Report on Governmental Health Research Policies
Promoting Gender or Sex Differences Sensitivity

Prepared for Institute of Gender and Health

by

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Report on Governmental Health Research Policies
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1. Introduction

The Institute of Gender and Health has requested an overview of initiatives – and especially any evaluations thereof – implemented to promote or support research taking into account gender and sex differences. This report attempted in the first instance to identify initiatives and evaluations directly relevant to the IGH. This meant, in particular, identifying initiatives and evaluations put into effect by public institutions supporting medical research.

We identified few policies which had been systematically evaluated. Two such cases are the policies promoting inclusion of women in clinical trials in NIH-funded projects, and in clinical trials overseen or evaluated by FDA. Evaluation in both cases was realised by the General Accounting Office reporting to the American Congress.\(^1\) A third case is found in Europe, where many programmes of the Fifth Framework Programme of research were subjected to a Gender Impact Assessment Protocol.\(^2\) The study of the Quality of Life programme interested us in particular, because it includes health research.

These three institutional evaluations are examined below, in this report (see 2.1.2 and sub-sections (NIH), 2.1.3 (FDA) and 2.2.1.3 (EU)).

In the American context just mentioned, the inclusion of women policy generated comment and debate and, ultimately, evaluations done by scholars and published in peer-reviewed journals which gave other perspectives on the significance and relative success or failure of the inclusion of women in clinical trials policy. A number of these evaluative papers are reviewed.

To complement the relative paucity of data with regard to evaluations, the report identifies and examines a number of other relevant policies, programmes or initiatives

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1 United States, GAO 2000 and United States, GAO 2001. See Bibliography, below, for complete references of all documents consulted. We consulted material listed in Bibliography. Additional references found in the footnotes were not necessarily consulted.

which exist or are in the process of implementation. These documents do not constitute evaluations per se of specific programmes or policies. However, the issues raised or explicitly discussed are of direct relevance to our subject of interest: Why promote or support or "do" research which takes into account sex differences or gender differences? What is entailed in such research? What are the conditions necessary for such research to advance? What are the barriers?

We found it useful to present these documents as well.

The reader will find, below, in chapter 2, the substantive analysis of initiatives considered useful to examine for this report. The chapter 3, a first section reviews in summary form the principal findings related strictly to the above-mentioned evaluations. The second section of chapter 3 presents a summary thematic analysis of the findings, including observations and identification of relevant policy issues found in our study of all the initiatives.

The hurried reader might now wish to jump to chapter 3, which we hope will suffice in place of an executive summary.

1.1. Mandate

The Institute of Gender and Health (IGH) requested an examination of international health research policy or programmes intended to promote gender/sex-difference sensitive research.3

We report on this mandate in the following text. We identify and examine some existing evaluations of such policies. We review some policies aiming to implement support to research taking into account gender and sex differences. Finally, we report on texts discussing criteria essential to successful implementation of such policies.

1.2. Methods of Inquiry

To begin our identification of relevant programmes and policies, we consulted standard electronic databases. The main databanks consulted were Medline, CISTI Source and Sociological Abstracts (Sociofile). In this way we identified published American (and Canadian) sources for the most part.

3 E-mail, Miriam Stewart & Kaysi Kushner to Joseph Caron, 20 Nov. 2002.
Personal contacts were used to help identify more recent initiatives, particularly in the European Union and in some European countries; and to verify the existence of others, especially in Canadian governmental agencies. Personal communications were used successfully to contact knowledgeable persons in Canada and in Europe (Sweden, Germany, Spain, The Netherlands and the European Institute of Women's Health). See the section on Acknowledgements for details.

Further sources were gleaned from references found in published material.

Finally, as the area of concern is in the public policy arena and we considered that public knowledge and awareness of the existence of such policies would be a reasonable condition of their success, we felt justified in using internet sources as a major input to complement the above inquiry methods. Internet publication is commonly used in many of the Western countries by public authorities. However, it is clear that evaluations of public policies should not be considered to be accessible in routine fashion through such sources, and they were not.

Given the time we had to complete the turn-around on this project, we do not suggest that all initiatives have been covered. We feel confident, however, that the principal ones have been examined.
2. Policies or programmes concerning gender- and sex-sensitivity in health research

In this section, we review our findings in light of the above-mentioned mandate. We have found three evaluated programmes: they are dealt with in sections 2.1.2 (in the three sub-sections thereof), 2.1.3 and 2.2.1.3. The NIH policy guidelines, FDA guidance and the European Union gender mainstreaming activities are analysed.

We have, however, organised the material by political or administrative entities. The reader will find, in fact, a review of a mixed bag of material in the following pages. We found documentation which was directly or indirectly relevant to our concern in the United States, in the European Union and some of its Member States, in Canada, and in some other agencies.

The reader will note that complete bibliographic details are given in the bibliography. Reference is made in the bibliography to the URLs of material available on internet. Those electronic versions are available in an electronic database, which has been delivered to IGH.

2.1. United States

In the United States, important initiatives have been put into place by the National Institutes of Health (NIH) to address the issue of sex and gender differences in research. The Office of Research on Women’s Health (ORWH) at the NIH, created in 1990, has had a significant role in these initiatives. We shall first discuss the role of the ORWH, then the targeted policy implemented by the NIH to foster the inclusion of women in clinical trials. Finally, in this section, a similar inclusion of women policy implemented at FDA – the Food and Drug Administration – is examined.

2.1.1. The Office of Research on Women's Health (ORWH) of the NIH

The ORWH was created to address inequities linked to an absence of women in policy-setting bodies in biomedical research institutions, and to lack of knowledge concerning

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4 For early history, see also Johnson & Fee 1994 in IOM 1994a, and Oberman 1994. Early studies on women's participation in clinical studies are documented in Appendix A in IOM 1994, a report solicited by the ORWH.
disease and health in women, as compared with men. A triple mandate was given to ORWH to begin to answer these inequities. The mandate, as reported by its director, relates to a) strengthening, developing and increasing research into diseases, disorders and conditions associated with women, b) ensuring appropriate representation of women in clinical trials, and c) strengthening access to women to careers in biomedical careers.5

The specific event that led to the creation of the ORWH was a report by the U.S. General Accounting Office in June 1990 that women were routinely excluded from medical research studies supported by the NIH, and that although NIH policies encouraged researchers to analyze study results by gender, the policy for the inclusion of women in clinical research was not well communicated or understood.6

The ORWH was not set up to fund research directly. Rather, this Office provides funds through NIH institutes and centers to, in a sense, leverage more research in areas considered of priority. Thus new research initiatives may be augmented, and ongoing studies may be expanded so as to address high-priority areas regarding women's health.7 This type of targeted joint funding allows ORWH to operate as a catalyst and as a facilitator.

Women's Health Initiative

The ORWH also has played a "collaborative advisory role" in the Women's Health Initiative, an important disease-prevention study (estimated 10 to 15-year, 625$M study on 165,000 women aged 50 to 79, of diverse racial and ethnic backgrounds8) examining major causes of death, disability and frailty in older women of all races and from all socioeconomic strata.9

Policy on inclusion of women in clinical studies

Further, since 198610 NIH had put into place guidelines concerning the inclusion of women in clinical studies. As mentioned above, a 1989 GAO report demonstrated that "while women were not being systematically excluded from studies, they were not systematically included and were, in fact, excluded from several landmark studies that affected public health practice".11 Changes were called for in the NIH and the ORWH

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5 Pinn 1994, p. 698.
was charged with monitoring. In 1990 revisions to NIH guidelines were made. Shortly thereafter, the NIH Revitalization Act of 1993, Public Law 103-43, made the inclusion of women and minorities in clinical trials a legal obligation. Guidelines were revised once again. In the next section we shall return to the inclusion policy.

Let us first, however, take a short look at other facets of work piloted by the ORWH.

Towards definition of a research agenda

Early in its history, the ORWH challenged the scientific community interested in the issues within its mandate, to collaborate in giving direction and leadership to the research agenda which the ORWH could pilot with the NIH. This resulted in what was called the Hunt Valley Report, which helped define NIH's research priorities in women's health for 7 years.

In a new initiative, the ORWH, with the assistance of the Task Force on the NIH Women's Health Research Agenda for the 21st Century (Task Force) and the NIH Advisory Committee on Research on Women's Health, convened three regional meetings and a final, national meeting to review the NIH's scientific agenda for research on women's health issues. Moving "beyond Hunt Valley," these meetings aimed to "foster collaboration among representatives of the NIH community and the broader women's health community to revise the research agenda on women's health," encouraging broad participation through public hearings and workshops, and supporting ongoing collaboration among individuals and groups of women, advocates, scientists, health care practitioners, and public health policymakers.

The Hunt Valley Report embodied certain underlying principles that continue to inform current NIH research orientations. Therein one found a redefinition of parameters of health to include research to better understand sex and gender differences between women and men in development, health and disease, including sub-populations previously less well represented in clinical research in the past. This agenda "recognizes the full spectrum of research from basic to clinical research and trials, epidemiological and population studies, clinical applications, and health outcomes." All stages of life are embraced, from the prenatal stage to the frail elderly. Women's health implies more than

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the reproductive system. Basic science investigations are emphasized, not just human subject research.16

The Task Force on the Research Agenda for the 21st Century suggests avenues for research which should lead to new analysis and treatment interventions adapted to groups, individuals and circumstances.

A first set of recommendations concerns the research agenda per se. First among these is the following recommendation concerning clinical trials: "Enroll more women in efficacy and safety trials, including pregnant women." This implies both conducting more clinical trials on women’s health issues and enrolling more women in clinical trials wherein women were previously insufficiently represented.17 Six means are proposed to facilitate fulfillment of this recommendation:

- Subject participation and compliance. Conduct research on how to increase recruitment and retention in clinical trials and how to enhance compliance with treatment regimens.
- Clinical trials of treatment protocols. Undertake well-controlled clinical trials with gender-sensitive models (single vs. mixed gender, mixed gender, gender sensitivity absence or presence).
- Inclusion of gender as a research variable. Develop an integrative strategy to include women in all phases of research, including both biological and biomedical studies.
- Effect of combination therapies on prevention and treatment. Conduct human research on incremental effectiveness and safety of combination therapies. These combinations include simultaneous administration of calcium, vitamin D, male and female hormones, and visphosphonates or other pharmaceutical agents.
- Treatment models. Expand research examining the development and effectiveness of treatment models, specific to the unique needs of women, for treatment of psychiatric disorders such as depression, anxiety, PTSD, and eating disorders. These models must also be culturally relevant and address developmental life span issues.
- Stratification of data. Stratify future and existing data from basic and clinical studies for sex and age of subjects.18

Three other sets of issues complement this first one.

The health care needs and concerns of particular sub-populations of women need to be addressed. Sub-populations distinct for any number of reasons (underserved in terms of health care, the elderly, victims of overt or subtle discrimination, etc.) may have special

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needs, may show greater vulnerability, and may in consequence show different etiologies, needs, and outcomes "compared to middle-class women from easy-to-reach populations." The means to address this issue are:

• Diversity. Address diversity in all research studies. Many measurement tools were normed on Caucasian male reference groups. Re-examine these tools and validate them for use with females and diverse ethnic groups. Similarly, there is need for female-centered models of treatment. In developing these models, researchers need to be cognizant of the variables important in women’s mental health, including race, religion, socioeconomic status, and sexual orientation.\(^{19}\)

Multidisciplinary research is said to be needed "to expand and strengthen research." It is recommended to "include behavioral and social science components in research," notably in the following ways:

• Alcohol and other drugs and biological effects. Develop collaborative research programs to examine the relation of alcohol and drug use to biological effects; gender differences; psychosocial, behavioral, cognitive, psychiatric, general health, family, and legal consequences; specific sexually transmitted diseases; and reproductive effects.

• Resource sharing. Increase sharing of resources among researchers — including sharing of clinical samples, DNA banks, serum banks, animals, and reagents.

• Collaboration. Foster interagency and public-private collaboration in order to carry out the full range of research recommended for studying health issues in women, including pregnant women.

Information systems need to allow easier access to archival material on clinical and genetic studies.

Finally, other areas of concern are discussed, in support of the research agenda.

**The significance of the action of ORWH**

In summary, ORWH is the organisation which was charged with overseeing the application by NIH of its policy concerning inclusion of women in clinical trials. Its mandate, in more general terms however, also enables it to 1) advise the NIH Director and staff "on matters relating to research on women’s health;" 2) strengthen and enhance research related to diseases, disorders, and conditions that affect women; 3) ensure that research conducted and supported by NIH adequately addresses issues regarding women’s health; 4) ensure that women are appropriately represented in biomedical and biobehavioral research studies supported by the NIH; 5) support

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research on women’s health issues; and other activities related to career advancement of women in biomedical careers.\textsuperscript{20} The five elements noted are all potentially of direct relevance to the issue which interests us.

We feel that four elements are significant in relation to the actions of ORWH.

First, it is important to signal the central role of ORWH in developing the tools and in being an important moving force in the implementation of the NIH inclusion of women in clinical trials policy. This points to the importance of an institutional leader to effect this form of change.

Second, the process of involving a broad constituency in the definition of policy orientations with regard to women’s health research seems to be a contemporary and useful strategy. We point this out as having advantages, in policy terms, far beyond the primary policy material produced by the participants in the process.

Involvement in the process itself may stimulate stronger awareness of the issues, broader commitment to avenues of action chosen, and aid in bringing about adherence to the proposed policies.

Third, the issues suggested to be relevant and useful to the women’s health research agenda are of interest \textit{per se}. The overarching themes are of direct significance for the issue of gender and sex-difference sensitivity: 1) "Women’s health’ is expanding into the larger concept of gender-specific medicine;" 2) "Research on women’s health must include the full biological life cycle of the woman (...);" 3) "Multidisciplinary research is essential;" 4) "The importance of social and behavioral science to research on women’s health is unquestionable;" and 5) "[T]he collection of first-hand information from women [is needed] to correct male models of normal function and of the pathophysiology of disease."\textsuperscript{21}

Fourth, it is of interest to return to the fact that ORWH has developed a number of useful tools to support in particular the implementation of the inclusion policy. These tools have continued to be updated over time. An example is the \textit{Outreach Notebook for the NIH Guidelines on Inclusion of Women and Minorities as Subjects in Clinical Research}. The document has more than doubled in volume over a very few years, and the content has progressively incorporated new issues as they have evolved through public debate and

\textsuperscript{20} United States, ORWH 2001.
ongoing scientific research. An example of this is found in the discussion newly integrated in a recent edition concerning successful strategies of recruitment and retention strategies.

2.1.2. NIH inclusion policy

2.1.2.1 Evaluation (2000) by GAO

The General Accounting Office (GAO) prepared, in 2000, a Report to Congressional Requesters entitled *Women’s Health: NIH Has Increased Its Efforts to Include Women in Research*. GAO presents the context of its report as follows: "In the 1980s, public health leaders and advocates brought attention to inequities in the health research agenda and the fact that in particular women and minorities were being excluded from research studies.²²² It was therefore uncertain whether the studies’ results applied also to women. In 1990, the GAO found that policy developed by NIH in late 80s to include women in research study populations, had been implemented slowly and ineffectively.²³²

GAO was asked to look at the situation a decade later. GAO published in 2000 an assessment of "NIH’s progress in implementing its new guidelines on including women in clinical research, including the requirement that certain studies be designed to permit analysis of differences between women and men."²⁴² Information for GAO’s assessment was collated from a variety of sources, so as to better understand the extent and variety of actions implemented, and their efficacy.

The assessment of the GAO is based on generally accepted government auditing standards and, more particularly, upon meetings with directors and officials of several NIH institutes, centers and offices,²⁵² review of documents related to the review and approval of a sample of grants and cooperative agreements from some Institutes, and

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²¹ United States, NIH 1999, pp. 13-14, as noted in IOM 2001, p. 15.
²⁵ Including the National Cancer Institute; National Heart, Lung, and Blood Institute; National Institute of Allergy and Infectious Diseases; National Institute of Arthritis and Musculoskeletal and Skin Diseases; National Institute on Aging; National Institute of Child Health and Human Development; ORWH; and Warren Grant Magnuson Clinical Center for intramural research, the National Cancer Institute; National Heart, Lung, and Blood Institute; National Institute of Allergy and Infectious Diseases; National Institute of Arthritis and Musculoskeletal and Skin Diseases; National Institute of Child Health and Human Development; ORWH; and Warren Grant Magnuson Clinical Center for
analysis of NIH’s tracking data on the inclusion of women and minorities in clinical research, and NIH’s expenditures on women’s health.

The NIH initiated action in response to criticism on its lack of progress on research on women’s health, and in 1990 established the Office of Research on Women’s Health (ORWH) within the Office of the Director and launched, the following year, the Women’s Health Initiative (WHI). In 1993 the NIH was required, by passage of the 1993 NIH Revitalization Act, to strengthen its previous policy on the inclusion of women and members of minority groups in clinical research supported by NIH. Five sets of activities or objectives were identified by GAO, in light of the provisions of the Act. Respect or attainment of these objectives is the standard by which GAO evaluates NIH's policy.

The requirements of the NIH, as set out in the Act, according to the GAO, are as follows:

a) "ensure that women and minority groups are included as subjects in clinical research except in cases in which it is inappropriate with respect to the health of the subjects or the purpose of the research or under circumstances that NIH’s Director designates,

b) "conduct or support outreach programs for recruiting women and members of minority groups as subjects in clinical research,

c) "ensure that clinical trials that include women and minorities are designed and carried out in a manner sufficient to provide for the valid analysis of differences in effect for them,

d) "establish guidelines about including women and minorities as subjects in clinical research projects, and

e) "establish a data system to collect, store, analyze, retrieve, and disseminate information about women’s health research that NIH supports or conducts."

We shall see that GAO notes important efforts by NIH concerning inclusion of women as clinical research subjects, but relatively little effort concerning analysis of differences by sex. Below, the letters in parentheses (a through e) refer to the five activities listed above, required of NIH by the 1993 legislation.

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26 United States, GAO 2000, Women’s Health : NIH…, pp. 6-7.
1. NIH has made significant efforts in ensuring that women are included in studies (a, b, d):

1.1. NIH guidelines (1994) implementing the 1993 Revitalization Act:

1.1.1. addressed all relevant provisions of the Act (concerns points a, b, c, d, e of the list above),

1.1.2. strengthened previous policies on inclusion of women and minorities in clinical research (from a requirement of inclusion concerning biomedical and behavioral research involving human subjects, guidelines broadened the definition of clinical research to include all research involving human subjects) (a),

1.1.3. required that some phase III clinical trials be designed to permit analyses of differences by sex (c),

1.1.4. eliminated cost as a motive for excluding the designated women and minorities from clinical research (a),

1.1.5. revised the application form for new grants to indicate the policy changes (e.g., application for Public Health Service grant instructs on compliance with inclusion policy, reporting of data on population by sex and by racial and ethnic group, composition of proposed study population, and annual reporting on current enrolment data; however, on the contrary, in requests for proposals and requests for applications for clinical trials issued by NIH, instructions concerning inclusion of women were included, whereas mention of necessity of analysis of outcomes by sex was not included – see also list element 3.2 below) (a, d),

1.1.6. instructed reviewers to consider the planned study population in light of new guidelines when assessing scientific merit (a, d),

1.1.7. offered extensive training and information on the new requirements,
internally (reviewers, programme officers and grants management staff)\textsuperscript{33} and externally (broader scientific community and grant applicants) (a, d),\textsuperscript{34} and

1.1.8. determined to conduct or support outreach programmes to ensure recruitment and retention of women and minorities as subjects in clinical research (b).\textsuperscript{35}

1.2. NIH staff continue to work with funded researchers to ensure ongoing attainment of inclusion requirements (a, b).\textsuperscript{36}

1.2.1. Attention appears to continue to be accorded to inclusion issues, in the course of research, as evidenced by mention of recruitment and lagging enrolment issues within investigator reports, and by ongoing NIH support toward recruitment of women (a, b, d).\textsuperscript{37}

1.3. The NIH intramural research program has also implemented the inclusion policy (a).\textsuperscript{38}

1.3.1. The members of institutional review boards, which are involved in overseeing research protocols, receive since about 1994 training and orientation which focus \textit{inter alia} on inclusion policy (a,d).\textsuperscript{39}

2. NIH has made less substantial progress in implementing the requirement that phase III clinical trials be designed and conducted to permit analysis by sex (c).\textsuperscript{40}

2.1. NIH was required by the Revitalization Act to enable sex differences (or whether interventions affect women and men differently) to be able to be analyzed within clinical trials. In turn, NIH required phase III clinical trials to include women in sufficient numbers to enable valid analysis of sex differences.

This entailed two limitations. First, the application of the Congressional requirement to phase III trials only, in the belief (of NIH officials) that what was aimed at were studies well advanced enough to contribute more immediately

\textsuperscript{33} United States, GAO 2000, \textit{Women's Health : NIH...}, pp. 7, 9.
\textsuperscript{34} United States, GAO 2000, \textit{Women's Health : NIH...}, p. 9.
\textsuperscript{35} United States, GAO 2000, \textit{Women's Health : NIH...}, p. 8.
\textsuperscript{36} United States, GAO 2000, \textit{Women's Health : NIH...}, p. 7.
\textsuperscript{37} United States, GAO 2000, \textit{Women's Health : NIH...}, p. 11.
\textsuperscript{38} United States, GAO 2000, \textit{Women's Health : NIH...}, p. 7.
\textsuperscript{40} United States, GAO 2000, \textit{Women's Health : NIH...}, pp. 7-8, 11 ss.
than basic research to development of policy and standards. The second limitation involved the preparation of "a special definition of clinical trial to distinguish these trials from other types of clinical research that NIH supports. NIH defined clinical trial as 'a broadly based prospective Phase III clinical investigation, usually involving several hundred or more human subjects, for the purpose of evaluating an experimental intervention in comparison with a standard or control intervention or comparing two or more existing treatments.' Phase I and phase II clinical trials are earlier phases of research in which interventions or treatments are tested in a smaller number of people."\(^{41}\)

Thus, certain clinical trials are exempted from the requirement, notably in cases where "substantial scientific data demonstrate no significant difference between women and men".\(^{42}\) In practice, however, GAO noted that these guidelines left room for interpretation\(^{43}\) and, thus, led to decisions open to interpretation, as in clinical trials designed to include women but involving numbers too small to allow valid analysis of difference of outcomes between men and women (a).\(^{44}\)

2.2. Although analysis of grant documents by GAO provided strong evidence of "routine" (regular, constant) focus on the studies' "general inclusion of women, evidence as to whether [NIH staff and reviewers] were taking care to implement the requirement related to analysis by sex was scant."\(^{45}\) As mentioned above (1.1.5), instructions concerning necessity of study of outcomes by sex were missing in some instances of NIH requests for proposals or applications (c).\(^{46}\)

3. Assessment of progress was subject to some difficulty, due to lack of documentation in some cases and in other cases inconsistencies in use of measurement tools (e).

3.1. In extramural research proposals, the proposed study populations are now routinely examined in the context of the evaluation of the scientific merit of projects (peer reviewers are guided in this process by a scientific review administrator who is part of NIH staff). Based on the evaluation, an overall

priority score is attributed to each application. This score affects decisions of NIH concerning funding of proposed studies (a, d).\textsuperscript{47}

3.1.1. Ostensibly, this score reflects at least in part the level of adherence to the inclusion policy. However, GAO was not able "to assess the extent to which observations about study populations affected the priority scores given specific applications" (a,d,e).\textsuperscript{48}

3.1.2. About 4 percent of extramural research applications including human subjects were found to be unacceptable on the basis of policy concerning inclusion of women and were barred from funding (a).\textsuperscript{49}

3.2. NIH has made some progress in implementing,\textsuperscript{50} since 1995, a centralized data tracking system which would permit production of measures of progress concerning inclusion of women as subjects in clinical research (e).\textsuperscript{51} Data are generally two years old, given lag time for reporting data, and then compiling and processing.\textsuperscript{52} Ten different categories of studies need not report on their inclusion of women and minorities (basic research, studies involving only tissue or body fluid specimens, very small studies, or studies wherein double accounting might occur – multi-centre study, or a study under a supplemental grant, in cases where it is presumed that the coordinating or the parent study will report). Just over 40 % of NIH studies were in fact tracked (with a range from 13 % to 60 %, according to the particular Institute) (e).

3.2.1. However, this system suffers from inconsistencies in the data, because of differing interpretations of which studies should be tracked. Initial training was given but update training has not been conducted. The system continues to be bettered, on an ongoing basis (e).\textsuperscript{53}

3.3. Women constitute a significant proportion of research subjects. "More than half of the participants in clinical research studies NIH funded in fiscal year 1997

\textsuperscript{47} United States, GAO 2000, \textit{Women’s Health : NIH...}, p. 9.
\textsuperscript{48} United States, GAO 2000, \textit{Women’s Health : NIH...}, pp. 9-10.
\textsuperscript{49} United States, GAO 2000, \textit{Women’s Health : NIH...}, p. 10.
\textsuperscript{53} United States, GAO 2000, \textit{Women’s Health : NIH...}, pp. 7, 15.
were women, according to NIH’s tracking data.\textsuperscript{54} Minority women were well represented, except that the representation of Hispanic women enrolled in studies was below their proportion in the general population.

NIH officials consider that the goal of NIH policy is to conduct biomedical and behavioral research so as to be able to generalize the knowledge gained to the entire U.S. population. Toward this end, they consider that the appropriate numbers of women or minority subgroups should be dependent on the scientific issue addressed in the study and on the prevalence among the particular subgroups of the particular disease, disorder or condition under investigation.\textsuperscript{55}

GAO did not examine change of representation of women in NIH studies over time. In the fiscal year 1997, most studies (52.5 \%) had enrolled between 30 and 60 percent women participants. Seventy percent of the studies were based on populations including at least 40 percent women (a, e).

3.4. Despite finding inconsistencies in NIH staff methods for production of annual expenditure figures,\textsuperscript{56} and notwithstanding the difficulty of predicting what group may eventually benefit from basic research, GAO reports that spending on women’s health, discounting inflation, has increased by 39\% between fiscal year (FY) 1993 and FY 1999. By comparison, men’s health research increased by 23\% and research affecting both men and women by 27\%.\textsuperscript{57} This data is to be "interpreted with caution." Further, dates of growth for specific women’s conditions varied greatly, from over 70\% in the case of osteoarthritis to 16\% for osteoporosis (e).

4. Implementation of the inclusion policy and general leadership in the area of women’s health research agenda development has been assumed by the Office of Research on Women’s Health.\textsuperscript{58} Implementation involved a variety of activities, including development of guidelines; training and education thereon; organisation of public hearings concerning the guidelines; ongoing collaboration with institutional review

\textsuperscript{54} United States, GAO 2000, \textit{Women’s Health : NIH…}, pp. 15 ss.
\textsuperscript{55} United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 17.
\textsuperscript{56} United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 23. “One official noted that sufficient judgment is involved in making these decisions to suggest that even the same person might not make the same judgment twice” (p. 24).
\textsuperscript{57} United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 23.
\textsuperscript{58} Other areas of concern for women’s health also are part of the mission of ORWH, for instance recruitment, retention, reentry, and advancement of women in biomedical careers; United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 19.
boards; organisation of standards, definitions and tools for tracking data on inclusion; and establishment of a database concerning research on women’s health, including a clinical trials registry, for health care providers, researchers and the general public.\textsuperscript{59} ORWH has specific mandate for carrying out guidelines on inclusion and coordinating the data tracking system. It conducted training and education at onset of inclusion policy.\textsuperscript{60}

ORWH took the lead at NIH and, with internal and external collaboration, helped develop an agenda for research on women’s health. According to the Director of ORWH, the Report of an early ORWH action, a 1991 scientific workshop, served as the basis for NIH’s research priorities in women’s health for 7 years.\textsuperscript{61} A recent (1999) report, \textit{Agenda for Research on Women’s Health for the 21st Century}, sets a new agenda (d).\textsuperscript{62}

ORWH provides leverage funding (ORWH does not fund research projects directly)\textsuperscript{63} for research on women’s health by NIH institutes and centers. Almost US$90 million were provided through various funding mechanisms such as making supplemental grants and cofunding studies, over fiscal years 1991 through 1999.\textsuperscript{64}

4.1. "ORWH does not have a formal mechanism for monitoring how NIH’s institutes and centers implement the women’s health research agenda."\textsuperscript{65} Liaison is assured through a Coordinating Committee for Research on Women’s Health, whose members include institute or center directors or, more commonly, their delegates (d, e).

4.2. The Women’s Health Initiative has two co-study directors: the ORWH director and the National Heart, Lung, and Blood Institute director (a).\textsuperscript{66}

To summarize, then, GAO determines that NIH has made "significant progress" toward the goal that all NIH-funded studies "answer (...) research questions for as wide a segment of the population as is scientifically appropriate."\textsuperscript{67} Compared to the 10-year

\begin{itemize}
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 18.
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 21.
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 21.
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 22.
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 22.
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 21.
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 21.
\item United States, GAO 2000, \textit{Women’s Health : NIH…}, p. 22.
\end{itemize}
earlier report, considered "scathing" by observers, widespread awareness and understanding of the policy is now evident. It seems clear, however, that if inclusion of women has to some important extent been achieved (but see below for other opinions on this matter), the analysis by sex or gender is still incompletely achieved: "For the policy to have its intended effect, however, NIH needs to expand its focus beyond simple inclusion and to ensure that, when it is scientifically appropriate, researchers conducting clinical trials enroll populations and analyze study data in ways that enable them to learn whether interventions affect women and men differently." 

Underplayed as the language of the GAO is, the implicit criticism is nonetheless clear. The reader understands that the gender analysis dimension of the inclusion policy has not been attended to in sufficiently conscientious fashion; grant applicants were not informed in systematic fashion that trials should in general aim to allow for sex-based differences analysis; reviewers should explicitly consider whether the study is structured to allow for analysis by sex. Decisions on grant applications should check off on respect of the policy or, on the contrary, on the reasons justifying exclusion from application of the policy.

A data tracking system has been put into place by NIH, but GAO determines that follow-up on its efficacy and on its application – with training, in consequence, for NIH personnel – is needed.

2.1.2.2. Independent study of effects of NIH policy

These criticisms are confirmed by other, published sources in the medical literature and in literature dealing with women's health. In this material, other forms of evaluation are adopted, most notably analysis of published material and evaluation of whether this material indicates change which may have been generated by the NIH policy on inclusion of women in clinical trials and on analysis by gender.

Enrollment of women in NIH trials insufficiently changed; analysis by sex, also

Harris & Douglas obtained, through access to information legislation mechanisms, list and descriptions of cardiovascular clinical trials conducted from 1965 to 1998 through the National Heart, Lung, and Blood Institute (NHLBI). A total of 121 clinical trials had

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68 Helmuth 2000, p. 1562.
commenced posterior to NHLBI requiring researchers to document the sex of subjects enrolled in clinical trials. These trials were categorized according to the type of cardiovascular disease being investigated (heart failure, coronary artery disease, hypertension, etc.). Numbers of men and women enrolled were tabulated, according to category of disease and according to whether the trial was a mixed or single-sex trial. Finally, comparison is made with sex-specific prevalence of the diseases, as obtained from the American Heart Association.\textsuperscript{71}

More women are seen to be studied over the time period observed (a significant increase, $r=0.57$, $P=0.002$). However, excluding all single-sex trials from the analysis, the percentage of women did not increase significantly over time ($r=0.08$). One half of the marked increase in the enrollment of women occurred, in fact, within two large single-sex trials investigating primary prevention of coronary heart disease, the Women's Health Study (started in 1991) and the Women's Health Initiative (started in 1992).

These authors suggest that the efforts to increase the representation of women in clinical trials was "moderately successful".\textsuperscript{72} However, their analysis suggests that the implementation of the federal mandate on inclusion of women in trials and the temporal patterns of enrollment "appear to be unrelated."\textsuperscript{73} The sex composition of clinical trials is seen to have been altered "primarily through institution of large trials restricted to women."\textsuperscript{74} This observation is viewed with concern as under-representation of women persists in studies of particular types of cardiovascular disease. The large single-sex trials instituted have not covered the broad spectrum of cardiovascular diseases which affect women as well as men.

It is suggested that sub-group analysis must be included in the study design. Data suggests that such analyses are performed only infrequently.

Vidaver et al. examined publication in four major medical journals in four separate years, of original research articles funded by NIH, and reporting on non-sex-specific studies. Thus the New England Journal of Medicine, the Journal of the American Medical Association, the Journal of the National Cancer Institute and Circulation furnished over 800 articles, the analysis of which generated the following observations.

\textsuperscript{71} Harris & Douglas 2000.
\textsuperscript{72} Harris & Douglas 2000, p. 475.
\textsuperscript{73} Harris & Douglas 2000, p. 478.
\textsuperscript{74} Harris & Douglas 2000, p. 478.
One fifth of the studies excluded women as subjects, thus "apparently violating the NIH guidelines." The proportion of women included as research subjects did not change significantly between 1993 and 1998 (p=0.22)\textsuperscript{75} (total coverage included four publication years: 1993, 1995, 1997, 1998). Differences were noted between journals, an increase being noted in the case of \textit{JNCI}, but no clear trends observed for the other journals.

Further, the proportion of women included as research subjects in NIH-funded, non-sex-specific clinical trials increased over time also, from 81% inclusion in 1993 to 93% inclusion in 1998. This increase, however, is not significant (p=0.63). All journals except \textit{Circulation} showed improvement in regard to reporting inclusion of women in clinical trials.\textsuperscript{76}

Of the non-sex-specific studies including women, it was found that between one half and three fifths made no mention of either presence or absence of effects due to the sex of the subjects. The analysis by sex did, however, increase significantly (p=0.011) over the five-year period. The increasing trend was observed in \textit{JAMA} between 1993 and 1997, with diminution in 1998.\textsuperscript{77} This author (jc) notes that in the case of the other three journals, the increasing trend in between 1993 and 1998 is subject to important variations, thus suggesting the interest of further measurement over time to ascertain the stability of the observed significantly positive trend.

Of the clinical trials including women, very few made any mention of analysis of outcomes in relation to sex of the subjects, and no significant change occurred in this regard between 1993 and 1998 (p=0.48).\textsuperscript{78} Telephone interviews were initiated with primary investigators of articles published in 1998 whose data covered men and women but in which no analysis by sex was offered. Of 18 studies thus explored further, 6 involved samples too small to adequately analyse, 3 included significant outcomes which had resulted in separate publications, 1 showed significant outcome so well known (sex difference in onset and treatment of acute lymphoblastic leukemia) that no separate publication was deemed useful; 3 authors noted no sex differences and therefore refrained from discussing this result, and 5 authors gave no reason for excluding analysis by sex of the subjects.

\textsuperscript{75} Vidaver et al. 2000, p. 497; see correction, p. 1042.
\textsuperscript{76} Vidaver et al. 2000, p. 497; see correction, p. 1043.
\textsuperscript{77} Vidaver et al. 2000, p. 497; see correction, p. 1043.
\textsuperscript{78} Vidaver et al. 2000, p. 499; see correction, p. 1043.
Another study, Ramasubbu et al. (2001), documented patterns of enrollment seen in *New England Journal of Medicine* articles published from 1994 to 1999. A first selection was made of articles describing randomized clinical trials in which the primary end point was total mortality or included mortality in a composite end point. Trials were then further analysed for enrollment of women with respect to disease state, funding source, site of trial performance, and use of gender-specific data analysis. Of 1322 original articles, 442 randomized, controlled trials led to retention of 120 articles meeting the inclusion criteria. Forty-three percent of the trials involved cardiovascular diseases; the remaining 57% were distributed among eight other medical specialties. In the 120 trials, over 160,000 participants were enrolled, of which less than 40,000 were women (24.6%). One-way analysis of variance (ANOVA) showed no significant differences in the enrollment of women among the various disease areas. Representation of women did not differ significantly with regard to funding source, or site of trial.

This study compared the enrollment of women before and after the 1993 legislatively imposed changes at NIH. Results showed "no significant changes in the enrollment of women over the last decade." Further, it is pointed out that these results are representative of findings in the international research scene.79

Results were analysed by gender in only 17 of the 120 trials, 12 of which involved cardiovascular diseases.80

One older study documents underrepresentation of women in medical studies more often than men, in publications of *JAMA* from 1990 to 1992. Further, data from studies including both men and women was in many instances not analysed by gender or sex.81 Beyond the evident advantage which could accrue to women in terms of better understanding of health and illness, with consequent betterment of health care, Bird points out that "a thorough understanding of men's and women's physiological responses to treatment may lead to better medical treatments for both men and women."82

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79 Ramasubbu et al. 2001, p. 761.
80 Ramasubbu et al. 2001, p. 760.
81 Bird 1994.
2.1.2.3. NIH’s monitoring of adherence to policy (2002)

A recent update (December 2002) presents NIH’s report on monitoring adherence to the policy on inclusion of women and minorities as subjects in clinical research.\(^{83}\) The report notes, as well, recent initiatives taken in light of the above-mentioned GAO report (2000) on NIH’s policy.

NIH notes that the 1993 Revitalization Act “essentially reinforced” existing NIH policies encouraging the inclusion of women in clinical trials and requiring a rationale for exclusion. The 2000 GAO report is noted as having stimulated some changes in NIH actions, including October 2001 update in *Inclusion of Women and Minorities Policy Implementation*.\(^{84}\)

Indeed, in our first stages of research, on 23 October 2002 we accessed from the web site of NIH a version of the guidelines as amended in August 2000. Having now in hand the current version (October 2001)\(^ {85}\), we note that there are some significant changes between the two versions, in particular:

- addition\(^ {86}\) of a clear presentation of the legislation itself, in everyday language with reference to the original legislative text;

- adjustment of the text of the policy, replacing the text "biomedical and behavioral research projects involving human subjects" by the term "clinical research";\(^ {87}\)

- changes in the nature of the obligations of researchers in regard to Phase III clinical trials. Pre-2000, researchers were requested to be attentive to possible "gender" differences; as of 2000, *sex* differences are also signalled. *Analysis* of gender and sex differences is more clearly obliged after amendments of 2001, as in planning, conducting, *analyzing* and reporting on Phase III clinical trials in 2000.\(^ {88}\)

The Outreach booklet, an exceedingly useful document for presentation in easy-to-

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\(^{83}\) United States, NIH 2002.


\(^{85}\) Research contracts and research grants are treated differently, but this difference was not deemed of particular relevance to the issue under study, and was ignored.

\(^{86}\) Our downloads came from different "areas" of the large NIH web site. This may explain the addition we noted. Notwithstanding, we found it surprising to have been able to download a version more than one year out of date.

\(^{87}\) Yet, it is clear (see GAO report, above) that it has always been Phase III clinical trials which were the object of the present policy.

\(^{88}\) United States, NIH 2000, and United States, NIH 2001, last paragraph of section B in both documents.
understand form, was also recently updated and made available on Internet.\textsuperscript{89}

Guidelines and instructions for reviewers and Scientific Review Administrators were developed, whereupon training was provided to staff, management, and current and prospective research investigators.\textsuperscript{90}

Having furnished this background, NIH reports on inclusion data and enrollment figures, noting that its policy does not aim to satisfy quotas for proportional representation but rather to generate scientific knowledge generalizable to the population of the U.S. The number of women or minority subgroups included in any particular study is a function of the precise scientific question and the prevalence among women and minorities of the disease, disorder or condition under study.

Aggregate data is summarized, showing that for all extramural research protocols, women represent 61.6\% of subjects in studies funded in FY2000, a marginal decrease of 0.3\% compared with FY1999.\textsuperscript{91} Excluding one-sex only protocols, women represent one half of the subjects (50.2\% in FY2000, 50.1\% in FY1999) in extramural research protocols.\textsuperscript{92} Extramural Phase III protocols are made up of 70.9\% women subjects in FY2000, compared to 63.3\% in FY1999.\textsuperscript{93} These last figures are respectively 45.5\% and 45.9\% in the case of Extramural Phase III studies excluding one-sex only protocols.\textsuperscript{94} Aggregate data, by minority group, is presented by institute or center. However, there is no presentation of data disaggregated by sex.

Further, it bears noting (see Table 1) that, excluding male-only and female-only protocols, aggregate enrollment data for extramural research protocols and for extramural phase III research protocols show a decrease in the percentage of women participating as clinical subjects, over the years for which data are available.

\begin{itemize}
  \item \textsuperscript{89} See United States, NIH [1997] and United States, NIH 2002a.
  \item \textsuperscript{90} United States, NIH 2002, pp. 5-6.
  \item \textsuperscript{91} United States, NIH 2002, Tables 1 and 2.
  \item \textsuperscript{92} United States, NIH 2002, Tables 3 and 4.
  \item \textsuperscript{93} United States, NIH 2002, Tables 5 and 6.
  \item \textsuperscript{94} United States, NIH 2002, Tables 7 and 8.
\end{itemize}
Table 1. Aggregate Enrollment Data for Extramural Research Protocols (FY97 – FY2000) and Extramural Phase III Research Protocols (FY98 – FY2000) (in all cases, excluding Male-Only and Female-Only Protocols)

<table>
<thead>
<tr>
<th></th>
<th>Aggregate Enrollment Data for Extramural Research Protocols, excluding one sex only protocols</th>
<th>Aggregate Enrollment Data for Extramural Phase III Research Protocols, excluding one sex only protocols</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FY97\textsuperscript{95}</td>
<td>FY98\textsuperscript{96}</td>
</tr>
<tr>
<td>Women</td>
<td>52.1%</td>
<td>55.0%</td>
</tr>
<tr>
<td>Men</td>
<td>46.6%</td>
<td>43.7%</td>
</tr>
<tr>
<td>Unknown</td>
<td>1.3%</td>
<td>1.2%</td>
</tr>
<tr>
<td>Total</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
<tr>
<td>Women</td>
<td>2,536,104</td>
<td>2,475,680</td>
</tr>
<tr>
<td>Men</td>
<td>2,016,445</td>
<td>2,426,526</td>
</tr>
<tr>
<td>Unknown</td>
<td>57,381</td>
<td>44,066</td>
</tr>
<tr>
<td>Total</td>
<td>4,609,930</td>
<td>4,946,272</td>
</tr>
</tbody>
</table>

Source: NIH (see notes in table).

2.1.3. FDA oversight needs improvement

In 1992 GAO published a review of FDA's study of gender differences in prescription drug testing. In brief, GAO then reported that FDA recommended testing of new drugs on "representative" patient populations without defining "representative". Inconsistency of application of the recommendation characterised manufacturers' actions. Half of manufacturers claimed to have not been informed of recommendation to include women in drug trials. Women were included in clinical trials for all drugs in GAO's early-1990s survey, but they were generally underrepresented in those trials. However, even when sufficient numbers of women were included in drug testing, trial data often did not analyze responses by sex.\textsuperscript{102}


\textsuperscript{95} United States, NIH 2000a, GAO Report Table 2, no page number.
\textsuperscript{96} United States, NIH 2001a, Table 3, p. 18.
\textsuperscript{97} United States, NIH 2001a, Table 4, p. 18, confirmed in United States, NIH 2002, Table 4, p. 21.
\textsuperscript{98} United States, NIH 2002, Table 3, p. 21.
\textsuperscript{99} United States, NIH 2001a, Table 7, p. 22.
\textsuperscript{100} United States, NIH 2001a, Table 8, p. 22, confirmed in United States, NIH 2002, Table 8, p. 25.
\textsuperscript{101} United States, NIH 2002, Table 7, p. 25.
In 2001, the GAO makes the link between their previous report and the more recent one in the following terms:

*In 1992, we reported that the Food and Drug Administration (FDA) was not adequately ensuring the representation of women or the study of sex differences in clinical drug trials conducted by the pharmaceutical industry. Although FDA subsequently has taken some steps to increase the participation of women in clinical drug trials, concerns remain that women continue to be underrepresented and that sex differences in responses to drugs continue to go unexamined during drug development.*

GAO’s assessment is done in the following way.

GAO examined new drug applications (NDAs) submitted over some 28 months ending 31 December 2000. For eligibility in this study, the NDAs for new molecular entities (NMEs) needed to have been approved or have been categorized as approvable in that time frame, and be labeled for use in both men and women. Some biologic products were excluded. Three critical summary documents submitted by the sponsor of the drug were analyzed, as well as one produced by the FDA Medical Officer Review, thus obtaining prescribed summaries of clinical trial data. Further, 100 annual reports for investigational new drugs (INDs) were randomly sampled. INDs are drugs in development for which, typically, FDA approval has not yet been sought.

**FDA recommends** (i.e., not binding) in 1993 that clinical studies include enough men and women to detect clinically significant sex differences in drug efficacy and safety, and that sex-differences be reported in NDAs.104

In 1998, a regulation (therefore binding) replaces the guidance but it "is less specific than the guidance."105 It is required that safety and efficacy data already collected be presented separately for women and men in NDA summary documents. (It is useful to remember that each NDA requires report of at least one pivotal clinical trial, a Phase 3 study, "adequate and well-controlled," demonstrating the efficacy or effectiveness of the drug.106) The distinction between data presentation and data analysis is not explained in the regulation. No criteria exist for determining number of women needed in clinical studies. No requirement is specified concerning analysis of the data. Tabular

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102 United States, GAO 1992, *Women’s Health. FDA …*
presentation of study participants by sex is required in IND annual reports.\textsuperscript{107}

The regulation of 2000 permits FDA to stop some trials if women are excluded from participation based solely on their reproductive potential, but the regulation does not require inclusion of any particular number of men or women.\textsuperscript{108}

\textbf{Non-compliance}

GAO reports that these rules were in many instances not followed by drug sponsors, with seemingly no consequences. Data presentation requirements of the 1998 regulation were "often" not met. In about one third of NDAs summary documents did not fulfill "requirements for the presentation of available safety and efficacy outcome data by sex."\textsuperscript{109} 39\% of IND annual reports failed to include the demographic information required by regulation.

All of the NDAs examined by GAO included enough women to demonstrate efficacy of the drug in women. It is clear then that the absence of safety and efficacy outcome data by sex, noted above, is an issue of non-compliance.

Women represented, overall, 52\% of study participants. Women represent a larger percentage of participants in clinical drug trials in this period compared to the study of GAO done approximately a decade earlier. The percentage of women participants in small-scale efficacy and full-scale safety and efficacy trials increased from 44\% to 56\% in NDAs examined in 1992 and 2001, respectively. However, early safety studies are used to set dosing levels for larger-scale trials, and women represent only 22\% of participants in these initial, small-scale safety trials.

GAO points out that NDAs usually contained sex-related analyses of safety and efficacy, although outcome data presented in summary documents might be absent despite regulatory obligation in this regard. Many of the NDAs reviewed by GAO reported differences in men and women's responses to drugs, some of which were statistically significant. However, GAO found no evidence of any of these sex differences being judged to be clinically relevant by NDA sponsors or by FDA reviewers, and no dose adjustments based on sex were recommended.\textsuperscript{110}

\begin{thebibliography}{9}
\end{thebibliography}
GAO notes that there "is no management system in place to record and track the inclusion of women in clinical drug trials or to monitor compliance with relevant regulations, so FDA is unaware that many new drug application submissions failed to meet standards." Absent, also, are routine following of annual reports for drugs in development; and routine following of medical officers' reviews of NDAs, who in turn are not required to discuss sex differences in their reviews of NDAs and who do not systematically entertain this discussion. Recent initiatives (worksheet to be used by reviewers, so as to standardize the application review process) were being tested by FDA, the GAO reports, and they might would possibly answer some of these issues.

Compared to the actions taken at NIH, it seems that FDA's activities may perhaps have been implemented with somewhat less attention to the conditions of success. We shall return to this case, along with the others, in our discussion.

2.1.4. National Centers of Excellence in Women's Health

We shall give short attention to the American programme, created in 1996, of National Centers of Excellence in Women's Health. This item merits a brief justification.

The issue before us is one of aiding and supporting increased attention to gender and sex differences in health research. We have seen that some of the clearly relevant initiatives, examined above, concern women's health in particular. Just as the Canadian Centres of Excellence for Women's Health are described as one of three important measures (the 3rd is creation of CIHR, including IGH) to better research gender and sex differences, so the American programme merits at least a summary review.

The Office on Women's Health of Health and Human Services in the U.S. compared the impact of National Centers of Excellence (CoEs) with a national sample of hospital-sponsored clinical health women's health centers. We are less concerned with results pertaining to health delivery issues than with results which speak to research issues.

It is important to note, however, that the CoEs contribute to "an expanded knowledge..."
base on women's health in multiple ways: enhancing the biomedical and health services research agenda in women's health; obtaining funding for women's health research; increasing opportunities to translate research into clinical practice; and expanding resources for recruiting women (including minority women) into clinical studies.¹¹⁴ Further, CoEs are "substantially more likely than centers in the [U.S.] national sample (75% VS. 21%) to report having implemented a commitment to women's health research."¹¹⁵ Research is of course a required component of the CoE program. CoEs also have a greater likelihood of providing clinical training than in the national sample.¹¹⁶ Authors of this study conclude:

> the CoE program has encouraged – or is giving visibility to – academic health centers that are furthering the institutional integration of women’s clinical care, women’s health research, and medical education in women’s health. Furthermore, because of their location in academic health centers, the CoEs may provide for a new generation of clinicians, administrators, and researchers committed to women's health issues.¹¹⁷

### 2.2. Europe

#### 2.2.1. The European Union

Attention to gender and to sex differences in research is seen as one part of a set of broader gender and women’s issues within the European context. This context is marked notably by a policy of "mainstreaming gender equality,"¹¹⁸ which appears to be an effective policy mechanism for advancing women’s issues in general in Europe since 1996.

Our examination of the specific issue of sensitivity to gender and sex differences in research is best understood as a dossier or issue which has been advanced within this larger context of "mainstreaming".

In overview, the European Union has, recently, initiated a number of important activities dealing with "women in science" issues.¹¹⁹ Changes brought about in the Fifth

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¹¹⁴ United States, OWH 2000, p. 2.
¹¹⁵ Weisman & Squires 2000, p. 252.
¹¹⁸ See European Commission, "Incorporating equal opportunities for women and men into all Community policies and activities," Communication COM (96) 67 final.
¹¹⁹ European Commission, "Women and Science: mobilising women to enrich European research," Communication COM (99) 76 final; hereafter referred to as Europe, Commission 1999, "Women and
Framework Programme, will be examined in more detail below.

The ETAN Report of 2000 examined science policies in the European Union, and the place of women in the implementation of such policies, as researchers, as decision-makers, etc. That report noted, *inter alia*, that women form 7% or less of full professors in 6 Member States. Although they constitute half of the undergraduate population, a continuous drop in numbers of women is manifest at each level of the academic ladder. Such loss of highly trained women to science is obviously to be deplored. Employment and promotion procedures in some academic institutions have not sufficiently evolved to more sophisticated means of evaluating merit. In Sweden, the peer review system was shown to be affected by both sexism and nepotism, and follow-up studies elsewhere generated equivocal results. Mainstreaming gender equality is proposed to be implemented into the Sixth Framework Programme.\textsuperscript{120}

The report produced in 2002 by the "Helsinki Group" (a group of national civil servants whose work started in 1998 in Helsinki, from whence its name) contributed further to documentation of under-representation of women in European research; horizontal segregation of women, with restricted numbers in certain disciplines; vertical segregation of women, for instance in relation to representation in decision-making bodies; differential pay levels; and differential success rates within the research environment. Obviously, these are issues of discrimination and bias, but also of lost opportunity to benefit from a wealth of experience and creativeness. The Helsinki Group’s work contributed to production of sex-disaggregated statistics and to developing gender sensitive indicators to better monitor women's participation in European research.\textsuperscript{121}

\textbf{2.2.1.1. Toward "mainstreaming" of gender equality in research}

Gender mainstreaming – or integrating gender into all major European policy areas – has formed the European Commission’s strategic approach to the issue of *equal opportunities* between women and men in the European Community. Equal opportunity, established as a concept in the 1950s in Europe, originally was limited to the principle of equal remuneration. Since 1996, after the 1995 UN World Conference on Women in Beijing, the concept is applied to gender equality and constitutes a policy to be implemented in all institutions, policies, programmes and practices of the European
Mainstreaming of gender equality in the area of science and technology was made explicit at the time of the launching of the Fifth Framework Programme for research and technological development (1998-2002). This policy approach has thus been on the public agenda in Europe for a number of years.

When launching the Fifth Framework Programme for research and technological development (1998-2002), the Commission decided to include the equal opportunities dimension by promoting the participation of women in European research. It had announced its intention to do so in its progress report on the follow-up of the communication: "Incorporating equal opportunities for women and men into all Community policies and activities" (COM(98)122 final).

2.2.1.2. Gender equality in research: by, for and on women, a three-pronged approach

The commitment to mainstream gender equality in regard to research has led to encouragement of the participation of women in research and technological development (RTD) within the Fifth Framework Programme (1998-2002), commonly referred to as FP5. This promotion takes place at several levels: "the aim must be to promote research by, for and on women." "Research by women" constitutes the dominant approach supported by gender mainstreaming in the European context ("research by women means the promotion of women as research workers and as involved in the various stages of the process of consultation and implementation for the 5th Framework Programme"). It has also been qualified as a largely "quantitative approach, which consisted of simply counting the number of women and men involved in our research programmes".

Through this work on gender equality in Europe, many new and well-documented studies have characterized the positions which women occupy in the scientific community, their numbers relative to the total population of researchers, by country and

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121 Europe, Helsinki Group 2002.
122 Europe, Gender in Research 2001, p. 8. The legal framework within which are set these initiatives and activities in Europe is the following: "When the Community was set up, the concept of equal opportunities for men and women was limited to the principle of equal remuneration. Equality of opportunity is now enshrined in Articles 2 and 3 of the Treaty of Amsterdam as one of the European Union’s objectives. The Treaty’s new Article 13 will enable appropriate measures to be taken against discrimination, while Article 141 provides the specific legal basis for equality of treatment between men and women" (Europe, Commission 1999, "Women and science," p. 5).
in all of Europe, etc. Further work has attempted to clarify issues raised by this situation for science in Europe, and for women: lost opportunities, obstacles to change, and avenues for transformation. Insofar as these studies do not deal directly with support of gender- and sex-difference-sensitive research, we do not report on them. However, these studies shed important light on some aspects of research and science, to which we shall return in discussion.

"Research on women" focuses on "the contribution which research can make to our knowledge of what it is to be a woman, and of gender and gender relationships and of the impact of these concepts on European society". Again, we do not report in detail on this part of the European approach, but we shall comment on it in discussion.

Concerning research for women, the Fifth Framework Programme (1998-2002) (FP5) in Europe was oriented towards funding research aimed at answering human and social needs and the pursuit of socio-economic objectives, in contrast to previous scientific and technological discipline-based support. In this context, the programme on "Quality of life and management of living resources", for example, aimed to support research into chronic and degenerative diseases and into genomes and diseases of genetic origin, neurosciences, public health and health services research. This concern, part of a three-pronged approach, "implies vigilance when drawing up the work programmes and an in-depth analysis of how all the fields covered by research affect women".

The Work Programme as locus of gender mainstreaming

Within FP5 (subject to calls for proposals), the Work Programme is the main reference document for proposers of research projects. One finds therein the research objectives and the topics to be researched. The Work Programme guides the formulation of proposals, assigning priorities with respect to strategic objectives of each FP5 programme and outlining quality criteria to be applied in the evaluation and selection process.

It is clear, then, that the Work Programme constitutes a pivotal element for the success of mainstreaming of gender in FP5.

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126 Europe, Gender & Research 2002, p. 5.
The Commission Communication (1999) Women and Science states that: “...When drawing up and implementing the Work Programmes, account will be taken of a possible gender dimension in the problems and challenges addressed by the Key Actions and, in a broader sense, by the specific programmes as a whole. Where ever the topic merits consideration from a gender point of view this will be stated in the Call for Proposals...” It is recognised that this is part of a process, and its effectiveness will depend upon the gender awareness of the Commission officials responsible for the Work Programme. until the overall level of gender expertise is improved and opportunities to incorporate the gender dimension are made explicit. The gender impact assessment studies will contribute to the latter.

These Gender impact assessment studies are reported on the in the next section.

2.2.1.3. Gender impact assessment studies

Seven gender impact assessment studies were carried out on specific programmes or sub-programmes of the Fifth Framework Programme (1998-2002) (FP5) of the EU. These studies formed part of a gender impact assessment exercise launched with the objective of understanding how gender issues were addressed within FP5.

We shall review the overall conclusions of the synthesis report produced on the basis of the seven studies. However, we shall concentrate particularly on one of those seven studies, one which deals with health research, the Quality of Life (QoL) study.

Figure 1. FP5 programmes studied for gender impact assessment (GIA)

- Quality of Life Study – Quality of Life and Management of Living Resources programme
- IST Study – User-Friendly Information Society programme
- Energy Study – Energy sub-programme of the Energy, Environment and Sustainable Development programme and the specific component “Research and training in the field of energy” of the Euratom programme
- Environment Study – Environment and Sustainable Development sub-programme of the Energy, Environment and Sustainable Development programme
- INCO Study – Confirming the International Role of Community Research programme

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130 Europe, Gender in Research 2001, p. 19.
132 Europe, Gender in Research 2001.
• **Innovation and SME Study** – Promotion of Innovation and Encouragement of Participation of Small and Medium-sized Enterprises programme

• **Human Potential Study** – Improving Human Research Potential and the Socio-economic Knowledge Base programme.

**Method of evaluation**

In each of the studies, the researchers first produced an overview of the current state of knowledge of gender and sex issues in the specific area (through bibliographic search and use of known key documents in the area). This research furnished the standard against which the study could evaluate FP5-supported actions (research projects). Assessment was also made of the implementation process.

In the case of the QoL study, principal documentary and bibliographic sources included an earlier critical assessment of FP5,\(^{133}\) other published studies,\(^{134}\) development and exploitation of an inventory of international bibliographies on gender and science, gender and health, and gender and technology,\(^{135}\) and keyword searching in IIAV (International Information Centre and Archive for the Women's Movement) and Medline, two databases respectively specialised in gender literature and in health related literature.\(^{136}\) A Gender Impact Resource (GI-Resource) was thus developed to be used for assessment of QoL programme. An analytical tool was developed for assessment of funded research, (Gender Impact Assessment (GIA) Protocol), inspired by a number of existing gender impact assessment instruments designed to evaluate topics as diverse as research, health education, curriculum development and policy decisions, from a gender perspective.\(^{137}\) Further assessment of the nature of the projects, their implementation, analyses, etc. was structured through consultation of recent work on state of the art of gender and science research (Schiebinger), proceedings of recent conferences (e.g., on advances in women and health research: toward gender sensitive strategies) and the gender-based analysis guide prepared by Women's Health Bureau.

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\(^{134}\) See Klinge & Bosch 2001, pp. 53-58.


\(^{136}\) See Klinge & Bosch 2001, pp. 63-103.

\(^{137}\) Klinge & Bosch 2001, p. 45.
The GIA Protocol permitted to identify, for evaluation: research projects concerning humans. Studies were differentiated as to whether they addressed or not sex and gender differences documented in state of the art literature review (see the following questions 2a and 2b, with accompanying summary tables, reproduced from the protocol\textsuperscript{138}). Finally, the presence or absence of commonly-known problems of gender bias\textsuperscript{139} involving over-generalisation, gender insensitivity and double standards is elucidated and documented through study of the research projects’ supporting proposal documentation.

### Figure 2. QoL GIA Protocol extract: Tool for identifying sex and gender differences

2a) Are sex or gender differences with respect to the object of study documented in the literature?

2b) Does the study address sex or gender differences?

<table>
<thead>
<tr>
<th>sex differences</th>
<th>documented in the literature</th>
<th>not documented in the literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>addressed in the proposal</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>not addressed in the proposal</td>
<td>-</td>
<td>0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>gender differences</th>
<th>documented in the literature</th>
<th>not documented in the literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>addressed in the proposal</td>
<td>+</td>
<td>++</td>
</tr>
<tr>
<td>not addressed in the proposal</td>
<td>-</td>
<td>0</td>
</tr>
</tbody>
</table>

+ Adequate - Missed sex and / or gender aspects
++ Innovative 0 Sex and / or gender aspects remain to be studied


In summary, then, the gender impact assessment studies aim to analyse the implementation of each specific programme, including the **participation of women and**

\textsuperscript{138} Klinge & Bosch 2001, p. 29.
men and the mainstreaming of gender in programme management and implementation processes, for example proposal writing material and evaluation criteria. Also, assessment is made of the gender impact on the research area in terms of how the gender dimension has been incorporated into the content of each Work Programme and the proposals submitted.\textsuperscript{140}

**Results of gender impact assessment (GIA) studies: conceptual background**

The results of the seven studies of the gender impact assessments have many common characteristics.

In common with views of other observers, these studies point to the need to distinguish gender and sex issues. It is pointed out, further, that other forms of diversity need also be considered, such as age, ethnicity and sexual orientation.

It is suggested, in a European Union perspective, that the "studies highlight the need to reach beyond a sex-counting approach by recognising the transformation implicit in a more far-reaching gender mainstreaming policy." It is suggested that:

\begin{quote}
A true integration of gender into research would profoundly affect the way in which scientific knowledge is defined, valued and produced, the methodologies that are invoked, and the theoretical reflections to which such new modes of knowledge give rise.\textsuperscript{141}
\end{quote}

New epistemological approaches are favoured, suggesting that the scientific agenda would benefit from integration of natural, technological and social sciences and use of interdisciplinary and transdisciplinary research and methods. Thus one could surpass gender-biased epistemological assumptions of science and build a "re-constructive" perspective allowing for basic research to encompass a gender perspective, to include the use of a diversity of research subjects, and to ask different and new research questions.

Other issues touched upon by all the studies are: Gender-disaggregated statistics are, in many areas, non-existent, scarce or fragmented. Education in science and technology is affected by gender bias and gender stereotypical approaches. There is unequal representation of women in decision-making processes and in positions of leadership within scientific institutions.

\textsuperscript{139} Cf. Eichler 1988 for early presentation of these issues.
\textsuperscript{140} Europe, Gender in Research 2001, p. 6.
\textsuperscript{141} Europe, Gender in Research 2001, p. 12.
Results of GIA studies: participation of women

The Commission has set a target of at least 40% female participation in a number of institutional structures (Marie Curie Scholarships, advisory groups and assessment and monitoring panels of the FP5). The participation of women in the FP5 implementation process is, of course, considered highly significant in integrating gender into European research.

It is recognised in the gender impact assessment studies that statistical data on participation of women is easier to access than previously, although the process of bettering this capacity is still in its early stages. The principal transferable observations of GIA studies are the following: the assigning of quantified targets should represent a challenge yet be realistic (a target insufficiently ambitious is of little use, one overly-ambitious is potentially demobilising); and targets should take into account the potential basin from whence participants will be recruited. The following observations, indicate the nature of difficulties which influence the participation of women in research:

- lack of women in some instances (e.g., shortage of women in Commission's expert database),
- practical constraints (family-work conciliation difficulties),
- constraints due to selection practices (tendency to select within the circle, or among known entities (persons)),
- ascending learning curve (under-representation of women in hierarchical positions of research organisations, and time and encouragement and incentives necessary before change occurs),
- strong vertical segregation in most programmes,
- perceived male-dominated culture (difficulty of raising awareness of gender issues, in situation of perceived or real male-dominated culture; discouragement of female participation in a programme with a masculine face.

Results of GIA studies: FP5 implementation cycle and research areas (Work Programmes)

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142 Europe, Gender in Research 2001, p. 15.
Finally, as concerns the content of the *Work Programmes*\(^{143}\) the major observations are:

- multidisciplinary and multisectoral activities, part of FP5 programming,\(^{144}\) facilitate integration of gender aspects by allowing consideration of socio-economic dimensions in research, and encouraging involvement of a variety of actors (researchers) from different sectors;

- it was noted that, except in the Quality of Life programme, gender dimension was introduced via consideration of socio-economic aspects. In QoL programme, entry-points for gender dimension are not limited in this way. "For example, if biological differences between women and men are not taken into account, medical research takes the male body as a norm, resulting in medical advances which are not tailored to the needs of women"\(^{145}\);

- the gender mainstreaming approach is currently incomplete: proposal preparation material clearly promotes equal opportunities for women and men, and encourages participation of women. In other words, solely research by women is addressed by such a formulation. "The current statements (…) do not concern the integration of the gender dimension in the content of policies, programmes, specific research topics or FP5 actions, failing to address research for and about women"\(^{146}\);

- implementation of a "pre-proposal check" is suggested, thus permitting early feedback and explicit recommendations regarding the integration of gender into proposals;

- the evaluation process ensures conformity to priorities and common criteria of Community research policies. However, the Guide for Evaluators makes no explicit mention of gender in the evaluation criteria, in terms of participation of women and men in the proposal, attention to equal opportunities, or gender issues within the project's objectives and activities.\(^{147}\) Supporting documents make no mention of gender either (for instance, in explanation of the evaluation criterion "Contribution to

\(^{143}\) Most studies based the gender impact assessment on the Work Programme of 1999. The Quality of Life study assessed the 2000 version (with review of 2001).

\(^{144}\) Europe, Gender in Research 2001, p. 19.

\(^{145}\) Europe, Gender in Research 2001, p. 20.

\(^{146}\) The evaluation criteria are: scientific and technological quality and innovation; Community added value and contribution to EC policies; contribution to Community social objectives; economic development and scientific and technological prospects; and resources, partnership and management. See Europe, Gender in Research 2001, p. 21.
Community social objectives," there is no mention of gender;\footnote{In this section of the report on Gender impact assessment studies, reference is indeed made solely to gender, as reported here. Europe, Gender in Research 2001, p. 21. However, in Klinge & Bosch 2001, p. 41, the issue of sex differences in public health (n.b., in coronary heart disease, cancer, osteoporosis and depression) is also discussed.}

- "The studies concluded that the gender dimension is not yet integrated into the evaluation criteria and procedures and so limited attention is currently paid to gender issues during evaluation."\footnote{Europe, Gender in Research 2001, p. 22.} Assessing integration of gender in proposals is said to be a task not reducible to quantitative measure, requiring on the contrary specific gender competence of expert evaluators and of the Commission officials involved;

- "The main outcome of the analysis is that the gender dimension is not being integrated in proposals."\footnote{Europe, Gender in Research 2001, p. 22.}

**Results of GIA studies: the Quality of Life (QoL) programme of FP5**

The thematic programme, *Quality of Life and Management of Living Resources* (QoL), of the Fifth Framework Programme dealt to a strong degree with health, health care and public health, and for this reason a focus, in the assessment study, on gender and health was considered appropriate.\footnote{Klinge & Bosch 2001, p. 8.}

Following on the presentation of the previous section, the main results of this study may be summarized in this way:

- Concerning "science by women," the QoL study argues for "a more contextual approach to target figures." "For decision-making bodies such as the Programme Committee (which is not mentioned in the EC Communication but should be included), the External Advisory Groups and the High Level Expert Groups a 40 to 50% representation of women is justified and realistic." Women represent only 24% of the members of the Programme Committee (8 of 34). Nine of fifteen member states are represented by men only; two by women only. External Advisory Groups achieved a mean participation of women of 37%, from a database composed of 15% women approximately. As with the other GIA studies, vertical and horizontal segregation is observed.\footnote{Klinge & Bosch 2001, pp. 10-11, 112, 114-115, 117-119.} It may be said, nonetheless, that in general, in this programme women are fairly well represented, at levels above their presence in the
respective basins of population.\footnote{Europe, Gender in Research 2001, p. 24.} Further, the authors of the GIA QoL study conclude:

*that during the short time that the inclusion of more women in various committees and evaluation panels has been on the agenda [in QoL], this policy has been very fruitful. Even if we have no precise data about women’s participation in FP4, nor about women working in the field of the life sciences in the EU countries, from the scant information there is, we may conclude that the gender balance for the important committees, as well as for the projects is rather good. This success deserves to be mentioned explicitly.*\footnote{Klinge & Bosch 2001, p. 141.}

Two drawbacks to this positive development are signalled: overwork for women involved in the process and the need for more women recruits; and the possibility that this could lead to lower quality standards. Open discussion and monitoring of the issue are called for.

- Concerning "science for and about women," it is fairly clear "that the qualitative aspects of integrating the gender dimension in science are as yet hardly a systematic part of any agenda." Interviews\footnote{Klinge & Bosch 2001, p. 131; e.g. in Key Action 2, p. 159.} with EC officials who were not part of the Women and Science Group (within QoL) revealed that they were only vaguely aware of the GIA study, and it had not been part of any agenda. Moreover, the issue of gender expertise as part of qualities required for participants in the various groups involved in the FP5 decision-making bodies has never been raised.\footnote{Klinge & Bosch 2001, Key Action 1 (Food, nutrition and health), p. 144.} However, changes have been brought to the Work Programme 2001, by comparison to that of 2000, in regard to attention to gender.\footnote{Klinge & Bosch 2001, Key Action 2 (Control of infectious diseases), p. 146, Key Action 5 (Sustainable agriculture...), p. 149, Key Action 6 (The ageing population and disabilities), p. 150, Generic Activity 7 (Chronic and degenerative diseases...), p. 151, Generic Activity 8 (Research into genomes and diseases of genetic origin), p. 152, Generic Activity 9 (Neurosciences), p. 153, Generic Activity 10 (Public health and health services research), p. 154.}

- Individual Work Programme action lines (i.e. encompassing both Key actions and Generic Activities) announce the general tenor of actions and activities to be funded. The researchers conclude that (quite systematically) categories in these Work Programmes remain undifferentiated,\footnote{Klinge & Bosch 2001, Key Action 1 (Food, nutrition and health), p. 144.} aspects of diversity covered in the relevant literature are missing,\footnote{Klinge & Bosch 2001, Key Action 2 (Control of infectious diseases), p. 146, Key Action 5 (Sustainable agriculture...), p. 149, Key Action 6 (The ageing population and disabilities), p. 150, Generic Activity 7 (Chronic and degenerative diseases...), p. 151, Generic Activity 8 (Research into genomes and diseases of genetic origin), p. 152, Generic Activity 9 (Neurosciences), p. 153, Generic Activity 10 (Public health and health services research), p. 154.} gender aspects documented in the literature are absent\footnote{Klinge & Bosch 2001, Key Action 1 (Food, nutrition and health), p. 144.}
or potentially not sufficiently exploited, mention of sex or gender is made not at all or just marginally, etc.

- Abstracts of funded research projects were assessed according to the schema noted above in Figure 2. The gender dimension is missing from proposals. 83 projects involved humans as objects of research and thus were assessed using this tool. In the QoL study, only 21% of Key Action proposals (14 of 66) and 18% of Generic Activity proposals (3 of 17) addressed sex and / or gender differences. This was not considered surprising, given the text of the Work Programmes at the time. "The evaporation of gender was evident." Even where Work Programme highlights relevance of the gender dimension, yet some projects did not specifically address the issues.

- The manner in which sex and / or gender differences were addressed "was open to critique." Risks of overgeneralization and gender insensitivity were present. A "common characteristic of projects which do not address sex and/or gender differences is that they do not address differentiated human populations." In some portfolios, not one project addressed sex and / or gender differences. The projects in the portfolio on ageing, on the contrary, showed substantial awareness for sex differences.

- Even within research projects dealing with one sex only, it is suggested to address more completely the diversity which may exist within the population studied (as in variation of ethnicity or of class origin or belonging). It is suggested, furthermore, that projects not designed to take sex differences into account should at least ensure that results are analyzed and reported upon in a sex-disaggregated form.

The gender impact assessment studies help understand integration of the gender dimension in FP5, ostensibly to better plan and implement progress in this area in FP6.

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161 Klinge & Bosch 2001, Key Action 3 (The "cell factory"), p. 147, Key Action 4 (Environment and health), p. 147, Key Action 6, p. 150.
162 Klinge & Bosch 2001, Key Action 3, p. 147.
163 Klinge & Bosch 2001, Key Action 6, p. 150.
164 Europe, Gender in Research 2001, p. 22.
165 Klinge & Bosch 2001, p. 163.
166 Europe, Gender in Research 2001, p. 25.
167 Klinge & Bosch 2001, Key Action 1, p. 158.
168 Europe, Gender in Research 2001, p. 25.
169 Klinge & Bosch 2001, chap. 4, notably Key Actions 3 and 5, and Generic Activity 12 (Bioethics).
170 Europe, Gender in Research 2001, p. 25.
To that end, recommendations were formulated for proposals for the next (the 6th) framework programme and specific programmes.\(^{171}\)

It is to be noted that programmes proposed for FP6 are quite different from those of FP5 to which the gender impact study applied. Recommendations were made concerning three priority thematic areas of FP6: Genomics and biotechnology (area 1.1.1), Food safety and health risks (area 1.1.5) and to Anticipating the EU's scientific and technological needs (1.2).\(^{172}\)

The recommendations formulated by Klinge & Bosch concern priorities within each of the thematic areas deemed relevant, and overarching recommendations concerning the conduct of gender sensitive research. In the process leading to identification of priorities for specific research initiatives encompassing concerning gender and sex differences, these researchers take account of the emphasis to be given in EU life sciences research under FP6 to genomics and biotechnology.

Recommendations concerning the conduct of gender sensitive research aim to enable more adequate integration of gender into FP6-supported research. Integration of gender dimension as an evaluation criterion is called for, as are guidance material and training for researchers and evaluators respectively. An integrated approach is said to be necessary in regard to health-related problems, to benefit from biological and social inputs and their interrelationship. Basic and molecular research is singled out in regard to integration of sex differences sensitivity, in light of new FP6 emphasis on genomics, and the anticipated therapeutic impacts. Guidelines, such as those implemented by NIH, are suggested concerning inclusion of women in clinical trials (phases III and IV, taking into account pragmatic aspects, and noting debate about application of guidelines to phase I and II trials).\(^{173}\)

It is too early to judge how these recommendations will be implemented in FP6. However, policy statements give us some sense of the ongoing process of integration of gender dimension into European research.

2.2.1.4. FP6 to continue and strengthen efforts in mainstreaming

We know that special effort will be made "to increase the participation of women in all

\(^{171}\) See Europe, Commission 2001 and Europe, Commission 2001a respectively.

\(^{172}\) Klinge & Bosch 2001, p. 19.

the activities of the framework programme [FP6] and boost, through these activities, the place and role of women in science and research in Europe. It is not clear whether the gender dimension will indeed be considered to be at the core of the European research area, itself now "the reference framework for research policy issues in Europe".

Building upon the multiannual framework programme 2002-2006, the specific programme for research, technological development and demonstration, priority thematic areas of research represent "the bulk of expenditure under the framework programme 2002-2006," states specifically that "Gender aspects in research will be taken into account in implementing this programme." Expenditures of 2 billion euros (\textit{circa} 3.3 billion $\text{C}^\text{175}) will be allotted over the period for Genomics and biotechnology for health, one of seven thematic research areas.

In all of these thematic research areas, the issue of women in science is to be kept in focus:

\begin{quote}
The priority thematic areas of research are described in terms of their overall objectives and the main research focus. The associated work programme will elaborate further on the detailed research content. Community action in each priority area will be pursued through integrated projects and networks of excellence which, in addition to research and technological development, may incorporate the following types of activity, where they are of specific relevance to the objectives sought: demonstration, dissemination and exploitation; co-operation with researchers and research teams from third countries; human resource development, including the promotion of training of researchers; development of research facilities and infrastructure of specific relevance to the research being undertaken; and promotion of better links between science and society, including women in science.;\textsuperscript{181} (…)
\end{quote}

In the implementation of Genomics and biotechnology of health area activities, it should be noted that gender-sensitive research protocols, methodologies and analysis of results

\begin{flushleft}
\textsuperscript{174} Europe, Commission 2001, p. 4, and on p. 12 the Proposal 2001/0053(COD), preamble art. 12, recalling relevant resolutions of the Commission, the Council and the European Parliament, and noting the existence and current implementation of an Action Plan (see Europe, Commission Staff 2001). Incidentally, the same elements are part of Proposal 2001/0054(CNS) concerning EURATOM, one of the founding pillars of European cooperation in the late 1950s and still one of the major European science projects.
\textsuperscript{175} Europe, Commission Staff 2001, p. 16.
\textsuperscript{176} Europe, Commission 2001, p. 2.
\textsuperscript{177} Europe, Commission 2001a, "Proposals...", p. 16.
\textsuperscript{178} Europe, Commission 2001a, "Proposals...", p.12 : decision 201/0122(CNS), preamble art. 7.
\textsuperscript{179} At conversion rate of 1.6487, late January 2003.
\textsuperscript{180} Europe, Commission 2001a, "Proposals...", p. 51.
\textsuperscript{181} Europe, Commission 2001a, "Proposals...", p. 16, emphasis added.
\end{flushleft}
are henceforth requisites:

1.1.1 Genomics and biotechnology for health

The sequencing of the human genome and many other genomes heralds a new age in human biology, offering unprecedented opportunities to improve human health and to stimulate industrial and economic activity. In making its contribution to realising these benefits, this theme will focus on integrating post-genomic research into the more established biomedical and biotechnological approaches, and will facilitate the integration of research capacities (both public and private) across Europe to increase coherence and achieve critical mass. Integrated multidisciplinary research, which enables a strong interaction between technology and biology, is vital in this theme for translating genome data into practical applications. In addition, an essential element will be to involve key stakeholders, in particular, industry, healthcare providers and practitioners, policy makers, regulatory authorities and patient associations, in implementing the theme. Gender equity in the research will also be ensured (15).182

[Note] 15. Causes, clinical manifestation, consequences and treatment of disease and disorders often differ between women and men. Therefore, all activities funded within this thematic priority must take the possibility of gender differences into account in their research protocols, methodologies and analysis of results.

Women and science issue remains on the European public agenda

The Council of the European Union invites the Commission "to continue and intensify its efforts to promote the role of women in science and technology and to ensure an effective mainstreaming of the gender dimension when implementing the Sixth Framework Programme and developing the European Research Area."183 The Commission is also invited to report on progress in the area of women in science within two years.

2.2.2. Sweden

Sweden is one of two Nordic countries (with Finland) to have raised the issue of women in science in the early 1980s. In 1982 it was decided by the Swedish government that gender equality should be given high priority in all research.184 A report from the National Council for Equality was requested by the government, and the report, If half were women..., prepared by a committee including female scientists of high standing, furnished analysis and recommendations for action.

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182 Europe, Commission 2001a, "Proposals...," p. 18, emphasis added in article 1.1.1 and in note 15.
183 Europe, Council 2001, p. 5.
184 Europe, ETAN 2000, p. 4.
In 1998 the Swedish Medical Research Council stated that gender should be taken into account in the process of doing medical research. A policy document issued that same year also authorizes research ethics committees to require additional information concerning choice of study population. This Council in 1999 adopts a policy that one-sex-only designs in principle not be funded.

"A new clause has been introduced in the instructions of the research councils and the sector research bodies stating that the councils have the task of promoting equality between women and men."

The Swedish Medical Research Council has since been merged with the Swedish Research Council (although it retains its separate identity as one of three separate councils, one for medicine, one for natural sciences and technology, and one for humanities and social sciences). The new Swedish Research Council (Vetenskapsrådet) exists since 1 January 2001 and it is this council that supports basic research in all scientific and scholarly disciplines. It also provides government with analysis of research policy and provides advice on research issues.

The Swedish Research Council has a committee for gender research, whose task it is to coordinate the efforts of the research councils with regard to equality, gender research and interdisciplinary approaches. Indeed, there is a programme concerning "gender research." According to Research secretary of the Council, this is not the same as research wherein gender differences and sex differences are taken into account.

The Swedish Research Council promotes gender equality in research, helping to "bring in new perspectives and ensure that new research problems are tackled." This seems to be the dominant perspective in Sweden. According to the Minister for Education and Science, gender equality issues are an area of high priority in Sweden.

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185 Personal communication from Gunnel Karlsson, National secretariat for gender research, Gothenburg, e-mail, 20 January 2003. No answer was received from Medical Council in response to our request for confirmation.
186 Soderstrom, Margareta, "Why researchers excluded women from their trial populations" [article in Swedish], Lakartidningen 98 (13), 28 March 2001: 1524-1528, information from English-language summary furnished kindly by Gunnel Karlsson, personal e-mail communication, 20 January 2003.
187 Europe, ETAN 2000, p. 43.
189 Sweden, MES 2000.
192 Vera Novakova, Swedish Research Council, personal communication, e-mail, 16 December 2002.
193 Sweden, SRC 2002.
This concerns medicine and the life sciences as well as the humanities and social sciences. A gender perspective can give an understanding of values that are of great importance when it comes to the choice of scientific problems and issues. The person who defines a scientific problem, is the person to influence the result of the research as well as the conceptions of the world that the science builds up and the techniques that it develops. I believe that an increase of women in science results in other questions being asked and other problems being highlighted. In this way, more equal recruitment of researchers and scientists contributes to a more equal society.194

Sweden has been moving toward public statistical accounting which disaggregate figures in terms of gender. This is seen as an important means for attaining a society providing equal opportunities for women and men. So, since 1997 results have been presented by gender for different groups reported upon in Sweden’s Public Health Report.195 So, one may, for instance, more easily see different patterns of usage of drugs, or of treatment offered to patients, or of cost of drugs, on the basis of distinction between men and women. It seems likely to us that the very presentation of data in this way may well stimulate important and new research questions.196

The Secretary of State for the Swedish Ministry of Education and Research states, with satisfaction, that the preoccupation with gender is now a government policy. The government is obliged to consider equality in all areas of decision making and policy forming, including research.197 Gender perspectives are to be integrated into all postgraduate education courses of study. A school of research on gender studies is being strongly supported, and the National Science Council has been enjoined to allocate substantial sums for gender research.198 In more general terms, Sweden uses what it terms double strategies, consisting both of mainstreaming and special measures to ensure progress in gender equality work.199 This includes some 10 million Swedish krona (1.8 million $C) par year for "genus research" including research on social and biological gender issues. Two points are significant in this regard: the money (for some part of support to these issues) is not necessarily recurrent, and in Sweden there is still lack of consensus, even controversy, on the meaning given to words such as "genus"

195 Personal communication from Gunnel Karlsson, National secretariat for gender research, Gothenburg, e-mail, 20 January 2003.
(gender in Swedish) in particular institutional settings.\footnote{200}

Moving from research to the introduction of research results into education, in Sweden as of 1995, development projects have been financed with the aim of integrating issues concerning women’s health into the basic medical education as well as in further training programmes for medical doctors.\footnote{201}

2.2.3. Germany

In Germany, in 1989, a national report was issued concerning the Promotion of Women in Science.\footnote{202} The first update to this report was presented in 1996. Other reports signal continued concern both at the national level and in lower jurisdictions.

It is noted that the Wissenschaftsrat (German Council of Science) presented a series of recommendations in a 1998 report entitled \textit{Equality for Women in Science and Research}. Most elements related to increasing the female scientific workforce. One element should be at least indirectly of interest for our present concerns: "The realisation of equality for women in science and research is a strategic task for every higher education and research institution."\footnote{203} The measures envisaged, however, concern the issue of female participation as researchers, rather than the content of the research \textit{per se}.

Mainstreaming has been adopted as government policy in Germany, in accordance with the European policy. Each Department has had to start a gender mainstreaming pilot study.\footnote{204}

There exists no policy of the nature of the inclusion of women in clinical trials in the United States. Nor is there in Germany any institutional research-supporting agency comparable to the Institute of Gender and Health.\footnote{205}

Research funding does not in general have a gender guideline in Germany, although individual programmes may increasingly include a linkage to gender such as a sentence "Gender differences should be analysed." However, there are no guidelines to direct

\footnotesize{\begin{itemize}
\item[\footnote{200}]{Vera Novakova, Swedish Research Council, personal communication, e-mail, 5 February 2003.}
\item[\footnote{201}]{Europe, Commission 1999, "Women and science," p. 43.}
\item[\footnote{202}]{Europe, ETAN 2000, p. 4.}
\item[\footnote{203}]{Noted in Europe, ETAN 2000, p. 128.}
\item[\footnote{204}]{Personal communication, e-mail, U. Maschewsky-Schneider, 17 January 2003.}
\item[\footnote{205}]{Personal communication, e-mail, U. Maschewsky-Schneider, 17 January 2003.}
\end{itemize}}
reviewers to be aware of gender aspects, and to specifically take them into account. 206

Some scientific associations have taken initiatives in promoting gender guidelines within the context of suggested best practices, as for instance in the German Epidemiological Association.207 Theses guidelines build on Eichler's work.208

2.2.4. The Netherlands

We understand that the ZorgOnderzoek Nederland (ZON, or Dutch Health Research and Development Council) had issued, in 2001, "a first and not fully developed recommendation to address sex, gender and ethnicity in research proposals." 209 No further information is available at this time on this recommendation.

The ZON and the MW-NWO (Medische Wetenschappen van NWO, or Medical Sciences – Netherlands Organisation for Scientific Research) have since been merged into the ZonMw (Netherlands Organisation for Health Research and Development).

2.3. Canada

Toward gender equality

In 1995 the federal government adopted a Federal Plan for Gender Equality, 210 a commitment to implement gender-based analysis of legislation and policies. Many of the recommendations included in that governmental document are relevant to our theme.

Objective 3 ("Improve Women's Physical and Psychological Well-Being") discusses how gender gaps in health policy and practice affect women's health, including clear recognition of knowledge gaps related to sex-differences, for instance as in cardiovascular disease. 211 It is proposed that gender differences be taken into account, where relevant, in regulatory and health promotion measures, as in measures to reduce smoking. 212 Gender bias in diagnosis of mental illness, in over-prescription of drugs to females, and in over-medicalization of women's health and normal life processes is

206 Personal communication, e-mail, U. Maschewsky-Schneider, 17 January 2003.
207 Personal communication, e-mail, U. Maschewsky-Schneider, 17 January 2003.
208 As cited in Maschewsky-Schneider et al. 2000, ¶ 3.7.4.
210 Canada 1995.
211 Canada 1995, ¶ 130.
212 Canada 1995, ¶ 132.
noted in most industrialized countries, including Canada.\textsuperscript{213}

It is further noted, in this 1995 federal plan, that:

\begin{quote}
Canada lacks a comprehensive source of data and analysis on women's health. The Medical Research Council estimates that only about five percent of Canadian health-research funding is spent specifically on women's health issues [footnote]. Consequently, women's health status may be being compromised.\textsuperscript{214}
\end{quote}

The government further commits itself, among other issues, to:

\begin{itemize}
\item "facilitating creation of a national research agenda, with priorities on policy-relevant research, to further understanding of the gender-specific determinants of health, health outcomes and best practices;"\textsuperscript{215}
\item "reviewing the issues of women's health research and the participation of women as subjects in clinical trials and establishing new guidelines for federally funded research programs;"\textsuperscript{216} and
\item "increasing knowledge and use of knowledge on a wide array of disease prevention and health promotion measures and interventions, including screening for major chronic diseases, physical activity and nutrition."\textsuperscript{217}
\end{itemize}

**Policy on inclusion of women in clinical trials**

In 1996-1997, Health Canada institutes its "Inclusion of Women in Clinical Trials".\textsuperscript{218} The intention of this guideline is to encourage the inclusion of women at the earliest stages of drug development, to ensure identification of potential sex-related differences, to facilitate their being taken into account when planning Phase III pivotal trials, and to generate the appropriate data so as to better inform physicians and potential users of sex-related characteristics of new drugs. Women of child-bearing potential are especially targeted for inclusion in clinical trials.

Subjects of both sexes should be included in trials in numbers adequate to allow detection of clinically significant sex-related differences in drug response. Analyses to detect the influence of sex should be carried out for individual studies and for integrated

\begin{footnotes}
\footnotetext{213}{Canada 1995, ¶ 134.}
\footnotetext{214}{Canada 1995, ¶ 139.}
\footnotetext{215}{Canada 1995, ¶ 153.}
\footnotetext{216}{Canada 1995, ¶ 157.}
\footnotetext{217}{Canada 1995, ¶ 158.}
\footnotetext{218}{Canada, Health Canada 1997.}
\end{footnotes}
analysis of efficacy and safety.\textsuperscript{219}

In 1999 a monitoring of this programme is promised in the Women's Health Strategy, of Health Canada:

- "2.7 The Women in Clinical Trials policy announced in September 1996 will be monitored."

We understand that the Women in Clinical Trials policy of Health Canada is provided to researchers and to those submitting drug review applications. The policy is taken into account in the drug review evaluation process, according to both the Therapeutic Products Directorate and the Women's Health Bureau of Health Canada. No systematic mechanism for monitoring the policy has as yet been put into place at the present time, although such implementation is possible in the future.\textsuperscript{220}

**Gender-based analysis**

In 1999 the Women's Health Strategy, of Health Canada, brings some of the above-mentioned challenges closer to realization. Notably, gender-based analysis (GBA) is to be fully integrated in all of the Department's programme and policy development work; and the Canadian Women's Health Network and the Centres of Excellence for Women's Health (created in 1996) are signalled as "pillars" of the strategy.\textsuperscript{221}

The first objective of the Women's Health Strategy aims to ensure responsiveness of Health Canada's policies and programmes to sex and gender differences and to women's health needs. Objective 2 aims to "increase knowledge and understanding of women's health and women's health needs." These objectives are to be implemented through a number of means, and in regard to research per se the following ones are of interest to us:

- "1.2 Tools, methods and training material will be developed to assist in implementing these gender impact assessments [application of gender-based analysis to programmes and policies in the area, inter alia, of research] across the Department and to orient senior managers to the requirements of this practice."

- "1.5 The inclusion of gender considerations and differential impact will be one of the

\textsuperscript{219} Canada, Health Canada 1997.
\textsuperscript{220} Catherine Kulisek, Women's Health Bureau, personal communication, e-mail, 31 January 2003.
\textsuperscript{221} Canada, Health Canada 1999, "Message from the Minister".
criteria when assessing research and demonstration proposals for which Health Canada funding is being sought."

In 2000 Health Canada’s Gender-based Analysis Policy was published, wherein the application of GBA is said to explain the development of the Inclusion of Women in Clinical Trials policy.\(^{222}\)

GBA implementation is ongoing, and development of GBA training modules has generated particular tools for gender-sensitive research and evaluation. Piloting of this material is being carried out in the science-based Health Products and Food Branch and other sectors of Health Canada. It is obviously too early to have any evaluation of progress in this regard.

It has been noted, above, that the GBA training tools were consulted and used by European colleagues\(^{223}\) in preparation of their own Gender impact assessment studies.

**Other fundamental initiatives**

The MRC has been turned about and in 2000 transformed officially into the Canadian Institutes of Health Research, including an Institute on Gender and Health, after important consultations on the themes of the institutes.

Health Canada plays a leading role in development of a comprehensive framework to monitor and address gender inequalities in health policies. The Women’s Health Surveillance Report project\(^{224}\) merits particular note for our concerns. European and American reports make abundantly clear that the availability of gendered data is an important issue to be addressed. In Europe, this is clearly mentioned in terms of personnel issues (women in science). Issues of gendered data in regard to diseases, disorders or conditions are mentioned both in Europe and in the United States.

The Women’s Health Surveillance Report focuses on many women’s health issues identified in collaboration with extensive national expert and stakeholder consultations. Gaps in women’s health surveillance information are identified. Sources include data documenting a wide variety of health determinants. Here, as elsewhere, it is recognized that a broad range of data must be considered to adequately portray the relevant

\(^{223}\) Klinge & Bosch 2001.
\(^{224}\) Canada, Health Canada 1999a.
women's health issues. Such data may then support the development of gender-sensitive monitoring systems, policies and programmes aimed at improving women's health across Canada.

Other important initiatives exist, perhaps less directly linked to research *per se* and relatively more toward policy, for example: Health Canada's Family Violence Initiative; and a federal cross-departmental initiative on women's health indicators, supporting September 2000 First Ministers' meeting commitment to report on health status, health outcomes and health services performance. This latter project supports GBA policy.

**Tri-Council policy on ethical conduct**

Finally, it should be mentioned that the then MRC, NSERC and SSHRC collaborated in developing a Policy Statement on Ethical Conduct for Research Involving Humans. As this policy document goes through occasional revision, we attempted to determine whether evaluation had been made of the particular dispositions concerning women.

Indeed, in Section 5 of this Policy Statement, it is pointed out that a principle of justice is the fair distribution of benefits and burdens. With the aim of applying this principle to the issue of research and women, section 5B. *Research Involving Women* states that "Article 5.2. Women shall not automatically be excluded from research solely on the basis of sex or reproductive capacity." We have not received written confirmation, after verification from inspection of files, but personal recollections by two persons active in ongoing revision of the policy indicate that no evaluations, formal or informal, have been made of this policy.

2.4. Other relevant policy orientations noted

2.4.1. Other countries

We understand that France, Nicaragua, Guatemala, Costa Rica and probably the

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226 Current orientations on Women's Health Surveillance Report project furnished by Catherine Kulisek, personal communication, e-mail, 31 January 2003.
229 Personal communication, Karen Messing, 17 October 2002.
other countries of Latin America have not implemented policies relevant to our focus.230

2.4.2. International development organisations

In international development work, the importance of gender was pointed out already in the 1970s; and research and field work was encouraged to take this dimension into perspective. Our literature search did not allow us to identify any evaluations of policies implemented supporting gender and sex difference research.

Personal communication with IRDC personnel in Ottawa did not allow us to identify any further documentation of the specific nature we were looking for. We were, however, directed toward the results of the Assessment of Social Policy Reforms (ASPR) programme initiative (1995-2000) in which "gender mainsteaming" was a specific element to be addressed.231

The results do not evaluate per se the initiatives put into place. Rather, they identify gender issues to be taken into account by researchers and agents of policy reform.

As we see in the extended quotation from an IRDC document on the subject, best practice would indicate the need for sensitivity to an exceedingly broad swath of cultural and socio-economic factors which have been shown to be of relevance in relation to women's access to resources, information, etc. and, of course, to health resources in particular. In this way, the health status of women is dependent on a broad set of determinants.

I. Defining the Research Area

What is the proposed subject of research? Is the research area relevant to men and women in different ways? How?

Who has defined the research subject? Are both men and women involved in the definition and design of the research? Does the researcher or research team possess adequate knowledge about gender issues to incorporate these into the research? If not, how can this be addressed?

What are the anticipated outcomes of the research? Who are the expected beneficiaries? Will men and women benefit equally from this research?

Does the research subject appear to be "gender neutral" (i.e. where the different experiences, status and resources of men and women are not a

231 Although the programme is no longer current, the information remains available on IRDC web site. See Canada, IDRC 1998.
relevant factor)? How has this conclusion been reached? What do women's organizations and researchers with gender expertise have to say about the research subject?

II. Methodology

Are gender differences reflected in the conceptual frameworks, objectives, methodology, expected outputs and anticipated impact of the research? How can attention to the different situations of men and women be incorporated into these aspects of the research design?

How will the design and implementation of the research address factors which often produce unequal opportunities for men and women? For example, where applicable, how will the research address the significance of the following issues:

-- differences between men and women in access to basic resources (e.g. differential access to education, health, social security, money, capital, collateral, land, information, transportation, technology etc.);

-- differences between men and women related to divisions of labour and responsibilities within the household (e.g. attention to limitations on time; gender-specific tasks and responsibilities, including childcare etc.)

-- differences between men and women related to participation within the informal and formal labour markets (e.g. different types of occupations, sectoral distributions, wage and benefit levels, full or part-time work; etc.);

-- differences between men and women related to legal status and entitlements (land ownership; inheritance law; marriage law etc.);

-- differences between men and women in terms of access to power and authority in political and policy arenas, at local, regional and national levels;

-- social traditions, customs, obligations, entitlements which produce different expectations, opportunities and constraints for men and women.

Who will participate in the research? Is the research process designed to create equal opportunities for the participation of men and women? What steps can be taken to ensure that this is so?

How will research methodologies address gender differences? Will methods of data collection and analysis be disaggregated by gender? Will relevant documents about the gender dimensions of the research area be identified and reviewed? Will there be attention to qualitative and quantitative data?

Will there be a need for gender-specific expertise or training? At what stages in the research would such training be most important? What resources are required-- budgetary or otherwise-- to ensure access to such expertise or training?

What criteria or indicators will be required in order to evaluate the success of the research in meeting its objectives and impact in relation to men and women?

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2.4.3. World Health Organization

First off, it must be stated that gender is very present as an issue within the World Health Organization (WHO), as our readers are surely well aware of. Nonetheless, we did not locate evaluations of gender and sex difference research policy produced by WHO or PAHO (Pan-American Health Organization, part of WHO). Literature search, contact with researchers\textsuperscript{233} and extensive consultation of web-sites and some web-site material were the modes of documentation in this respect. Mention, in some recent material, of certain documents discussed above, without reference to other, more recent material, produced by WHO or other parties, supports our determination.

Two points may nonetheless be made which are relevant to our concern.

First, social determinants of health are a high concern in some areas, for instance in the area of Tropical Disease Research (TDR). WHO participates with other international agencies in supporting research in which particular attention is given to gender, as gender roles and responsibilities impact on disease patterns, and on the effectiveness of prevention and control. Men and women experience different exposure and susceptibility to disease. Differential access to healthcare, and to prevention and control measures leads to gender inequality.\textsuperscript{234} Research and training is pursued in examining how gender inequalities affect TDR diseases, their control, and access to health care; in developing guidelines for gender-sensitive interventions; and in supporting research on equity in health and health care, of which gender is an important and neglected aspect.

Second, within the Women’s Health and Development programme in WHO, an interesting paper of 1998 makes a review of the literature on gender and health. This paper aims to make sense of change of exclusive focus on women toward focus on gender, that is on "the socially constructed differences and the power relations between women and men, as a determinant of health."\textsuperscript{235}

In this paper, WHO puts into circulation the idea that dialogue among researchers, women’s health advocates, users of medical technology and other relevant stakeholders

\textsuperscript{233} Personal communications, by telephone with Maria De Koninck of Université Laval, December 2002, telephone and e-mail with Peggy Maguire or European Institute of Women’s Health, January-February 2003, and by e-mail, Ulrike Maschewsky-Schneider, February 2003.

\textsuperscript{234} See WHO 2002.

\textsuperscript{235} WHO 1998, p. 6.
is essential in assuring an appropriate place for women in the research process. The report notes the important role of ORWH (in United States) in ensuring high-quality research into diseases, disorders and conditions unique to or more prevalent in women; notes strategies of positive action in regard to increasing numbers of female researchers; and legislation concerning inclusion of women in clinical trials.

Beyond the clear importance of these other approaches, the importance of dialogue is considered essential. It is suggested that models of such interventions may be found in meetings of researchers from various disciplines, along with groups of women's health advocates and non-governmental organizations (NGOs), resulting in useful determination of priority areas for development and introduction of fertility regulation methods.

Further, a call for better quantitative documentation of gender inequalities in health and well-being is made. Epidemiologists, clinical scientists and social scientists could use a range of methods to better understand broader health dimensions of women's and men's lives. Creative research methods are called for.

It is suggested that research taking gender into account must:

consider the differences between women's and men's roles and responsibilities, their knowledge base, their position in society, their access to and use of resources and the social codes governing female and male behaviour. Strategies to improve women's health need to be grounded in a rigorous analysis of the whole range of their productive and reproductive activities and of the way these change across the life span.

Getting "the whole picture" would involve taking account of women's activities, and notably work, both in the workplace and at home. Taking account of physical issues and psychological dimensions is necessary. Differences between female and male biology require more attention if impact of waged work on women's health is to be properly understood.

In summary, then, factors which would "contribute to reconfiguring research to be more gender-sensitive" would include:

236 WHO 1998, pp. 55-56. Dr Lesley Doyal is responsible for the original work on this unofficial WHO document, with input from WHO Working Group on Gender.
237 The parallel with the broad range of inputs considered in Health's Canada's Women's Health Surveillance Report project is evident.
239 In this regard, see K. Messing's much more detailed treatment of these issues, in Messing 1998.
• data collection disaggregated by sex, age and social;\textsuperscript{240}

• use of innovative quantitative and qualitative methods, needed to better elucidate and understand sex and gender differences, for instance in documenting evidence of risks for women and men in home and in workplace\textsuperscript{241,242}

• women as well as men should be included in design and implementation of epidemiological and clinical research as researchers and as subjects of research;\textsuperscript{243}

• research should analyze productive and reproductive activities across life spans.\textsuperscript{244}

Further, making the link between policy and research, it is suggested:

• the development of "gender-sensitive" policies (which acknowledge the reality and undesirability of inequalities between women and men) is necessary for the resolution of gender bias which oftentimes results in prioritization of men in the allocation of resources.\textsuperscript{245}

2.4.4. A.M.A.

The American Medical Association is a professional organisation, promoting the interests of professionalism in medicine and setting standards for medical education, practice and ethics.

\textit{JAMA}, the \textit{Journal of the American Medical Association}, is one of the prestigious journals in the field of medical research.

In light of these facts, it is relevant to note that AMA has adopted policy supporting what it perceives as a trend toward increased research on women's health and participation of women in clinical trials. In particular, the AMA recommends that "all medical/scientific journal editors require, where appropriate, a sex-based analysis of data, even is such comparisons are negative." AMA supports educative actions concerning sex- and gender-based differences in health and disease, as pursued for instance by federal agencies, medical associations and women's health organisations.\textsuperscript{246}

\textsuperscript{240} WHO 1998, p. 60.
\textsuperscript{241} See Messing 1998.
\textsuperscript{242} WHO 1998, p. 60.
\textsuperscript{243} WHO 1998, p. 60.
\textsuperscript{244} WHO 1998, p. 60.
\textsuperscript{245} WHO 1998, p. 61.
\textsuperscript{246} CSA, AMA 2000, p. 18.
In its Report on sex- and gender-based differences in health and disease, the Council on Scientific Affairs of the AMA points out that "the realization that research findings on men cannot be extrapolated to women, combined with the relative lack of evidence-based information on which to guide treatment decisions in women" has fostered change in a number of sectors including, notably, medical school curricula. AMA encourages developments in this area, for instance development of women's health/gender-based biology curricula in medical schools, and continuing medical education for physicians in the area.

The CSA report notes that sex- and gender-based differences in cardiovascular disease have been much studied, but that there exists debate as to the success of these efforts. "Although women comprised a majority of subjects included in trials sponsored by the National Institutes of Health (NIH) from 1993-1998, only a fraction of the final reports of these studies provided sex-based analysis of the data. Furthermore, although women were adequately represented in studies of coronary artery disease and hypertension, they were underrepresented in studies of heart failure."

This report then reviews the principal research results available concerning "the prevention, diagnosis, and management of conditions or diseases that may be unique to women; that are more prevalent in women than in men, or that manifest differently in women than men," with focus on the latter two categories.

This report ignores reproductive physiology and some other issues unique to women because while "these traditional areas of women's health continue to receive appropriate research emphasis, there is now widespread recognition that women's health must be approached in a more broad-based fashion, examining how differences in sex factors, gender, culture, ethnicity, and socioeconomic background influence the causes, diagnoses, progression, and treatment of diseases unique to women, as well as those that are not sex-specific." Sub-populations noted in the report may be differentiated by age, economic status, ethnicity, lifestyle, access to health care, incidence of co-existing disease, etc.

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248 CSA, AMA 2000, p. 2.
250 CSA, AMA 2000, p. 2.
251 CSA, AMA 2000, p. 3.
2.4.5. Institute of Medicine

The mission of the Institute of Medicine (IOM), established by the American National Academy of Sciences (NAS) in 1970, is to advance and disseminate knowledge to improve human health, thus advancing policy matters of interest in public health. The NAS advises the American government on scientific and technical matters.

A recent (2001) publication has been signaled widely as a major contribution to the questions Does sex matter?, When does sex matter? and How does sex matter?. The committee was charged with considering biology at the cellular, developmental, organ, organismal, and behavioural levels. The committee focused its efforts on nonreproductive areas of biology, where differences between the sexes are much less expected than in reproductive systems, but these differences "do occur, and some of these differences have important consequences."252

We shall not review the biological contributions to human health as detailed in this volume. Our aim in noting its content is rather to point out the policy implications for research in the area. The suggestions on that count are useful.

Being male or female affects health and illness throughout the human life span. The genetic and physiological constitution of individuals, and their interactions with environmental and experiential factors contribute to observed differences between individuals and also to differences observed between the sexes. In many of these cases, sex differences may be traced to direct or indirect effects of reproductive hormones. But the differences cannot be solely attributed to hormones. "Therefore, sex should be considered when designing and analyzing studies in all areas and at all levels of biomedical and health-related research."253

"The study of sex differences is evolving into a mature science. There is now sufficient knowledge of the biological basis of sex differences to validate the scientific study of sex differences and to allow the generation of hypotheses with regard to health. The next step is to move from the descriptive to the experimental phase and establish the conditions that must be in place to facilitate and encourage the scientific study of the mechanisms and origins of sex differences."254 This report states that investigators are

now able to explore sex differences (or sex-based differences in biology) at the basic cellular and molecular levels.

These differences have been insufficiently explored because "the research community assumed that beyond the reproductive system such differences do not exist or are not relevant." Scientific experts from diverse disciplines concurred in the message that "sex – that is, being male or female – is an important basic human variable that should be considered when designing and analyzing the results of studies in all areas and at all levels of biomedical and health-related research."256

The committee was asked to consider current and potential barriers to further investigation of sex differences, including ethical, financial, sociological, and scientific factors. The barriers posing challenges to progress in scientific knowledge about sex differences in health and illness are varied, as noted below.

- **Terminology:** It is necessary to clarify terminological inconsistency and confusion surrounding the use of the terms sex and gender in the scientific literature and the popular press.257

- **Research tools and resources:** "Detection of modest differences may require studies with more complex experimental designs, the use of more complex model systems, and the use of more subjects to achieve statistical power; and, thus, in some cases detection of modest differences may require additional financial resources." Research sponsors and peer-review committees are singled out for attention to the consequence of potential need for additional resources.

- **Information difficult to glean from published literature:** In its evaluation of inclusion of women in clinical trials, GAO experienced difficulties in determining whether analysis of data by sex was occurring or not. Reporting of negative results is often discouraged by journal editors. In addition, when sex differences are reported, inappropriate or inadequate abstracting and indexing work may make difficult retrieval of material of interest.259

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Few journals have information or guidelines regarding analysis of data by subpopulations such as sex, in their instructions for authors. The *Journal of the National Cancer Institute (JNCI)* has "taken the lead in encouraging authors to include information on and analyses of subjects by sex."\(^260\) The amended *JNCI* information for authors, since October 2000, suggests where appropriate to analyse clinical and epidemiological studies "to see if there is an effect of sex or any of the major ethnic groups. If there is no effect, that should be stated so in Results."\(^261\)

The reporting of negative results is mentioned as a positive step. The multiplicity of interpretations surely to be applied to the term *appropriate* is signalled, presumably with concern.

- **Information on sex of origin of cell and tissue culture material.** "All somatic cells have a full complement of chromosomes, including the sex chromosomes. Despite this, useful information on the sex of origin of cell lines or tissue cultures is often lacking in the literature. Data suggests that many cells throughout the body display sex specificity. Sex of origin of biological research materials should be determined and disclosed."\(^262\)

  Origins and sex chromosome constitutions of cells or tissue cultures used for cell biological, molecular biological, or biochemical experiments should be elucidated, and should be reported upon when known. Journal editors should encourage routine inclusion of such information in Materials and Methods sections.\(^263\)

- **There is a lack of data on sex differences across the life span from longitudinal studies.** There is a lack of consideration of cycles (e.g., hormonal variability). These issues should be better studied.\(^264\)

- **Synergy is needed in the study of sex differences, between basic scientists, epidemiologists, social scientists, and clinical researchers.** Interdisciplinary collaboration, as in other areas of study, would provide mutual benefits to the researchers involved. Challenges include openness to mutual learning between specialists, and strategies for more effective communication and cooperation are

\(^260\) IOM 2001, pp. 177-178.
\(^261\) Quoted in IOM 2001, p. 178.
\(^263\) IOM 2001, p. 179.
needed.\textsuperscript{265}

- Bias needs "Scientific research is not separate from other practices of society." Bias in interpretation or reporting, well documented in social sciences, is less obvious in basic and clinical sciences. Studies on race, ethnicity, age, nationality, religion and sex "have sometimes led to discriminatory practices." "Ethical research on the biology of sex differences is essential to the advancement of human health and should not be constrained."\textsuperscript{266}

\textsuperscript{265} IOM 2001, p. 182.
\textsuperscript{266} IOM 2001, p. 184.
3. **Discussion**

Our discussion has two parts. First, we shall discuss the results of explicit evaluations. Secondly, we shall discuss the issues raised either within the aforementioned results or within other documents examined above.

3.1. *What do these evaluations tell us?*

**NIH**

The National Institutes of Health implemented change of policy concerning inclusion of women in clinical trials in the late 1980s. In 1993, the policy became strengthened, and took on the authority of legislation. The guidelines that NIH adopted to implement its policy have evolved over time (we shall return to this element, below).

Here are five comments about NIH and, more specifically, ORWH.

Firstly, it has been shown that NIH, notably at the instigation and through the initiatives of ORWH, made important efforts to augment numbers of women subjects in clinical trials. Educative actions in-house and outside NIH, training of personnel, production of information tools, changes of forms and instructions to concerned parties (researchers, staff, evaluators, management) were pursued with diligence (United States, GAO 2000).

Indeed, the role of ORWH is signalled for its leadership and positive contributions to the efforts put forward.

However, secondly, it has not been shown beyond doubt that these efforts resulted in the desired *quantitative* objective.

GAO shows that more than half of participants in clinical research studies in FY1997 were women. This is true also when one-sex only studies are removed from the calculation. However, recent NIH figures show that, excluding one-sex studies, women's participation as clinical subjects has not increased (see Table 1 above).

Three independent studies, based on results of peer-reviewed publications, suggest that there have been either "no significant changes" in enrollment of women over the past decade (Ramasubbu et al. 2001), or that the augmentation was not significant (Vidaver et al. 2000), and that the sex composition of clinical trials has been altered principally due to large-scale trials restricted to women (Harris & Douglas 2000).
Since NIH is perceived to have accomplished much, and as mention of NIH's actions often refer to the legislated policy on inclusion of women in clinical trials, it may be surmised that that action was indeed the effective mechanism. The data we were able to examine does not fully support that hypothesis. Major one-sex (women) studies account for one-half of increase in enrollment.

Third, NIH's data gathering system includes weaknesses causing difficulty to more completely evaluate the efficacy of NIH's inclusion policy. The lack of data disaggregated by sex and other relevant factors (e.g., by types of trials, by institute or center, etc.) in NIH's most recent monitoring of adherence to the policy appears to show that this weakness has not been sufficiently addressed.

These three comments referred to inputs to the system. Now, let us turn to outputs.

Fourth comment: few efforts were made by NIH to assure analysis by gender or by sex. Not surprisingly, then, despite the augmentation of numbers of women included in reports, these studies lack analysis by sex or gender. More particularly with respect to clinical trials, there is no significant change in this regard (Vidaver et al. 2000).

Fifth, and perhaps most important, it remains highly significant that the NIH initiative continues to maintain a fairly strong reputation as being an effective mechanism. Why is this? Here, we do not have hard data. However, at least three major elements seem clear from our study. A) It seems that the ORWH has maintained strong links with researchers, within NIH and without. ORWH piloted the development of two vast and important "research agendas" for women's health research in collaboration with a wide network of researchers and including other groups as well. B) The significance of the Women's Health Initiative, and other in-house collaborative efforts with individual Institutes, should not be under-estimated, as another mode of pushing forward the women's health research frontier. C) As a "champion" of the dossier within the institutional framework, it seems that through its outreach work and its internal agenda, ORWH has clearly succeeded in maintaining a dynamic impetus for women's health research in the public sphere and in the research community.

FDA

The FDA in 1993 recommends that clinical studies include enough men and women to detect clinically significant sex differences in drug efficacy, and that sex-differences be reported in new drug applications. This is a recommendation, not an obligation. The
parties applying the guidance are not researchers but, rather, the pharmaceutical industry. Increased obligation, as in adoption of a regulation in 1998, is accompanied by diminished requirements. Data should be presented separately for men and women, but no criteria exist for determining the number of women needed in clinical studies and no requirement is specified as to analysis of the data.

Non-compliance "often" characterizes drug sponsors’ response to data presentation requirements despite, in all cases examined, the material data necessary to comply. No consequences ensue for the drug sponsors. Indeed FDA is unaware of failure of new drug applications to meet standards, as no management system is in place to record and track the inclusion of women in clinical drug trials (GAO).

We do not think it exaggerated to suggest that the FDA mechanism was not seriously put into place (no champion within, no evidence of institutional commitment, no training to speak of, no educative tools, no monitoring mechanism, no evidence about results).

Effect of the policy? Unknown. But it may safely be presumed that the effect of the adoption and implementation of this policy, in these conditions, was negligible.

EU

The Gender impact assessment (GIA) studies of the European Union (EU) allow us to see to what extent the mainstreaming of gender equality is integrated into the Fifth Framework Programme (FP5) defining the EU's support for research and technological development over the period 1998-2002. Mainstreaming is a Community policy, and its application in research is the result of political will and official decisions.

Further, the GIA studies are concomitant with other initiatives in the EU concerning the under-representation of women among scientists and notably in decision-making positions in the research community. The GIA studies are remarkable in highlighting a need to go beyond issues of representation, suggesting (without rejecting the importance of more input of women into research positions) that a true integration of gender into research poses broader epistemological and methodological questions.

However, despite early efforts to mainstream gender into research, current work programme proposals fail to integrate the gender dimension into the content of policies, of specific research topics or FP5 actions. Efforts at mainstreaming are clearly effective in addressing issues of participation of women in science (research by women), but are not effective at addressing issues of research for and about women.
Guides for evaluators of submitted proposals make no explicit mention of gender in evaluation criteria. Not surprisingly, limited attention is therefore paid to gender issues during evaluation. Integration of the gender dimension into proposals is noted as requiring specific gender competence, from expert evaluators and from Commission staff. Implicitly, training is therefore necessary, but it is not available. The net result is that the gender dimension is not being integrated into proposals (Europe, Gender in Research 2001).

With respect to the Quality of Life programme (dealing *inter alia* with health research), the subject of one of the seven GIA studies, again the gender dimension in the scientific proposals is lacking in many respects, markedly absent or inadequately treated, compared with relevant published literature.

It seems clear (to this author) that the majority of research proposals and activities examined dealt more closely with issues of gender than those of sex differences. A quantitative count was not possible. However, it is clear that *both* kinds of differences are being examined and discussed (Klinge & Bosch 2001).

In conclusion, it must be noted that in the Sixth Framework Programme (and notably in Genomics and Biotechnology for Health research area), changes *have* been implemented. Research projects funded in this research area must address issues of gender equity in research in their research protocols, methodologies and analysis of results.

### 3.2. Issues raised by evaluations and review of health research policies and initiatives

In this last section we shall not draw conclusions. That is not our mandate. More importantly, policy is not an area lending itself easily to identification of "one best way." The success of policy, *inter alia*, resides very much in the process. Currently, good policy process in Western societies often includes sharing and exploring options among "stakeholders" and interested parties, including, in the health area, researchers, institutional and financial partners, and to an increasing extent, patients and specific advocacy groups (organized around gender, around specific diseases, etc.).

We shall simply point out a number of "issues" which it would seem useful to IGH to keep in focus during their own deliberations and decision-making process.

**The importance of an institutional "champion".** The presence of an institutional
leader seems to be key in the American experience; the relative lack of one seems to have been a hindrance in the European experience. Adjustments to policy or programming are facilitated (as noted, for instance, in the case of NIH).

The importance of working with constituencies and clients, partners and allies. It is useful to view IGH in the context of all its partners. The importance of a health research funding agency is founded upon its place in a network, pointing to the importance of practices and policies in a number of other institutions, and the importance of the relations between IGH and these other persons and institutions, such as:

- fellow institutions supporting research and in particular health research: CIHR institutes, NSERC, SSHRC, provincial agencies (e.g., FRSQ)
- loci of research (production, communication, distribution):
  - researchers, hospitals and universities as research institutions (medical or health research, and other more basic disciplines), and corporate entities involved in health-related research;
  - scientific and medical journals, social science journals;
  - higher education teaching establishments (universities and hospitals), professional associations, organisations offering continuing education of professional nature
- extramural funding sources: philanthropic sources, corporate sources, governmental sources not in direct line
- health care delivery: health care delivery establishments\(^{267}\) (hospitals), corporate entities active in selling health care products and services; citizens as patients and as participants in clinical research
- citizens as members and activists of civil society groups active in promoting issues related to medical knowledge, health care, citizens’ rights and notably women’s rights

This focus appears useful, given our reading of the material examined. Some groups could be sought out with which to establish alliances (e.g., more effectively reaching

\(^{267}\) For instance, to help overcome barriers to translating research outcomes into health care practice; Pinn 2001, slide 75.
researchers, through collaboration with sister Institutes). Others could be pressed into service (e.g., journals whose editorial policy could be brought more into line with gender and sex research objectives of IGH). Other partners have been noted in various contexts (strategic advantage, for research objectives, of close linkage between research and health care delivery establishments; the interest of quickly assuring transmission to young researchers of new gender-sensitive knowledge; the advantage of assuring better collaboration, in research, with heretofore poorly canvassed sub-populations as research subjects; and so on).

The collaboration of advocacy groups as well as researchers is pointed out as being of use in developing research priorities and in fostering support for research activities.

**Being clear on the mandate.** Key to the action of any organisation is, of course, its mandate, its prerogatives, its liberty to initiate (or not) actions, to enter into agreements with sister organisations, etc.

**Taking into account the whole picture.** There are two aspects to this issue: the focus on research, and the institutional (IGH) focus. From the point of view of research, we noted a remarkable consensus on the necessity to attempt to focus on gender and sex differences from the combined perspectives afforded by interdisciplinarity, building on collaboration and input from many disciplines (medical and more fundamental disciplines), from the clinical point of view and the epidemiological perspective, and including the social sciences, notably for their contribution to understanding of socio-economic and cultural influences and characteristics leading to better appreciation of women's health and the health of sub-populations. From another point of view, increasingly, researchers note the importance of considering gender and sex issues early in the formulation of research questions or in the design of experiments. So, in Europe, it represents a major gain in the Sixth Framework Programme that gender differences be taken into account in research protocols and in methodologies. Further, in looking towards publication of results, the explicit mention in FP6 of the analysis of results represents an equally important gain.

**The need to clarify terminology.** This is not a minor issue. In the context of interdisciplinary collaboration, thought by many to be essential to progress in research

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268 For example, in Vidaver et al 2000, p. 502: make sure that sample size and analysis by sex are addressed from the outset in design of protocols.
sensitive to sex and gender, confusion or uncomprehension across disciplinary lines only slows collaboration.

**More attention to diversity and to life span issues.** The links between health care and research need to be carefully attended to, notably in terms of assuring attention and sensitivity to diversity (e.g., ethnicity, age, socio-economic status, sexual preference, other alternative life-style choices) so that research needs (and health care, but that concern is secondary and strictly instrumental in this context) are met; thus the contacts with patients (and research subjects) must be culturally relevant, and attend to development life span issues.

**Sex disaggregated data.** The importance of data disaggregated by sex, and by other factors (such as age, socio-economic status, etc.), is considered of fundamental importance.

**Mechanisms of promoting gender and sex sensitive research.** We have seen examples of:

- a major programme of research (WHI),
- use of institutional leverage within an institution (ORWH),
- legislated obligation of inclusion of women as subjects of clinical trials\(^{269}\) except where explicitly justified (NIH, FDA, HC),
- expansion of gender mainstreaming policy to areas of research (EU),
- proposals to editors to adopt gender-sensitive author guidelines (SWHR)\(^{270}\),
- development with aid of broad constituency of a women’s health research agenda (NIH)\(^{271}\),
- compilation of research information available on sex and gender sensitive research

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\(^{269}\) An important initiative, the NIH inclusion policy, was applied to clinical trials only. This is considered too limited in scope by some observers; Klinge & Bosch 2001 proposed discussion of opportunity of extending inclusion policy to earlier phases of testing.

\(^{270}\) Vidaver et al. 2000, p. 503. The SWHR called on editors of leading journals to revise publications guidelines, in order to require a sex analysis; see Helmuth 2000, p. 1563. Recommendations to authors, to be made known to participants in the peer review process as well, are invited from journal editors, suggesting requirements for presentation of analyses by selected sample subgroups, such as gender; see Ramasubbu et al. 2001, p. 763.

\(^{271}\) Early on, the ORWH initiated a year-long process which served to contribute to determination of a research agenda for the ORWH; see Pinn 1994, p. 699. The 21st century Research Agenda action constituted an update of the earlier initiative.
• refusal to fund research on single sex projects without an adequate justification;\(^{272}\)
• demanding accountability of grant awardees;\(^{273}\) etc.

Only a small number of these varied initiatives have been the object of evaluation. Many of these initiatives were not implemented by a public health research funding agency. Some initiatives may not be appropriate for consideration by IGH, but the range of initiatives specifically addressing this issue was deemed of interest to be noted.

The specific conditions of implementation have been shown to be, in many circumstances, of primary importance.

Issues noted include:

• institutional issues of resistance to consideration of gender in discussions concerning science and research;\(^{274}\)
• institutional issues of political will to enforce policy;\(^{275}\)
• continuity in institutional support for research;
• need to stop underenrolling women in clinical trials;\(^{276}\)
• issues relating to diversity (see above), important in implementation of recruitment

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\(^{272}\) Suggested as an interesting course of action for funding bodies; Europe, ETAN 2000, p. 43. See also Sweden, above. In the case of funding of external research projects, the possibility of a “contract compliance” clause is noted. See Europe, ETAN 2000, p. 82.

\(^{273}\) Granting agencies could demand accountability of grant awardees in effectively meeting enrollment requirements in non-sex-specific (or gender-neutral) clinical trials. Success could be rewarded in future grants and failure to attract and retain women in studies could entail discouragement toward obtaining future grants unless corrective measures are clearly defined and implemented. Ramasubbu et al. 2001, p. 763.

\(^{274}\) Science, the scientific community and science decision-makers are resistant to the gender issue. Science is perceived as being gender-neutral. These are lessons learned from the Gender Impact Assessment exercise (“a learning tool for the Commission”). See Europe, Commission 2002, p. 6.

\(^{275}\) Even in jurisdictions where an important amount of preliminary work has been brought to bear on the conceptualisation of the integration of gender issues, and on the implementation process, yet shortcomings were noted at all levels of programming targeted for implementation. A lack of attention to gender was noted in definition of research programmes (Work Programmes), in information distributed to researchers and in the evaluation process at the time of decision-making on funding. Given those starting points, the way research takes gender into account is of course affected and, more often still, gender is therefore simply not taken into account at all. Even “in thematic areas where there is an obvious gender dimension, such as health research (…), this tends not to be given due consideration.” Another lesson drawn from the Gender Impact Assessment exercise.

\(^{276}\) Harris & Douglas 2000, p. 480. It has also been pointed out that “inequities in gender enrollment extend to studies funded by nongovernmental sources as well”; see Ramasubbu et al. 2001, p. 763. This issue is not dealt with here.
and retention strategies;\textsuperscript{277}

- importance of preparation and delivery of educative and training material, at many different steps in the process (administrators of programmes, researchers, evaluators, peer reviewers; and also journal editors);

- importance of appropriately addressing critical points in the process: research design, methodology, evaluation of proposals, analysis of research results, publication of research results;

- assuring the proper functioning of the peer review process.\textsuperscript{278}

\textsuperscript{277} Include recognition on a formal basis, within grant review process, of initiatives and creativity in identifying, recruiting and retaining women into clinical trials. See Ramasubbu et al. 2001, p. 762. Granting agencies should support in active fashion, through appropriate budgetary mechanisms, to facilitate retention of women in studies, by addressing needs related to transportation, child care and other barriers preventing participation in clinical trials. Ibid, p. 763 and Vidaver et al. 2000, p. 502.

\textsuperscript{278} Confidence in the peer review process is a foundation of the development of scientific knowledge. Transparency, regular scrutiny and review are deemed to be essential to maintaining confidence in the process. It is suggested that funding bodies are directly responsible for addressing this issue. See Europe, ETAN 2000, p. 44. An important document, in this regard, is Wennerås & Wold 1997 wherein nepotism and sexism were found to be clearly present in some peer review process.
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A useful source helping to ascertain presence or absence of material may be found in Commission 2002, Annex 1 concerning an overview of efforts made in European Member States to promote the role of women in science.

Thanks are extended to the persons whose names appear above. Of course, they bear no responsibility for errors or omissions in this report.
6. **Acronyms**

AMA American Medical Association
CIHR Canadian Institutes of Health Research
CoEs United States, National Centers of Excellence
EC European Commission
EU European Union
FDA United States, Food and Drug Administration
FP5 European Commission, Fifth Framework Programme
FP6 European Commission, Sixth Framework Programme
FRSQ Fonds de la recherche en santé du Québec
FY Fiscal year
GAO United States, General Accounting Office
GBA Gender-based analysis
GIA Gender impact assessment
HC Health Canada
IDRC Canada, International Development Research Centre
IGH Institute of Gender and Health
IND FDA, Investigational new drug
IOM United States, National Academy of Sciences, Institute of Medicine
JAMA Journal of the American Medical Association
MRC Canada, Medical Research Council (now, the CIHR)
NDA FDA, New drug application
NIH National Institutes of Health
NME FDA, New molecular entity
NSERC Canada, Natural Sciences and Engineering Research Council
ORWH National Institutes of Health, Office of Research on Women's Health
PAHO Pan-American Health Organization
QoL European Commission, Gender impact assessment study, Quality of Life and Management of Living Resources programme
SSHRC Canada, Social Sciences and Humanities Research Council
SWHR Society for Women's Health Research
WHI National Institutes of Health, Women's Health Initiative
WHB Health Canada, Women's Health Bureau
WHO World Health Organization