CPME/AD/Brd/150308/042/EN

At the CPME Board Meeting, in Ljubljana, Slovenia, on 15 March 2008, CPME adopted the following document **"CPME Statement on Unethical drugs testing"** (referring to CPME 2008/042 EN)

CPME Statement on Unethical drugs testing

A report published 19 February 2008 by the Centre for Research on Multinational Corporations (SOMO)[1] shows that 30 to 40% of phase III clinical trials are conducted outside the US and Europe, China, India and Russia being the countries used most for offshoring clinical trials. Most of the trials that the SOMO study identified as being performed in low and middle income countries concern the placebo-controlled testing of psychotherapeutic agents. The reason for this is that placebo-controlled trials for schizophrenia are not approved anymore by most European Medical Ethics Review Boards. Such trials are to be considered unethical, because patients in the control group are denied effective treatment and caused to relapse, a situation that can cause an irreversible worsening of their condition.
Par. 29 of the Declaration of Helsinki[2] states that *'The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists*. A footnote to this paragraph does allow for exceptions: '*The WMA hereby reaffirms its position that extreme care must be taken in making use of a placebo-controlled trial and that in general this methodology should only be used in the absence of existing proven therapy. However, a placebo-controlled trial may be ethically acceptable, even if proven therapy is available, under the following circumstances:*

- Where for compelling and scientifically sound methodological reasons its use is necessary to determine the efficacy or safety of a prophylactic, diagnostic or therapeutic method; or

- Where a prophylactic, diagnostic or therapeutic method is being investigated for a minor condition and the patients who receive placebo will not be subject to any additional risk of serious or irreversible harm. It is clear from the wording of this footnote that comparing new medicines to existing proven therapy is the rule.

Par. 30 of the Declaration of Helsinki furthermore states that '*At the conclusion of the study, every patient entered into the study should be assured of access to the best proven prophylactic, diagnostic and therapeutic methods identified by the study*.' In low and middle-income countries this is often not the case. Yet European authorities (and the FDA) still

[1] Ethics for Drugs testing in Low and Middle Income Counties – Considerations for European Market Authorisation; 19 February2008. http://www.somo.nl/index_eng.php
[2] http://www.wma.net/e/policy/b3.htm

require pharmaceutical companies to conduct placebo-controlled trials, also for schizophrenia. Similar observations have been made on trials for, *e.g.* hypertension drug trials, where patients were taken of their medication and received a placebo, for 52 weeks. Such trials are unethical.

European regulations do not in principle require placebo-controlled trials; in fact Directive 2003/63/EC mentions that … '*it may, in some instances, be more pertinent to compare the efficacy of a new medicinal product with that of an established medicinal product of proven therapeutic value rather than*
with the effect of a placebo.' Furthermore, Directive 2001/20EC requires that clinical trials conducted outside the EU, mentioned in marketing authorisation applications, meet the same standards for ethical conduct as trials in the EU: '*They shall be carried out in accordance with the ethical principles that are reflected, for example, in the Declaration of Helsinki.'* This is not always the case. It seems, therefore, that drugs are admitted to the European market that have been tested in trials that do not meet basic ethical standards.

The CPME therefore urges

- The European Commission and the European Parliament, to see to it that their relevant regulations are fully implemented.
- EMEA and national pharmaceutical authorities to no longer accept clinical trial data that are not in accordance with the Declaration of Helsinki.