

10th Summit Meeting Consensus: Recommendations for Regulatory Approval for Hormonal Male Contraception

The investigators at the Sixth Summit Meeting on Hormonal Male Contraception, Petersberg, Germany, held on 7-9 July 2002 recognized the need for standardized clinical trials to develop a hormonal male method and drafted several recommendations (Int J Androl 25, 2002: 375).

At the 9th Summit Meeting on Hormonal Contraception, Nyon, Switzerland, held on October, 9-11, 2005, the group of experts reviewed the status of clinical development projects for Male Hormonal Contraception and discussed the need to update the recommendations.

The following revised recommendation is the result of this discussion and presents consensus statement confirmed at the 10th Summit Meeting, New York, October 22-23, 2006:

It is stressed that the following recommendations are valid exclusively for hormonal methods for which the mechanism of action is based on the inhibition of sperm production. Methods with a different mode of action are outside the scope of this recommendation

The goal of hormonal male contraception is the reversible suppression of spermatogenesis to a level compatible with infertility. In principle this can be achieved by using an androgen alone or an androgen in combination with a gestagen or a GnRH-antagonist. The success of this principle in terms of lowering sperm counts in semen to azoospermia or to severe oligozoospermia has been demonstrated in multiple studies. Some trials demonstrated the contraceptive efficacy of this approach when couples used no other method of contraception. Investigators agree that information gained from preliminary studies on male contraception have reached a stage that hormonal contraceptive products for men should now be proposed for development for general use.

In order to bring a hormonal method to the market, large scale clinical trials are required. As no pharmacological method for male contraception is currently available, this represents a novel effort requiring new recommendations for testing and regulatory approval.

The investigators agreed that the following criteria should be fulfilled:

- In phase II dose-finding studies, the suppression of spermatogenesis can be used as the main parameter. As the surrogate parameter, sperm concentrations, measured according to WHO recommended methods, can be used and the goal should be ≤ 1 million/mL.
 - After cessation of treatment, each participant should be followed until reversibility of sperm production to criteria that are compatible with normal fertility has been shown. Usually return to sperm concentration of at least 20 million/mL provides sufficient evidence of fertility. These figures may be revised, probably downwards, as new data on fertility parameters emerge.
 - Currently only men with sperm concentrations ≥ 20 million/mL should be included. This threshold may be revised, probably downwards, in future as new data on fertility parameters emerge. Participants with known or suspected infertility should not be enrolled in clinical efficacy studies.
 - Open-label, non-comparative contraceptive efficacy studies are acceptable if the primary endpoint is not susceptible to bias, e.g pregnancy rate.
 - For contraceptive efficacy, two independent phase III trials for 1 year beginning when the male volunteer has suppressed to ≤ 1 million sperm / mL should be completed by 200 men/couples per trial.
 - For safety assurance for a new chemical entity, trials are required involving at least 300-600 men for 6 months at the intended combination and dose, 100 men exposed for 1 year and a total of 1500 men in phase I-III studies at the minimum.
 - Long-term safety will be monitored by post-marketing surveillance.
- The necessary laboratory investigations, especially semen analysis, need to be made under strict quality control.

These recommendations were drafted and approved by the participants in the 10th Summit Meeting on Male Contraception. This statement reflects the opinion of the individuals, but not necessarily the institution with which they are affiliated.

Pertti Aaltonen, Schering AG, Berlin, Germany

John K. Amory, University of Washington, Seattle WA, USA

Richard A. Anderson, Centre for Reproductive Biology, University of Edinburgh, UK

Hermann M. Behre, Martin-Luther-University, Halle, Germany

Gabriel Bialy, Center for Population Research, NIH, Bethesda MD, USA

Diana Blithe, NICHD, NIH, Bethesda MD, USA

Wilhelm Bone, Schering AG, Berlin, Germany

William J. Bremner, University of Washington, Seattle WA, USA

Doug Colvard, CONRAD, Arlington VA, USA

Trevor G. Cooper, University of Münster, Münster, Germany

Jörg Elliesen, Schering AG, Berlin, Germany

Henry L Gabelnick, CONRAD, Arlington VA, USA

Yi-Qun Gu, National Research Institute for Family Planning, Beijing, P. R. China

David J. Handelsman, ANZAC Research Institute, University of Sydney, Australia

Elof A. B. Johansson, Population Council, New York NY, USA

Wendy Kersemaekers, NV Organon, Oss, The Netherlands

Peter Liu, ANZAC Research Institute, Sydney, Australia

Trent MacKay, NICHD, Bethesda MD, USA

Stephen Matlin, Global Forum for Health Research, Geneva, Switzerland

Michael Mbizvo, WHO, Geneva, Switzerland,

Robert I. McLachlan, Prince Henry's Institute, Melbourne, Australia

Maria Cristina Meriggola, University of Bologna, Bologna, Italy

Stephan Mletzko, Schering AG, Berlin, Germany

Ellen Mommers, NV Organon, Oss, The Netherlands

Hilde Muermans, NV Organon, Oss, The Netherlands

Eberhard Nieschlag, University of Münster, Münster, Germany

Viveca Odland, University of Uppsala and Medical Products Agency, Uppsala, Sweden

Stephanie T. Page, University of Washington, Seattle WA, USA

Albert Radlmaier, Schering AG, Berlin, Germany

Regine Sitruk-Ware, Population Council and Rockefeller University, New York NY, USA

Ronald Swerdloff, Harbor-UCLA Medical Center Los Angeles, Biomedical Research Institute,
Torrance CA, USA

Christina Wang, Harbor-UCLA Medical Center Los Angeles, Biomedical Research Institute, Torrance
CA, USA

Frederick Wu, University of Manchester, Manchester, UK

Michael Zitzmann, University of Münster, Münster, Germany

