

## Red Alert for Women's Hearts

### *Summary for Regulatory Authorities*

*Compendio per le Autorità Regolatorie*

#### **FACTS AND STATISTICS ON WOMEN AND CARDIOVASCULAR DISEASES IN CLINICAL TRIALS**

- Gender differences have been identified in the clinical presentation of Cardiovascular diseases (CVD), as well as in their treatment (therapeutic options might not be equally effective and safe for men and women).
- Their understanding may improve the clinical management of CVD and, in the future, develop possible gender specific diagnostic and therapeutic strategies.
- Women are underrepresented in cardiovascular research:
  - The 62 randomized clinical trials published between 2006 and mid 2009 enrolled 380.891 participants, 127.716 of them only were women (33.5%)
  - The percentage of women enrolled in each trial ranges between 15 to 60
  - Only 31/62 trials (50%) reported the analysis of the results by gender
- This underrepresentation is particularly noticeable in the fields of cholesterol-lowering therapy, ischemic heart disease and heart failure.
- As a consequence, safety and efficacy of several drugs have been evaluated predominantly in male populations.
- Most of the clinical trials and metanalysis on CVD do not report a significant lower efficacy of interventions in the outcome of women when compared with men.
- Although gender issues are addressed, scientific guidelines do not generally provide specific recommendations for prevention or treatment of women.
- Regulatory agencies in the USA and in Europe (EMA released a document on gender considerations in the conduct of clinical trials in 2005) have tried to encourage the inclusion of a higher proportion of women in clinical trials. Other documents have been released by WHO: e.g. Women, ageing and health.<sup>1</sup>

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<sup>1</sup> (<http://www.who.int/mediacentre/factsheets/fs334/en/index.html>)



## ***Recommendations for Regulatory Authorities*** *Raccomandazioni per le Autorità Regolatorie*

- Clinical trials enrolling a significant proportion of women to allow for pre-specified gender analysis should be encouraged, especially in the fields of ischemic heart disease, cholesterol-lowering therapy and heart failure.
- Clinical trials should systematically allow for an analysis of the results by gender.
- Enrolment criteria and follow-up duration of clinical trials should allow the inclusion of women at risk of developing cardiac events.
- External barriers to the enrolment of women in clinical trials need to be addressed, and in particular the transportation difficulties for older women to go to the follow-up visits.
- Scientific guidelines should systematically address gender differences; when not relevant, the guidelines should still indicate this so that readers are informed that they have been addressed.
- Regulatory agencies in the European Union are urged to adopt strict rules on the inclusion of women in clinical trials and a systematic gender analysis
- Standardised rules on gender specific biomarkers in drug development should be identified, validated and qualified.