological evaluation. Since such an effort was not being made by international pharmaceutical companies, the World Health Organization as part of its Special

> Programme of Research, Development and Research Training in Human Reproduction established a task force to determine whether such a development programme could be launched outside the pharmaceutical industry.[30]

The WHO's HRP thus transformed and specified the demand for long-acting contraceptives into two explicit criteria for how these contraceptives should look: the contraceptives should be injectable, and they should be steroids.[31]

The next step was to build an R&D organization. The WHO did not have laboratories, nor did it build them. Rather, in July 1975, it consulted a group of leading steroid chemists with past or current experience in industry.[32] These experts, 'boundary élites' to use Hoch's felicitous phrase, provided HRP with precisely what was needed: a list of approximately 150 hypothetical steroid compounds, and a proposal involving a number of laboratories with the ability to synthesize these new compounds.[33] Geoffrey Waites, manager of HRP's Task Force for the Regulation of Male Fertility, described the birth of what was eventually called the Chemical Synthesis Programme of Steroids as follows:

> This Programme was initiated because of the realisation that, unless we have drugs developed in the public sector, we would always be at a disadvantage by being left to negotiate with the drug companies for drugs that they are developing.[34]

The WHO thus explicitly opted to become an independent R&D organization, particularly independent from industry.

The actual design of the programme, and its consequent realization, exemplify how many things and people need to be put in place if industry does not participate directly in drug development. The first problem was how to find laboratories with the necessary expertise and willingness to cooperate in a programme for the synthesis of novel steroid compounds. The programme got off to a promising start. The WHO staff in Geneva did not have to begin from scratch. Pierre Crabbé, named coordinator of the steroid synthesis programme, could rely on his informal contacts with the chemists who had designed the programme.[35] Crabbé approached the laboratories mentioned at the consultancy meeting in July to determine whether they would be willing to participate in the programme. Most importantly, he did not approach these laboratories with empty hands. Crabbé proposed an arrangement by which 'in addition to supplying literature, material, and chemicals', the WHO would fund 'each laboratory to the extent of $10,000 to

$15,000, the sole requirement being that 5-gram quantities of pure steroid would have to be delivered to the WHO headquarters. Patent rights would remain with WHO'.[36] The proposed arrangement was quite effective: eventually 16 laboratories agreed to participate in the programme. These laboratories, for the major part chemistry labs and some pharmacy labs, were located in Australia, Brazil, Bulgaria, China, East Germany, Iran, Israel, Korea, Mexico, Nigeria, Poland, Singapore, Spain, Sri Lanka, Thailand and Yugoslavia.[37] The choice of such a decentralized and multinational R&D network was not a necessary step for building an effective research organization for the synthesis of contraceptive compounds, but may be understood in terms of the WHO's broader institutional goals.

> This choice fitted the other part of the WHO's profile as much as anything. It would have been fully possible to go to one or two laboratories: they could have given huge contracts for a couple of hundred thousand dollars to two places. But particularly in the 1970s, when the HRP programme was in its infancy, one of the fairly perceived aims was institution strengthening and really distributing expertise in many places, and I suspect that putting these sums of money ($15,000 per year) to a number of laboratories was aimed at widening the interest in synthesis of antifertility compounds. They were committed to trying to increase the interest in antifertility work in developing countries.[38]

The next step was to find suitable laboratories in which to purify and test formulations of the chemical compounds once they had been synthesized in the chemical laboratories, and to perform the biological evaluations of these compounds. The WHO succeeded in making arrangements with the Department of Chemistry of the City University in London for purification and quality control, with the School of Pharmacy of the University of London for formulation, and with the Contraceptive Development Branch of the National Institute of Child Health and Human Development in Bethesda, Maryland, USA, which agreed to undertake the screening studies in rats and pharmacokinetic studies in monkeys.[39] The choice of the laboratories in London was made because of their specific expertise and skills in purification and formulation work.[40] The decision to concentrate the biological testing of the synthesized compounds in one laboratory — namely, the laboratory in Bethesda — was based on financial considerations and on the need to centralize the testing in a well-qualified location.

> The biological evaluation was done in one place for a very good reason. The person involved there, Dr Bialy, was very committed to this programme and used

> the part of the available budget from the NIH to collaborate with the WHO in that field. It would have been incredibly expensive for the WHO to actually fund a laboratory to do that kind of biological testing. It is very expensive: you need a large number of animals for each assay, and a lot of very highly skilled personnel. The quality of that data was actually critical to evaluating the whole programme so it had to be done in a very high quality laboratory. And so because NIH was providing that partnership with the WHO it was possible to do the whole programme. I am not sure whether they could afford it in another way.[41]

The WHO thus managed to translate the political demand for new contraceptives into a research programme which had to be performed in a variety of locations all over the world.

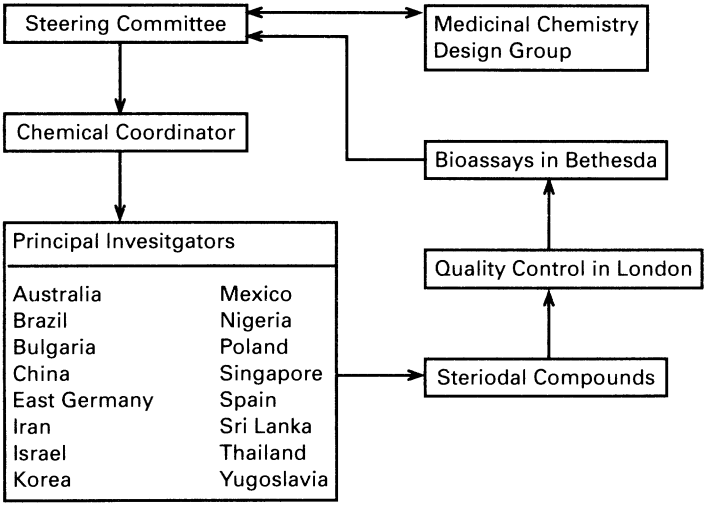
The Creation of Translocal Laboratory Practices

It is obvious that the WHO could only succeed in this ambitious programme if it put great effort into transforming the specificities of the local laboratory cultures into a translocal research practice. This part of the HRP's steroid synthesis programme is intriguing because it enables us to gain more detailed insight into the process of standardizing laboratory work. Some parts of the development of new contraceptives (such as the synthesis of steroid compounds) were spread over various laboratories and locations, whereas other parts (namely: the purification, formulation and the biological evaluation of the compounds) are centralized and synchronized in three central laboratories (see Figure 1).

This type of organizational structure demonstrates that standardization can be accomplished by centralizing those parts of laboratory work that lie at the end of the research trajectory. The two laboratories in London and the laboratory in Bethesda functioned as gatekeepers by selecting only those compounds that could pass the test of being pure and active compounds. The decision to centralize the purification and formulation work and the animal testing in three locations might thus be understood in terms of facilitating control over the selection of the desired compounds. I will elaborate this further in the next section.

Let us first turn to the synthesis work. The chemical synthesis of new steroid compounds was not restricted to a single laboratory. Due to HRP's policy of decentralizing the synthesis work, standardization was of crucial importance. The science studies literature on standardization outlines the problems that arise in creating uniform

FIGURE 1
Structure of the WHO Steroid Synthesis Programme



Source: Martin, op. cit. note 37, 5.

laboratory practices, and emphasizes the tensions that exist between locally specific routines and universal standards levied by centralized bodies. Recent studies on standardization practices describe how difficult it is to create uniform research practices.[42] Halffman, drawing on Shapin and Schaffer's distinction between social, material and literary technologies,[43] suggests that we can understand standardization processes in terms of the control and routinization of people, objects and texts.[44] First, authority and control can be mainly delegated to people. In this case, standardization may be achieved by training and disciplining people, and supervising their actions. Second, control and routinization can be delegated to objects: local laboratory cultures can be transformed into translocal research practices by applying standardized apparatus and materials. Third, standardization may be accomplished by texts: locally specific contingencies of laboratory work are diminished by the use of textual protocols or data report forms which contain highly detailed prescriptions for what needs to be done, and what must be avoided. According to Halffman, all three categories are essential in stabilizing research activities between different laboratory settings:

> [S]tability is obtained by the mutual control of these three elements: literary technologies such as textual protocols or data report forms control people's operations, people control the material design of a test and verify test performance, the material design controls the inscriptions produced and so on.[45]

At first glance, the HRP's steroid synthesis programme seems to reveal all three control technologies. A closer look reveals a pattern of standardization in which literary technologies, and, to an even greater extent, material technologies, dominated the process. Face-to-face supervision, assistance and control of the chemists who participated in the steroid synthesis programme were restricted to one or two visits by the programme's coordinator, Pierre Crabbé.

> During the first 3 years of the programme the coordinator visited most laboratories at least once. The purpose of the site visits was to brief the investigators about the precise objectives of the programme and operating details, to offer appropriate scientific information and advice, to become familiar with the local research facilities, and to solve a number of administrative problems. Each centre had difficulties, for example, inexperienced personnel, lack of sophisticated equipment and instruments, inclement weather conditions, or frequent power failures .... The coordinator acted as a general troubleshooter and was easily available to the various principal investigators.[46]

Direct feedback and control by the WHO staff was thus performed only in a very limited manner. This suggests that successful standardization does not necessarily require the presence of people who directly supervise and control the research activities. Nor does it require intensive communication between the participating laboratories: during the three years in which the programme was carried out, only three face-to-face meetings took place where the coordinator and the principal investigators discussed the proceedings of the synthesis work. This is not to say that these meetings did not have any impact. Matlin recalled that these meetings were characterized by a fair amount of peer group pressure: 'there is nothing more shaming for a scientist than to go to a meeting to admit defeat'.[47]

By contrast, literary technologies played a much more extensive role in the WHO's attempts to reduce the differences among the participating laboratories. The steroid synthesis programme consisted of a highly predesigned procedure which left only a limited degree of freedom to the participating laboratory scientists. The design of the programme, developed by the coordinator in consultation with the other leading steroid chemists, was clear and straightforward: each laboratory had to change the configuration of existing

steroid compounds by inserting specific chemical compounds (acid chains) at specified locations in the molecule (position 17 of the steroid nucleus). A blueprint of the desired compounds (steroid esters) was made by the HRP team: they compiled a list of 16 to 20 ester structures which was sent to the participating laboratories. Each laboratory was requested to submit a research proposal 'outlining how they intended to synthesize the acid chain to be introduced into the steroid molecule. The proposals were reviewed by the WHO secretariat, an outside referee, and the coordinator'.[48] These procedures reveal the highly predesigned and practical nature of the steroid synthesis programme, in which literary technologies played a crucial role in controlling the actions of the participating laboratories. Texts were central in all the different phases of the steroid synthesis programme. The WHO Secretariat in Geneva set up a control system to monitor all movements of materials from Geneva to the various chemical laboratories, and from these laboratories to the laboratories in London and Bethesda, and eventually back again to Geneva: 'every sample was followed by the WHO Secretariat and by the coordinator (appropriate forms were used at every stage of the programme) until the biological results were returned'.[49]

Up to this point, the participating scientists were allowed a certain degree of freedom. However, this freedom was further restricted by the use of material technologies to standardize a variety of research practices. Most importantly, the WHO team provided the participating laboratories with standardized chemical reagents, small equipment items and highly purified steroids that had to be used as 'mother-compounds': synthetic progestins (norethisterone and levonorgestrel) for the synthesis of compounds for female contraceptives and testosterone for the synthesis of compounds for male contraceptives. The only freedom allowed the chemists was to vary the length of the acid chain, the nature and degree of unsaturation, and ring size.[50] To quote Matlin:

> The methods of preparing the side-chains were very much left to the principal investigators, and they were able to consult with Pierre Crabbé if they had a proposal, or if they were getting into difficulties, and they could contact him and ask for suggestions.[51]

The only exception seems to have been that in some cases chemists had to synthesize new acids that were not previously described in the literature. This is the only phase in the synthesis work that was

left to the expertise and creativity of the local laboratories.[52] These research activities did not consist only of straightforward chemical work. To quote Matlin again:

> Some of these side-chains were very challenging and required very innovative chemistry and a high degree of skill; others were quite mundane, almost off-the-shelf chemicals, that had to be coupled together, but even the coupling methods used to join the side-chains to the steroid were not necessarily straightforward.[53]

This phase of the steroid synthesis programme thus shows that it is not necessary for an effective research programme to lock all research activities into uniform, centrally specified routines. Not all procedures and idiosyncratic practices need to be standardized, because the eventual results (in this case chemical compounds with data sheets) can be monitored and controlled by textual (and later testing) procedures. In some phases of research a too strictly uniform approach might even be counterproductive, because it does not stimulate scientists to explore alternative routes. The steroid synthesis programme thus vividly illustrates that some phases in research can be left to the expertise and skills of individual laboratory scientists, and do not require extensive direct control and supervision by people to adjust the locally specific activities to uniform standards. In Matlin's words:

> I think there was very little standardization of chemical procedures between the laboratories. They chose whatever methods and equipment they felt most suitable. Obviously, Crabbé visited each lab at least once so he could give advice, but by and large they were competent chemists who knew how to make compounds and they got on with the job. The standardization was only in the context of the reasonable chemical procedures for doing things, and that chemists by and large used the same kind of tools for investigating the purity of their products . . . . If you take a subject like synthetic organic chemistry and you give this task to people in different parts of the world they will be likely to come up with similar kinds of methods.[54]

This suggests that in laboratory work, routines are an important part of structuring activities, just as Berg has noted in connection with medical work.[55] This structuring role of routines does not imply that this part of the steroid synthesis programme was left entirely to the dynamics of the local laboratories. This phase of the synthesis programme exemplifies that locally specific routines were only allowed if they resulted in the desired end products:

> The laboratory working methods were the judgement of each competent scientist. They were asked to produce a product using good chemical techniques. The

> target was in a sense to complete the appropriate form on which they could say: I have this product and it has this series of constants, of physical properties and has such and such a purity. And we acted as the final check on that.[56]

Moreover, data reports showing the results of the individual researchers were sent twice a year to the Steering Committee of the Task Force on Long-acting Contraceptives, and the participating laboratories had to report on their methods and results at the three Principal Investigators' meetings that were organized over the five-year period of the programme. These reporting procedures had a tremendous impact not only on standardizing the synthesizing activities, but also on the productivity of the local laboratories. According to Matlin, there was a great rise in the number of compounds submitted to his lab in London shortly before each Steering Committee meeting took place. Moreover, the quality of the compounds also improved due to these monitoring procedures.[57]

Literary technologies, despite their decentralized mode of operation, thus defined to a great extent the 'proper' activities that were expected from the participating laboratories.[58] However, the steroid synthesis programme also shows that certain research activities cannot be organized in such a decentralized mode. As mentioned earlier, the compounds synthesized in the sixteen laboratories were eventually sent to three central laboratories for purification, formulation and biological testing. The compounds were thus subjected to additional, highly centralized procedures of testing. In this respect, the quality control lab in London seems to have played the most crucial role in standardizing the research activities. To quote Matlin again:

> The first real standardization step, I would say, was in my laboratory. Because everything came in whatever state of purity,[59] and unless it was a complete disaster we did not go back to the synthetic chemist . . . . By the time things left our laboratory they were all analyzed by standard protocol, and they were all to a common level of purity. The quality control step was the sort of critical bringing together of everything. This had to be done in one laboratory and with an approved kind of protocol and continuity over a long period of time as well. Basically everything passed through my hands in terms of paper work and the analysis of results before it went out. Although over the period of six years I had a number of PhD people working on it individually, I saw all the data they produced and I compiled the reports on that data myself.[60]

The chemical laboratory in London thus functioned to standardize the compounds produced by the other laboratories. Eventually,

the compounds were sent for animal screening to the National Institute of Child Health and Human Development in Bethesda. These standardization efforts paid off. In 1981, the coordinator could report that the programme, over a period of five years, had resulted in the synthesis of 380 steroids — approximately 310 progestin esters for female contraceptives, and 70 androgen esters for male contraceptives.[61] A decade later, the WHO Annual Technical Report (1992) described the completion of two major phase III clinical trials on two monthly injectable contraceptives (progestins) for women, and a phase I study with a three-month injectable androgen for men which, in combination with a long-acting progestagen, would be developed as a male contraceptive.[62]

Negotiating the Interests of Developing Countries

The role of the WHO as intermediary between family planning and population control politics and university laboratory research was actually much broader than the production of steroid compounds. In 1983, the coordinator and several of the participating chemical investigators evaluated the programme as follows:

> It is considered by the Authors that this chemical synthesis programme undertaken by WHO has, in addition to identifying potentially useful new contraceptive agents, also set the stage for further productive research in this area and other fields of chemotherapy.[63]

In another report on the programme, the initiators specified the productivity of the programme in terms of its contribution to new esterification methods for the field of steroid chemistry,[64] and its impact on extending the experience with steroid chemical research to laboratories in developing countries which had no previous experience in the field.[65] In this respect, the steroid synthesis programme realized a central theme of the WHO's agenda: the extension and strengthening of its networks with investigators in developing countries to increase their interest, expertise and involvement in research on contraceptives.[66] To quote Crabbé, one of the initiators of the programme:

> Excluding efforts by the military establishment,[67] this is probably the first instance in which an international public sector agency has launched successfully a programme of this nature, and it is reasonable to ask how economical the programme is. In terms of time, the chemical synthesis has taken longer than it

> would have in the steroid synthesis laboratory of a large pharmaceutical firm in the US, Western Europe, or Japan. However, part of that extra time was consumed in institution building and in creating technical capability in developing countries — two features that will be of long-lasting benefit .... What is important is that societal goals rather than pure economics have become the driving force.[68]

The WHO's steroid synthesis programme thus functioned as an important mediator in transferring knowledge, skills and equipment to Southern and Eastern countries, a process in which the compounds themselves played a crucial role:

> The Steroid Synthesis Programme has provided us with a few very useful steroidal compounds by which to extend and control the intervals between injections .... I think it has had other effects as well. As with gossypol,[69] these compounds have been valuable in a training mode. We have been able to provide them to investigators in multi-centre studies, and they have been able to undertake research from common protocols that have had a training end too.[70]

Again, we may conclude that material and literary technologies were of crucial importance, not only for the standardization of laboratory practices, but also for the transfer of knowledge.

The WHO's intermediary role was not restricted to the organization of an alternative R&D network. Most importantly, the WHO succeeded in negotiating a more privileged position for family planning and population control organizations in the contraceptive market. The very act of organizing the synthesis programme for steroids brought the WHO into a challenging position. This newcomer in the field of drug development had demonstrated that it was possible to do contraceptive R&D outside the control of industry, thereby providing a model of particular relevance to the development of the so-called 'orphan drugs' — drugs for which there exist societal needs, but which are not of interest to the pharmaceutical industry.[71] The WHO programme showed that the pharmaceutical industry was not essential, at least not during the early stages of drug development.

In the late 1970s, the WHO gradually became aware of its changing position in the biomedical networks of drug development. Until then it had been the WHO's policy to publish all results from its research projects without seeking to obtain patents. Their only concern was that relevant data should be accessible to a wider audience as soon as possible. Following its increased R&D efforts, the WHO decided to change this policy. In 1982, the World Health Assembly endorsed a resolution which stated that:

> It shall be the policy of WHO to obtain patents, inventor's certificates or interests in patents or patentable health technology developed through projects supported by the WHO, where such rights and interests are necessary to ensure development of the new technology, and to promote its wide availability in the public interest.[72]

By changing its policy on patents, the WHO established a much stronger position in its relations with industry: the WHO now came into possession of the proprietary rights of the new products it developed.[73]

> In the early days the policy was going to be that if WHO identified a new drug it would simply publish all the details so it could become public property. It was only in the early 1980s that they decided that the best way to protect the public interest was for the WHO to file a patent. I think it came down to economic realism that if you just publish a drug which is going to be active and anybody can make it, you can no longer license the drug, you cannot control the conditions of manufacturing, and you cannot control the public price. WHO felt that their only way to entice the pharmaceutical company into collaborating would be if they could offer them an exclusive license.[74]

The WHO successfully applied for patents for three of the four new progesterone compounds, as well as the new androgen compound that had been developed in the steroid synthesis programme.[75] The patent authors were the people who had designed the steroid synthesis programme in 1975, but all rights were assigned to the WHO.[76] In this manner the WHO put itself firmly on the map as a potential influential drug developer.[77]

The very fact that the WHO now holds the proprietary rights for potential contraceptives enables this organization to negotiate with industry about what types of drugs will be manufactured, and the specific markets for which these drugs will be produced. If the WHO had not taken the initiative to start contraceptive R&D projects, and if it had not decided subsequently to patent its products, it would never have gained such a position at all. Now the WHO approaches industrial partners for manufacturing and distributing its products, and tries to negotiate agreements which guarantee that a very specific sector of the potential market will be reserved for the WHO: notably the public sector, while the private market remains the domain of the pharmaceutical company. In this manner the WHO realizes the 'cornerstone of the Programme's relationship with industry': 'the promotion and protection of the interests of the public sector with special emphasis on the needs of

developing countries'.[78] By negotiating these agreements with industry, the WHO ensures that the drugs will be manufactured and distributed to family planning and population control organizations and other agencies in developing countries. Moreover, it uses its position as patent owner to negotiate a cheaper price for the public sector. Pharmaceutical firms cooperating with the WHO have to sign the following agreement:

> Proprietary rights owned by the parties prior to the agreement remain the property of the originator, but are licensed to the other party. In the case of the WHO, this may be on a royalty-bearing basis or the cost of the product to the public sector is reduced in proportion to the anticipated royalties. The company agrees to supply the public sector with the product, but in the event that it is unable, or unwilling to do so, it agrees to transfer the necessary technology and know-how to a mutually agreed third party with appropriate licensing arrangements, so that the public sector requirements can be met.[79]

In this manner the WHO played a major role in negotiating the interests of population control organizations.

Conclusions

Reflecting on the role of the WHO in building an R&D network for contraceptives outside traditional pharmaceutical industrial channels, we may conclude that the WHO has been very successful in establishing a position in this highly contested field. Notwithstanding this success, the WHO retains its dependency on industry, simply because it possesses neither the capital nor the facilities needed for large-scale manufacturing and distribution of the newly-developed contraceptive compounds.[80] Moreover, the WHO seems to have adopted a much more extended role in contraceptive development because industry, in contrast to the WHO's expectations, did not accept any partnership in the steroid synthesis programme:

> I think [the WHO] always thought that once they got a good active entity that industry was willing to go into partnership, and that that discovery could then be transferred and be licensed into a company. It actually took a lot longer than anybody thought to find a partner. They had to accept going further and further down the road of product development in order to try to entice people in. It was not enough just to show that there was an active entity, they had to do a lot of work with these clinical studies and they had to do a lot of work with these compounds, and they are still negotiating even now . . . But scientifically it was a success, they achieved the objective of finding long-acting agents.[81]

The WHO thus acted as a surrogate pharmaceutical firm in spite of itself. On the other hand, the very fact that industry was not interested in developing contraceptive compounds motivated those involved in the steroid synthesis programme to make the programme a success.

> There was the strong institutional commitment to develop these products, because for the whole of the time that this programme has been going on there was never a question of any competition from the outside. Nobody else was going to do it .... There was never any actor in the field to whom you could off load your responsibility .... The route that HRP has taken is: right, we will design drugs from here, and we will get the work done through university laboratories wherever that can be done in developed or developing countries, and we will try to bring a product to such a state that people have to take notice of it.[82]

The WHO's synthesis programme thus may best be portrayed as a 'demonstration network', following a typology of R&D networks introduced by Philippe Laredo. Demonstration networks are aimed at 'demonstrating the feasibility of a new technical option for a collective good'. The typical organization form of this type of network is 'a star shape around a central actor in charge of all integrative dimensions'.[83] The steroid synthesis programme fits nicely into this typology of research networks. The demonstration of the feasibility of long-acting contraceptive compounds, particularly those for men, was a crucial goal of the whole endeavour.

> I think what is special with male contraceptives is the attitude of people. What has been fundamental has been the lack of any desire of almost everybody to engage in developing male contraceptives. Traditionally, male contraception was always regarded as a non-starter by industry. There was a standing prejudice that men would not use a male contraceptive, and even if they did, women would not trust them to use it. The WHO is getting quite advanced with their steroid and I think this will help again to promote the idea of a sort of viable male contraceptive. I don't know whether it is really an ideal drug; that remains to be seen. At least it will extend the public exposure to the idea of practical working methods.[84]

This strategic goal of the steroid synthesis programme to capture the interest of industry seems to have had its impact on industry. Despite its reluctance to invest in the technical and cultural novelty of male chemical contraceptives, industry subsequently seems to have taken initial steps into the R&D of male contraceptives. Very recently, Organon has decided to initiate a feasibility study to explore whether they can use some of their steroid products —

which do not require long-term animal toxicology testing — to develop a male contraceptive.[85] The WHO has clearly played an important role in clearing the atmosphere for industry to take an interest in R&D for male contraceptives. To quote Bergink, Organon's programme manager of reproductive medicine:

> If you ask me why we are doing this [the feasibility study for a male contraceptive], it's simply because we are getting signals from the WHO, from the researchers. We see the results, we review the literature. Then you get an idea how it works. They showed that it is scientifically and clinically do-able. Well, to make up the economic picture is not so difficult. There will definitely be a market for it.[86]

The demonstrative character of the WHO's synthesis programme is not unique: demonstration networks have been developed in other cases as well, particularly in the energy and health sector.[87] What is exceptional is that this research network has succeeded in reaching its goal: the synthesis of new contraceptive compounds. Most other cooperative research networks initiated and coordinated by intermediary organizations seem to be rather unsuccessful.[88]

My major argument throughout this paper has been that an analysis of the role of intermediary organizations in science and technology enables us to go beyond a too-narrow focus on the micro-sociological dynamics of laboratory work in two different ways.

First, a focus on intermediary organizations enables us to learn more about the manner in which locally specific laboratory cultures are transformed into translocal research practices. I have shown how literary technologies, and to an even greater extent material technologies, are important tools in accomplishing standardization of local laboratory cultures. Materials can function as control technologies because they make scientists work with the same research materials (in this case standardized chemical reagents and highly purified steroids to be used as 'mother-compounds'). Moreover, materials can be subjected to centralized tests.[89] We have seen how the purification and formulation work, and the animal testing of the locally produced compounds, were centralized in three locations. Texts can function as tools to create translocal research practices because they can be used to specify what work should or should not be done. Texts can also be used to monitor all the phases of laboratory work. I have shown how the WHO standardized the work of all participating laboratories by the use of protocols and

data reports which forced scientists to follow highly predesigned procedures, and which enabled the WHO to monitor what had happened to the locally produced compounds. Thus, texts and materials were the major tools to accomplish standardization. We have seen how texts and materials, and not people, frequently travelled all over the world to create translocal research practices.

Second, a focus on intermediary organizations enables us to study how concerns that go beyond the laboratory help to shape laboratory practices. An analysis of the trajectory of the synthesis reveals an intriguing mixture of factors which shaped laboratory work (see Figure 2). Reflecting on this heterogeneous list, it is not easy to decide which considerations dominated the laboratory work. Of course, the 'blueprint' of the desired contraceptives provided by family planning and population control organizations was of crucial importance because it steered the search for new contraceptive compounds in the direction of long-acting compounds. However, this blueprint could have been translated into a number of possible trajectories. The choice of steroids was made by the WHO team, not by family planning or population control organizations. This choice can best be understood in terms of the scientists' preference for 'do-able problems', to use Joan Fujimura's phrase.[90] Since the 1950s, the steroidal approach has dominated contraceptive R&D: the WHO team could thus simply continue in this line of research and build on a firmly established routine of laboratory skills with steroidal

FIGURE 2
Choices and constraints in the WHO Steroid Synthesis Programme

Choices	Constraints
1) long-acting injections	population control politics
2) steroids	domination of edcrinology; do-ability
3) new derivatives of known, rather than novel steroids	do-ability and safety
4) specific 'mother-compounds': norethisterone, levonorgestrel, testosterone	patents, litigation and acceptability
5) network of laboratories in Northern and Southern countries	development policies

compounds, as well as on animal and clinical testing data on the efficacy and safety of steroids.[91] The decision to develop new derivates of known steroids rather than new steroids may also be understood as a choice to construct 'do-able problems', particularly to avoid toxicological problems.

> If you started synthesizing a new steroid it would be a very much bigger business, synthetically more difficult, but also you have a lot more unknowns in terms of toxicity. So the likelihood of success was relatively good with our programme because they were working with known principles .... What was taken from existing knowledge was the fact that the steroid nucleus had a known activity and that you could increase the duration of action by adding things on to the side.[92]

The choice for specific steroids as 'mother-compounds' was shaped by the existence of earlier patents, litigation problems related to the safety of specific compounds and the acceptability of compounds in terms of side-effects.[93] Finally, the choice to create a decentralized, multinational R&D network, including laboratories in Northern and Southern countries, was clearly initiated by organizational concerns of the WHO — in particular, its aim to strengthen R&D capacities in developing countries. This case study thus shows how macro-political concerns and meso-organizational concerns are important factors in shaping local laboratory practices.

• NOTES

I would like to thank Willem Bergink, Jane Cottingham, Herman Kloosterboer, Stephen Matlin, Alvin Paulsen and Geoffrey Waites for granting me interviews, and Robert Bud, Adele Clarke, Willem Halffman, Philippe Laredo, Bernike Pasveer, Ad Prins and three anonymous referees who were so kind as to comment on earlier versions of this paper.

1. The promotion of collaborations and alliances both between companies and with public sector organizations is one of the major characteristics of EC programmes and EUREKA projects. See Philippe Laredo, 'EC and EUREKA Promoted Networks. Toward a Redefinition of European Public Interventions?' (paper presented at the colloquium on Management of Collaborative European Programmes and Projects in Research, Education and Training, Oxford, 11–13 April 1994), 2, 4.

2. There is one major exception: Philippe Laredo, B. Kahane, J.B. Meyer and Dominique Vinck, 'The Networks Built by the Fourth Medical and Health Services Research Programme' (Bruxelles: Commission Communitaires Européenes, 1992).

3. See, for example: Karin Knorr Cetina, *The Manufacture of Knowledge: An Essay on the Constructivist and Contextual Nature of Science* (Oxford: Pergamon Press, 1981); Bruno Latour and Steve Woolgar, *Laboratory Life: The Social Construction of Scientific Facts* (Beverly Hills, CA & London: Sage Publications, 1979); Michael Lynch, *Art and Artifact in Laboratory Science: A Study of Shop Work and Shop Talk in a Research Laboratory* (London: Routledge & Kegan Paul, 1985).

4. Authors who have criticized constructivist approaches in STS for neglecting the political and normative dimensions of science and technology are, among others: Hans Radder, 'Normative Reflections on Constructivist Approaches to Science and Technology', *Social Studies of Science*, Vol. 22 (1992), 141–73; Langdon Winner, 'Upon Opening the Black Box and Finding It Empty: Social Constructivism and the Philosophy of Technology', *Science, Technology, & Human Values*, Vol. 18, No. 3 (Summer 1993), 362–78; Brian Martin, 'The Critique of Science Becomes Academic', ibid., No. 2 (Spring, 247–59. These and related criticisms are debated at length in a Special Issue of *Social Studies of Science*: Malcolm Ashmore and Evelleen Richards (eds), 'The Politics of SSK: Neutrality, Commitment and Beyond', *Social Studies of Science*, Vol. 26, No. 2 (May 1996), 219–468.

5. The role of the WHO as intermediary organization in the area of contraceptive technologies is not restricted to promoting and coordinating R&D in the field of long-acting contraceptives, but includes a much wider range of activities which I describe in the section 'Building an Alternative R&D Network'. I have chosen to restrict my analysis to the WHO's R&D programme for long-acting contraceptives because it enables me to study how intermediary organizations operate in mediating between the demands of population control politics and the microdynamics of laboratory work.

6. R. Christian Johnson, 'Feminism, Philanthropy and Science in the Development of the Oral Contraceptive Pill', *Pharmacy in History*, Vol. 19 (1977), 63–79.

7. Michael J.K. Harper, *Birth Control Technologies: Prospects by the Year 2000* (Austin, TX: University of Texas Press, 1983).

8. Barbara Seaman and Gideon Seaman, *Women and the Crisis in Sex Hormones: An Investigation of the Dangerous Uses of Hormones from Birth Control to Menopause and the Safe Alternatives* (Brighton, Sussex: Harvester, 1978), 76.

9. Roy O. Greep, M.A. Koblisky and F.S. Jaffe, *Reproduction and Human Welfare: A Challenge to Research. A Review of the Reproductive Sciences and Contraceptive Development* (Cambridge, MA & London: The MIT Press, 1976), 4.

10. Ibid., 3.

11. Seaman & Seaman, op. cit. note 8.

12. Harper, op. cit. note 7, 9. The implicit assumption in the cafeteria discourse is 'that more technologies automatically equal more choices'. Feminist health advocates have argued that contraceptive choice is not such a simple matter. Individual choices are defined and constrained by power relations in sexual relationships, dependencies between users and providers, and the availability of methods. See Betsy Hartmann, 'Contraceptive Choice: A Multitude of Meanings', in Helen B. Holmes (ed.), *Issues in Reproductive Technology: An Anthology* (New York & London: Garland, 1992), 3–9.

13. Barry Smart, *Modern Conditions, Postmodern Controversies* (London & New York: Routledge, 1992).

14. John F. Marshall, 'Acceptability of Fertility Regulating Methods: Designing Technology to Fit People', *Preventive Medicine*, Vol. 6 (1977), 65–73, quote at 65.

15. David J. Handelsman, 'Bridging the Gender Gap in Contraception; Another Hurdle Cleared', *The Medical Journal of Australia*, Vol. 154, No. 4 (18 February 1991), 230–33, quote at 230; Fred C.W. Wu, 'Male Contraception: Current Status and Future Prospects', *Clinical Endocrinology*, Vol. 29 (1988), 443–65.

16. Pierre Crabbé, Egon Diczfalusy and Carl Djerassi, 'Injectable Contraceptive Synthesis: An Example of International Cooperation', *Science*, Vol. 209 (29 August 1980), 992–95; Diczfalusy, 'World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, The First Fifteen Years: A Review', *Contraception*, Vol. 34, No. 1 (July 1986), 3–119. In this context, it is important to emphasize that the need for long-acting contraceptives was articulated by population control organizations and not by the eventual users. Population control organizations and reproductive scientists have, by and large, ignored women's perspectives on contraceptives. The history of contraceptive research indicates that there has been hardly any social science research on consumers' concerns. All through the history of contraceptive development there have been, and still are, severe conflicts between the population control perspective and women's perspectives on birth control. These different perspectives have also shaped the terms in this domain. In the 1920s and 1930s, feminists, most notably Margaret Sanger, used the term 'birth control' which reflected the incentive that contraceptives should enhance women's control over their reproductive life. The term 'family planning' was introduced in the 1940s, when more conservative men began to dominate the birth control movement. During the last three decades, the term 'population control' has been used by feminists and other progressives to refer to 'national and international organizations and movements which have focused on controlling the size of particular populations over and against both the specific desires and interests of women and the distribution of resources across such populations' (personal communication, Adele Clarke, 11 May 1995). Throughout this paper I use the term 'population control' in cases in which the actors consider the reduction of the size of populations as the major incentive for contraceptive development, and the term 'birth control' in cases in which users' concerns are considered as the major incentive for contraceptive R&D. For a detailed analysis of the debates on population policies, see: Judith Bruce, 'Users' Perspectives on Contraceptive Technology and Delivery Systems: Highlighting Some Feminist Issues', *Technology in Society*, Vol. 9, Nos 3/4 (1987), 359–83; Holmes (ed.), op. cit. note 12; Ruth Dixon-Mueller, *Population Policy and Women's Rights: Transforming Reproductive Choice* (New York: Praeger Press, 1993); Gita Sen and Rachel Snow, *Power and Decision: The Social Control of Reproduction* (Cambridge, MA: Harvard University Press, 1994); Gita Sen, Adrienne Germaine and Lincoln C. Chen (eds), *Population Policies Reconsidered: Health, Empowerment and Rights* (Cambridge, MA: Harvard University Press, 1994). I am grateful to Adele Clarke, who clarified these points for me.

17. Madeleine Akrich, 'Comment décrire les objects techniques?', *Technique et Culture*, Vol. 5 (1987), 49–63; Bruno Latour, 'Mixing Humans and Nonhumans Together: The Sociology of a Door-Closer', *Social Problems*, Vol. 35 (1988), 298–310. In medicine, 'proper' use of prescribed drugs is called patient compliance.

The implanted contraceptive Norplant is, for example, advertised by Wyeth-Ayert as 'Compliance Free Contraception': Clarke, loc. cit. note 16.

18. Anneline Gelijns and C. Pannenborg, 'The Development of Contraceptive Technology: Case Studies of Incentives and Disincentives to Innovation', *International Journal of Technology Assessment in Health Care*, Vol. 9, No. 2 (Spring 1993), 210–32; Philip J. Hilts, 'Birth-Control Backlash: Years of Litigation and Agitation Have Left America in the Dark Ages of Contraception', *New York Times Magazine* (16 December 1990), 41, 55, 70, 72, 74.

19. Seaman & Seaman, op. cit. note 8.

20. Gelijns & Pannenborg, op. cit. note 18; Seaman & Seaman op. cit. note 8.

21. Karen M. Hicks, *Surviving the Dalkon Shield: Women versus the Pharmaceutical Industry* (New York: Teachers College Press, 1994).

22. The concerns about health produced an enormous increase in the number of liability suits, initially against US manufacturers of the Dalkon Shield intra-uterine device, and later against manufacturers of oral contraceptives. In the 1980s, 'there were more liability suits for oral contraceptives annually than for any other drug category': see Gelijns & Pannenborg, op. cit. note 18, 227; and Carl Djerassi, 'The Bitter Pill', *Science*, Vol. 245, No. 35 (28 July 1989), 356–61. In the United States this dramatic increase in lawsuits led to a situation in which liability insurance for manufacturers became temporarily unavailable. Nowadays, the liability costs in the field of contraceptives are higher than for any other drug category (Djerassi, ibid., 357). Moreover, the public demand to reduce health risks led to more stringent rules and procedural regulations for the production and approval of new drugs. The requirements for contraceptives are even more stringent than for other types of drugs because contraceptives are normally used by healthy people for many years: see Greep, Koblisky & Jaffe, op. cit. note 9, 352. In response to concerns about the long-term effects of oral contraceptives, the US FDA has demanded more stringent premarketing requirements for long-term animal research and clinical testing. These more extensive testing requirements significantly increased the R&D cost for drugs and contraceptives. Within two decades, the average R&D cost of developing a new chemical compound has increased from $65 million to $344 million: see World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, *Inter-Agency Consultation on Meeting the Challenges of the 1990s in Human Reproduction Research* (Geneva, 1990). Other sources suggest, however, that the decline in industrial involvement in contraceptive R&D can be ascribed to the role of American health agencies such as Planned Parenthood US, and international agencies such as the WHO and Planned Parenthood International, who have adopted the policy of bargaining for lower prices for contraceptives with pharmaceutical firms, thus lowering the firms' profits from these products. Pharmaceutical companies and population control organizations usually blame feminists who have fought for contraceptive safety for the decline in interest of pharmaceutical firms to invest in contraceptive R&D (Clarke, loc. cit. note 16). See also: Luigi Mastroianni, Peter Donaldson and Thomas Kane (eds), *Developing New Contraceptives: Obstacles and Opportunities. Committee on Population, Commission on Behavioral and Social Sciences and Education, National Research Council and Division of International Health, Institute of Medicine* (Washington, DC: National Academy Press, 1990).

23. Laura Fraser, 'Pill Politics', *Mother Jones* (San Francisco, CA), Vol. 12, No. 5 (1988), 30.

24. Gelijns & Pannenborg, op. cit. note 18, 216. The European industry has been able to continue research in contraceptives since liability issues have not played such a major role in Europe as in the United States: see WHO, op. cit. note 22, 14.

25. Linda Atkinson, S. Bruce Schearer, Oscar Harkavy and Richard Lincoln, 'Prospects for Improved Contraception', *Family Planning Perspectives*, Vol. 6, No. 2 (June 1980), 43–59.

26. Pierre Crabbé, Sydney Archer, Giuseppe Benagiano, Egon Diczfalusy, Carl Djerassi, Josef Fried and Takeru Higuchi, 'Long-Acting Contraceptive Agents: Design of the WHO Chemical Synthesis Programme', *Steroids*, Vol. 41, No. 3 (March 1983), 243–53.

27. Stephen Matlin, 'The Pill — 40 Years On', *Education in Chemistry*, Vol. 31 (September 1994), 123–27, quote at 125. For women's health and feminist perspectives on Depo Provera, see Jill Rakusen, 'Depo-Provera: the Extent of the Problem. A Case Study in the Politics of Birth Control', in Helen Roberts (ed.), *Women, Health and Reproduction* (London: Routledge & Kegan Paul, 1981), 75–108; Kim Yanoshik and Judy Norsigian, 'Contraception, Control, and Choice: International Perspectives', in Kathryn Strother Ratcliff (ed.), *Healing Technology: Feminist Perspectives* (Ann Arbor, MI: The University of Michigan Press, 1989), 61–92.

28. Stephen Matlin has been one of my major sources for information about the role of the WHO in developing new contraceptives, particularly about the HRP's Synthesis Programme that was created to synthesize new contraceptive compounds. Matlin was one of the principal investigators of this programme, and worked at that time at the Department of Chemistry of the City University in London, a laboratory that played a central role in the Synthesis Programme.

29. Interview, Stephen Matlin, University of Warwick, Coventry, 28 November 1994. For a similar analysis of the reluctance of the pharmaceutical industry to invest in the development of long-acting contraceptive methods, see also Djerassi, op. cit. note 22; Gelijns & Pannenborg, op. cit. note 18.

30. Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 992.

31. By taking the decision to develop long-acting contraceptives, the WHO, like the pharmaceutical firm Upjohn, had to face feminist criticism. Since the 1980s, the WHO has adopted the strategy of inviting representatives of women's health organizations to special meetings to discuss issues such as safety and acceptability of new contraceptives. See Bruce, op. cit. note 4; Anita Hardon, 'The Construction of Antifertility Vaccines: Contesting Assessments of Safety and Acceptability To Future Users', *Science, Technology, & Human Values* (forthcoming). Moreover, the WHO has appointed a special staff member to maintain contacts with women's health organizations 'to help integrate women's perspectives into the research and the institution strengthening work of the programme' (interview, Jane Cottingham, staff member of the WHO's HRP, Geneva, 2 February 1994).

32. Those present at the July meeting included Sidney Archer (Professor of Steroid Chemistry at the Rensselaer Polytechnic Institute, who had worked with Sterling Winthrop), Giuseppe Benagiano (Manager, Task Force for Long-acting Contraceptives, WHO Geneva), Pierre Crabbé (Professor of Chemistry at the University of Grenoble and, in the 1960s, general manager of the research division of Syntex in Mexico City, who was appointed coordinator of the synthesis programme), Egon Diczfalusy (Professor of Reproductive Endocrinology at the

Karolinska Institute in Stockholm, also affiliated with industry), Carl Djerassi (a leading chemist and research president of Syntex at that time) and Josef Fried (Professor of Steroid Chemistry at the University of Chicago, who had previously worked with Squibb).

33. Hoch introduced the concept of 'boundary élites' to describe the role of scientists who have regular and direct involvement with both business and academic science: Paul K. Hoch, 'The Crystallization of a Strategic Alliance: The American Physics Élite and the Military in the 1940s', in Everett Mendelsohn, Merritt Rue Smith and Peter Weingart (eds), *Science, Technology, and the Military* (Dordrecht: Kluwer, 1989), 87–116; Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 992.

34. Interview, Geoffrey Waites, WHO, Geneva, 2 February 1994.

35. The chemists were selected largely because they were known to the initiators of the synthesis programme. Djerassi, Fried and Archer were all steroid chemists with former PhD students in all parts of the world. Pierre Crabbé, who began his career in chemistry as a student of Carl Djerassi, was a chemist with a lot of experience in developing countries. The selected chemists, most of them working in laboratories in developing countries, had thus been trained mainly in the United States and Europe. Interview, Matlin (note 29); see also Carl Djerassi, *Steroids Made It Possible: Profiles, Pathways, and Dreams: Autobiographies of Eminent Chemists* (Washington, DC: American Chemical Society, 1990), 63.

36. Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 992.

37. Stephen Matlin, 'Pierre Crabbé Memorial Oration' (paper presented at the First International Conference of Andrology, Nenjiing, China, 4 March 1991).

38. Interview, Matlin (note 29). The extension and strengthening of networks with investigators in developing countries has been (and still is) a major incentive of the HRP: see Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 992, 993; Atkinson & Schearer, op. cit. note 25.

39. Crabbé et al., op. cit. note 26, 252.

40. The WHO approached the City University of London laboratory because of its expertise with a then not yet widely available purification technique (high performance liquid chromatography, HPLC). Formulation work included the testing of the compounds to decide which formulation (oily solutions, microcrystalline suspensions, or other forms) had the best profile with respect to the duration of action, since different formulations may give rise to different pharmacological activities, including the duration of action: see World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, *Task Force on Long-Acting Agents for Fertility Regulation: Meeting of Investigators Participating in the Chemical Synthesis Programme* (Singapore, 1981), 3. The formulation work was thus a crucial step in the developmental trajectory, because the development of long-acting compounds was the central aim of this programme.

41. Interview, Matlin (note 29). Gabriel Bialy was the chief of the Contraceptive Development Branch of NIH and member of several steering committees of WHO. NIH was then spending millions per year on contraceptive development. Bialy was able to use part of the available budget to collaborate with WHO and has acted as one of the scientists who published the results and evaluation of the synthesis programme (ibid.; interview, C. Alvin Paulsen, Professor Emeritus in Medicine at the Medical School of the University of Washington, Seattle, 18 October 1994). See also Crabbé, Diczfalusy & Djerassi, op. cit. note 16; Crabbé et al., op. cit. note 26;

Peter E. Hall, Gabriel Baily, R.P. Blye and P. Crabbé, 'Development of Certain Levonorgestrel Esters as Long-Acting Injectable Contraceptives', in Gerald I. Zatuchni et al. (eds), *Long-Acting Contraceptive Delivery Systems* (Philadelphia, PA: Harper & Row, 1983), 190–98.

42. Geoffrey Bowker, *Science on the Run: Information Management and Industrial Geophysics at Schlumberger, 1920–1940* (Cambridge, MA: The MIT Press, 1994); Peter Galison, *How Experiments End* (Chicago, IL: The University of Chicago Press, 1987); Joan Fujimura, 'Constructing 'Do-able' Problems in Cancer Research: Articulating Alignment', *Social Studies of Science*, Vol. 17 (1987), 257–93; Susan Leigh Star, *Regions of the Mind: Brain Research and the Quest for Scientific Certainty* (Stanford, CA: University of Stanford Press, 1989).

43. Steven Shapin and Simon Schaffer, *Leviathan and the Air Pump: Hobbes, Boyle, and the Experimental Life* (Princeton, NJ: Princeton University Press 1985), 25.

44. Willem Halffman, 'The Standardization of Chemical Risk: The Transformation of Expertise in Two Regulatory Regimes of the EPA', *Social Studies of Science* (forthcoming).

45. Ibid., 3.

46. Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 993.

47. Interview, Matlin (note 29).

48. Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 993.

49. Ibid.

50. Ibid.; interview, Matlin (note 29).

51. Interview, Matlin (note 29); Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 993.

52. Crabbé et al., op. cit. note 26; Hall et al., op. cit. note 41, 191.

53. Interview, Matlin (note 29).

54. Ibid.; Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 993.

55. Marc Berg, 'The Construction of Medical Disposals: Medical Sociology and Medical Problem Solving in Clinical Practices', *Sociology of Health and Illness*, Vol. 14 (1992), 151–80.

56. Interview, Matlin (note 29).

57. Ibid.

58. Most participating scientists readily adopted the regime set by the programme for synthesizing the predesigned compounds, not least because alternative compounds would very likely cost extra money: interview, Matlin (note 29).

59. The criteria for testing the purity of the compounds were set by the Steering Committee. This committee had set very strict purity limits of at least 99.5%, which is a much stricter condition than is normally found in the pharmaceutical industry. 'Part of the concern was that as they were looking for very long-acting injectable agents, it was appreciated that the physical form of the solid might have a critical bearing on the rate of release. So in order to avoid artifacts and confusion they decided that they wanted such a high purity': interview, Matlin (note 29). Due to these strict limits more than 50% of the synthesized steroids failed to pass the test.

60. Interview, Matlin (note 29).

61. WHO, *Task Force*, op. cit. note 40. Although most participating laboratories developed esters of both progestins and testosterone in parallel, the androgens were given 'a somewhat lower priority partly because it was mainly a female-oriented

focus in the Task Force': interview, Matlin (note 29). The fact that the Task Force for Long-acting Contraceptives was more interested in female contraceptives also resulted in a delay in the actual work on androgens: although 20 AET-1, which was eventually selected as an effective male compound, was first synthesized in 1979, it was only 'during a re-evaluation of the data at the end of the programme that people realized that there was actually an androgen there that was looking very good' (ibid.).

62. World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, *Annual Technical Report 1992* (Geneva, 1993), 10, 64; interview, Waites (note 34). The injectable for men, testosterone buciclate (code name 20 AET-1), is a long-acting androgen replacement preparation. Many strategies envisaged for controlling male fertility necessitate androgen replacement therapy. The development of long-acting androgens is therefore a crucial part of the development of hormonal contraceptives for men. See World Health Organization, Special Programme of Research, Development and Research Training in Human Reproduction, *Twelfth Annual Report* (Geneva, 1983), 71.

63. Crabbé et al., op. cit. note 26, 251.

64. According to Matlin, 'two or three laboratories designed new coupling procedures. Some of the publications that came out were actually to do with novel coupling procedures. This was one of the spin-offs. Obviously the motivation of the people who agreed to take part in the programme involved several factors, but one of them was the opportunity to develop something academic and get publications': interview, Matlin (note 29).

65. Crabbé, Diczfalusy & Djerassi, op. cit. note 16, 993.

66. Ibid., 992.

67. The antimalarial programme during World War II was organized by the military: ibid., 993.

68. Ibid.

69. Gossypol, a component of cottonseed oil, was discovered accidentally by Chinese scientists to have contraceptive properties. Although clinical trials with gossypol had already taken place since 1972, the news only reached the western scientific press in the early 1980s: National Coordinating Group on Male Antifertility Agents, 'Gossypol: A New Antifertility Agent for Males', *Chinese Medical Journal*, Vol. 4 (1978), 4. For a more detailed analysis of the role of Chinese scientists in contraceptive R&D see: Nelly Oudshoorn, 'Discourse Coalitions in Contraceptive Technologies. The Case of Male Contraceptives' (paper presented at the Annual Meeting of the Society for Social Studies of Science [4S], Charlottesville, VA, 18–21 October 1995). In 1982, the WHO initiated a synthesis programme, similar to the steroid synthesis programme, to synthesize gossypol analogues for the development of male contraceptives: 78 analogues were produced, of which 37 were passed for animal screening. The Gossypol Synthesis Programme had a similar impact and was particularly instrumental in stimulating contraceptive research in China. Or, as Waites put it: 'Gossypol, whose action as a potential antifertility drug was first described in China, has been very important for China. It was a useful entity to encourage research by Chinese scientists with not much experience with scientific method in the early 1980s because of isolation during the cultural revolution. Gossypol provided an entity to enable scientists in China to develop skills in the classical basis of scientific investigation. So it had an enormous

influence on the development of scientific work in China': interview, Waites (note 34). Unlike the Steroid Synthesis Programme, the Gossypol Synthesis Programme has not been successful. The Programme was confronted with many problems with compound stability and low productivity. In the late 1980s, HRP decided to stop the programme due to problems with toxicity. See Contraceptive Development Branch, Centre for Population Research, National Institute of Child Health and Human Development, Special Programme of Research, Development and Research Training in Human Reproduction, World Health Organization, *Consultation on the Chemical Synthesis of Fertility Regulation Agents* (Bethesda, MD, 1985), 9.

70. Interview, Waites (note 34).

71. Examples of such drugs mentioned by the WHO include remedies for tropical diseases, rodenticides and pesticides designed specifically for tropical pests: see Crabbé et al., op. cit. note 26, 252.

72. Diczfalusy, op. cit. note 16, para. 5.3.

73. Since 1974, the WHO has filed fourteen patent applications: seven were granted, six were abandoned, and one has been rejected: see ibid.; interview, Waites (note 34).

74. In the early 1980s, WHO's decision to patent its products was rather controversial, mainly because it involved ethical questions with respect to the organization's position as a public agency. According to Matlin, 'there were huge debates at that time of what was the right approach because one of the things that was held to be true was that WHO as a public agency could not be sued by anybody. What would be the ethical and moral position of an agency developing a drug which might go wrong or which might be abused by somebody if they could not be sued? It has never happened': interview, Matlin (note 29).

75. Diczfalusy, op. cit. note 16, 6; Task Force on Methods for the Regulation of Male Fertility, *Report Steering Committee Meeting* (Geneva, 23 March 1990), 26. WHO's decision to patent their products resulted in further restrictions for the scientists who participated in the Synthesis Programme (and other WHO programmes). During meetings with the principal investigators 'the participants were reminded of the confidentiality of the information exchanged at the meeting, and a Secrecy document was circulated for all participants to sign'. Moreover, scientists were only allowed to publish the results of their research after the compounds were patented (WHO, *Task Force*, op. cit. note 40, 2).

76. Ibid., 15.

77. The question that remains to be answered is whether alternative R&D networks, such as those organized by the WHO, can replace the role of industry in contraceptive R&D. I have described elsewhere that, notwithstanding their success, newcomers in the contraceptive arena retain their dependence on industry. Most of these new organizations do not have enough venture capital to start the large-scale manufacturing of the products they develop. The development of contraceptives, including all phases from synthesis to animal testing and clinical testing and the eventual large-scale manufacturing and distribution, requires long-term financial commitments that are beyond the capacities of the nonprofit organizations such as the WHO: see L. Mastroianni, P.J. Donaldson and T.T. Kane, 'Development of Contraceptives: Obstacles and Opportunities', *The New England Journal of Medicine*, Vol. 322 (15 February 1990), 482–85. Although these new organizations act as drug developers, they will never be able to replace industry: see Nelly Oudshoorn, 'Shifting Boundaries Between Industry and Science: The Role of the WHO in

Contraceptive R&D', forthcoming in Jean Pierre Gaudilliere et al. (eds), *The Invisible Industrialist: Manufacturers and the Construction of Scientific Knowledge* (Basingstoke, Hants & London: Macmillan Press, 1996).

78. Diczfalusy, op. cit. note 16, para. 5.2.

79. Ibid.

80. Due to a decrease of funding by its donors, WHO is presently re-evaluating its priorities, including its role in drugs development. According to Matlin, critics of WHO's role as a surrogate pharmaceutical firm suggest that 'it really should not have a role in drug development, that it is not what it is there for, and this is an activity that should be cut back. There are certainly a lot of questions around in WHO about whether this is the right thing to be doing': interview, Matlin (note 29). These critics consider the HRP's attempts to develop new contraceptives to be a failure and say '20 years almost down the line and you have not brought a product to market. You have spent how many millions on drug development and at this stage you have not found an industrial partner. The product still might fail at any stage along the way, and what is the public interest in this?' (ibid.). The outcome of this policy re-evaluation is not yet known. Other pressures were voiced at the World Conference on Population and Development held in Cairo in 1994, urging the WHO to continue its role in drug development, particularly with respect to male contraceptives. To quote Matlin again: 'Cairo's emphasis on male participation and sharing burdens of responsibilities is a clear mandate to WHO to look where it has its particular strength and advantages. Very few agencies are trying to do serious work in the male. Moreover, the FDA requirements for manufacturing drugs [the guidelines for Good Manufacturing Practices] set even more constraints on producing drugs; they require expertise and skills that are not present within HRP and obviously not easily borrowed from elsewhere' (ibid.).

81. Ibid. For a more extended analysis of the negotiations between the WHO and pharmaceutical firms to increase the involvement of industry in the development of long-acting hormonal contraceptives, see Oudshoorn, op. cit. note 77.

82. Interview, Matlin (note 29).

83. Laredo, op. cit. note 1.

84. Interview, Matlin (note 29).

85. Interview, Herman J. Kloosterboer, Director, Department of Endocrinology, Organon International BV, Oss, 1 July 1993.

86. Interview, Willem Bergink, Programme Manager, Reproductive Medicine, Organon International BV, Oss, 1 July 1993.

87. Laredo, op. cit. note 1, 2.

88. Laredo, op. cit. note 1. Bont recently described the tensions and conflicts in a WHO R&D network involving fifteen laboratories given the task of mapping the variety of HIV in different countries by collecting blood samples. WHO had to redelegate the tasks originally assigned to these labs to a central laboratory because it failed to reduce all the locally specific routines and practices of blood sampling in the participating laboratories: see Antoinette de Bont, 'HIV1ARWOOSWHO.01—1S—DASH0702-L002QA—N——A–A-OOOO: A Reconstruction of the Organisation of An International HIV Registration' (paper presented at the HSS/PSA/4S Meeting, New Orleans, 12–16 October 1994).

89. See Joseph O'Connell, 'Metrology: The Creation of Universality by the Circulation of Particulars', *Social Studies of Science*, Vol. 23 (1993), 129–73, who has described a similar role of standardized materials and equipment.

90. Fujimura, op. cit. note 42.

91. Economic histories of technology also show the cumulative nature of technology development in which 'one development appears to suggest the next', in the words of Wendy Faulkner, 'Conceptualizing Knowledge Used in Innovation: A Second Look at the Science–Industry Distinction and Industrial Innovation', *Science, Technology, & Human Values*, Vol. 19 (1994), 425–58; Giovanni Dosi, 'Technological Paradigms and Technological Trajectories: A Suggested Interpretation of the Determinants and Direction of Technical Change', *Research Policy*, Vol. 11 (1982), 147–62. For a detailed biographical account of the establishment of the steroid paradigm, see Djerassi, op. cit. note 35.

92. Interview, Matlin (note 29); Hall et al., op. cit. note 41, 190.

93. The choice of a 'natural' androgen, rather than a synthetic androgen, was made because synthetic androgens 'had a generally very bad image' because, as early as 1954, scientists had reported liver damage in experiments with these compounds (interview, Matlin, note 29); C. Djerassi, L. Miramontes, G. Rosenkranz and F. Sondheimer, 'Steroids: LIV: Synthesis of 19-Nor-17a-ethynyltestosterone and 19-Nor-17a-methyltestosterone', *Journal of the American Chemical Society*, Vol. 76 (1954), 4092–94.

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