MEMORANDUM

From:	Dr C. d'Arcangues, RHR	**To:**	Secretary, Expert Committee on the Selection and Use of Essential Medicines	**Date: 10 January 2007**
Our ref:		**Attention:**		
Your ref:		**Through:**	Director, RHR	
Originator:		**Subject:**	APPLICATION FOR HORMONES AND CONTRACEPTIVES TO BE ADDED TO THE WHO MODEL LIST OF ESSENTIAL MEDICINES	

Received in PAR 12 JAN 2007

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Action needed:

Action taken:

In response to the request of the Secretariat for the Expert Advisory Committee on the Selection and Use of Essential Medicines, the Department of Reproductive Health and Research (RHR) would like to take the opportunity to comment on the applications for the following contraceptives:

- The levonorgestrel-releasing implant
- The medroxyprogesterone acetate plus estradiol cypionate injection

and on the paper entitled the *Systematic review of contraceptive medicines: "Does choice make a difference?"*.

The Department strongly supports the applications for each of the proposed contraceptive agents. Both represent important modes of delivery for contraception, both are increasing in user prevalence worldwide and both methods are included in RHR's guidelines and recommendations regarding the safe use of effective contraceptive agents.

With regard to the *Systematic review of contraceptive medicines: "Does choice make a difference?"*, conducted at the request of the Expert Advisory Committee on the Selection and Use of Essential Medicines, RHR comments are presented here as issues pertaining to: the question presented by the paper and its interpretation, the overall construction of the paper, the methodology, the arguments used to support the questions, and finally, details in the writing or exemplification of specific issues.

The Question:

The question presented by the paper is whether or not a wide range of choice of contraceptive agents for a woman, as opposed to a limited range of choice, makes a difference in health outcomes. The authors approached the issue from the bio-medical and intervention literature, attempting to answer whether a wide range of options improve uptake, adherence, continuation, satisfaction,

reduction of unwanted pregnancy and improvement in maternal health. Accordingly, the authors found much indirect evidence, but little evidence directly supporting their hypothesis.

This question may have been approached more effectively from a biosocial science point of view. As an example, the paper by Sullivan, et al, in the Journal of Biosocial Sciences 2006, "Dynamics of Contraceptive Use" could be used to directly address the question whether reliance on one or two methods act as a barrier to attaining very high levels of overall contraceptive use. This would be a good starting point for a paper taking a social science approach.

In line with this approach, there is strong evidence that women do not make choices based only on all methods available, they form preferences based on the views and behaviours of their friends and families; unfortunately, much about the social-behavioural aspects of making a choice is missing from this review. An additional element of the impact of socio-cultural barriers on choice may have included an exploration of how poverty influences the expression of choice.

The Structure:

Comments regarding the structure of the paper address mostly its overall clarity and cohesiveness. The review commences with the title 'Systematic review of contraceptive medicines 'Does choice make a difference?'. This title reflects the origins and history of the paper; however, to those unfamiliar with it, the subtitle of the report may be unclear and misleading.

In general, conclusions at the completion of each research question throughout the paper, with a summary of evidence presented and its derived overall conclusion, would be appropriate and would facilitate comprehensive reading of the report. The conclusions are currently weak enough that one RHR reviewer felt like she could not ascertain whether any conclusions were made at all. Additionally, without a strong recommendation or overall assessment, one may mistake the statement in the second paragraph of the Executive Summary regarding 'lack of quality evidence' to mean that no evidence is available and therefore no conclusion may be made. Instead, the conclusion of the paper should include a firm recommendation to the Committee, based on the evidence that does exist in the paper, that a wide range of safe and effective contraceptives be included in the essential list of medicines.

Throughout the paper, some editorial help, for example, with the length of paragraphs and sentences, completion of incomplete sentences, as well typographical and spelling errors, would be useful in making this report more easily read.

The Methods:

The conduct of a systematic review, particularly of this scope, must have a very clear methodology for identifying, describing, evaluating and integrating the evidence. Although the authors report a sound systematic search, and go on to describe many papers and studies, they fail to mention the methods used to evaluate the quality of the evidence. Without clear quality assessment, it is difficult for either the reader or the author to compile evidence in a meaningful way. It is also helpful

when grading the evidence to include, often in an evidence table, the strengths and weaknesses of each study, thus making its quality grade transparent. However, this has also not been done in this review. Additionally, much of the text is actually data-free, and therefore impossible to interpret in the context of a systematic review.

A significant amount of the evidence cited in the report is irrelevant, or only very indirectly relevant to the questions presented. This increases the difficulty of synthesizing the evidence in a focused manner, which is essential in a systematic review. The assessments of quality and relevance, as discussed above, would have helped the presentation of the good quality, direct and helpful evidence that is instead presented along evidence that is of low quality and indirect. Some specific studies which seem irrelevant are the six Cochrane reviews and the non-Cochrane review (Curtis et al, 2006) mentioned on page 25, as well most of those discussed on pages 32-35.

The strongest evidence about method-choice and subsequent satisfaction/compliance concerns women who do not receive the method that they wanted. The Pariani et al result for east Java are confirmed by a multi-site IPPF study in Huezo et al in Proceedings of XIII th World Congress of Gynaecology & Obstetrics Vol 1:111-135, 1993, which the review misses.

The Arguments:

Many arguments are presented in the review to substantiate the claim that choice in contraceptive methods improves health outcomes. Some arguments are more successful than others. We suggest that more should be made of the evidence concerning contraceptive discontinuation. This is an important marker, as, according to the most recent UN Population Division report, some 30% of women stop using their chosen reversible method within 12 months of starting it (for reasons that imply health concerns or dissatisfaction). These women need an alternative method to choose from as most (60%) switch methods, and their ability to switch is constrained by limited alternatives.

A concept that also deserves more attention is the following: if the most successful contraceptive is determined by the client and not the provider or disease-state, then contraceptives are unique among the standard chronic disease drugs. Therefore, the Essential Medicines organizing concept of the fewest, most rationalized listing of similar medications should be adapted for this category of drugs. This is discussed in the review, but minimally, and late in the paper.

An argument not explored in this review is that the idea that 'choice' actually presupposes informed choice, or patient education. If one follows this line of reasoning, the authors could explore the literature that exists showing that increasing patient education is positively correlated with compliance in long-term treatment of chronic diseases. Essentially, having choices about contraception are a necessary but not a sufficient condition for continuation of contraceptive use- understanding of the side effects, and proper use are important for successful use.

A final thought which also was not explored are that there are a variety of combined oral contraceptives, with substantial variability within the class. Therefore, the contraceptive methods

discussed may benefit from an exploration of the benefit of variability within a single type of contraceptive. This may be appropriate in the case of contraceptive devices as well.

The Details:

Additional comments mostly pertain to places in the text where further clarification, reference or detail is warranted. Towards the beginning of the report, there is a discussion on page 6 that contraceptives should provide against unwanted pregnancies as well as protect against HIV acquisition and future infertility. Condoms are the only method that meet all of these criteria but they are not the only contraceptive that should be recommended. It should be clear that RHR recommends that contraceptives be used as individually or in combination to address each individual's desired qualities of protection.

A specific study in which it is difficult to see its relevance is the Kalaca study, mentioned on pages 7 and 18. These couples had no options to choose from and therefore could not exhibit 'choice'; therefore, this study documents only the efficacy of Standard Days Method (SDM). Additionally, those who did not use SDM were not discussed.

Similarly, it is difficult to assess the importance of the Baveja paper mentioned on page 8, as the review does not describe how many women received their first choice, and how this affected their continuation. It would also have been helpful to include whether a non-choice environment was compared to in the Stevens-Simon paper, also on page 8. Other difficulties arise assessing relevance with the studies that are presented without their results, but only the author's interpretations of them, which impedes the reader from ascertaining the importance or relevance of the results.

Although there is a nice summary of current contraceptive practices worldwide on page 11, the current trends of contraceptive use are not discussed. If they were included, they would indicate the increasing use of both implants and injectables by the world's women.

The references cited as 'Anonymous' should cite instead the authors' organization, such as, the WHO Task Force on Service Research in Family Planning, for example, and should include the date.

It is interesting that the authors chose, on page 18, to define 'uptake' as user prevalence. The word 'uptake' suggests new users to the method and hence, the incidence of that contraceptive's use. If this definition was determined from another source, it would be helpful to cite its origin.

In general, throughout the report, 'free' choice should be written as 'increased' choice, to be truly accurate.

Finally, the list of factors that are identified as affecting choice should include the contraceptive's mode of delivery, as this is a key factor in deciding on a contraceptive for most women.

Conclusion

This review is thorough, and attempts to break down the question of whether a wide choice of contraceptive methods improves health outcomes for women and their families into manageable research questions. Overall, the strength, quality and relevance of the evidence presented is absent, and this affects the ability of the reader to synthesize a relevant and accurate conclusion from the review.

RHR appreciates the opportunity to comment on this paper.