30 March 2011

Submission of comments on 'EMA Reflection paper on the need for active control in therapeutic areas where use of placebo is deemed ethical and one or more established medicines are available' (EMA/759784/2010)

Comments from: Medicines in Europe Forum (MiEF), Association Internationale de la Mutualité (AIM), International Society of Drug Bulletins (ISDB)

Name of organisation or individual

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*

The EMA proposal clearly shows that the European Medicines Agency does not have the interest of the patient and public health as primary objective.

- Indeed, EMA states “Where feasible, three-arm trials including experimental medicine, placebo and active control represent a scientific gold-standard and there are multiple reasons to support their use in drug development”; however, the EMA proposals consists in normalising a practice which is in contradiction with this scientific gold standard.

- EMA not only falls behind from the scientific gold standard, but is also in contradiction with the World Medical Association’ "Declaration of Helsinki – Ethical principles for medical research involving human subjects" (2), which states:

“The benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention, except in the following circumstances:

The use of placebo, or no treatment, is acceptable in studies where no current proven intervention exists; or

Where for compelling and scientifically sound methodological reasons the use of placebo is necessary to determine the efficacy or safety of an intervention and the patients who receive placebo or no treatment will not be subject to any risk of serious or irreversible harm. Extreme care must be taken to avoid abuse of this option.”

The World Medical Association considers that the comparison of new medicines with "best current proven intervention" should be the ethical rule, and that the use of a placebo be the exception: “Extreme care must be taken to avoid abuse of this option”. We note that EMA reverses this ethical principle, considering that the use of a placebo is generally acceptable, unless in a limited number of cases.

- Finally, EMA even falls back behind ICH recommendations (which have been written in accord with the pharmaceutical industry). ICH guideline E10 states very clearly that: “In most cases, evidence of efficacy is most convincingly demonstrated by showing superiority to a concurrent control treatment. If a

superiority trial is not feasible or is inappropriate for ethical or practical reasons, and if a defined treatment effect of the active control is regularly seen (e.g., as it is for antibiotics in most situations), a non-inferiority or equivalence trial can be used and can be persuasive."

There is a huge difference between this position and the one proposed by the EMA although the EMA reflection paper refers to ICH guidelines!

We refuse to comment on the details of the proposals described in the EMA reflection paper as it moves away from the EMA's acknowledged scientific gold standard, ethical rules of the World Medical Association, and even ICH guidelines.

The EMA proposal is completely unacceptable and need to be firmly rejected.

References

1- European Medicines Agency "Reflection paper on the need for active control in therapeutic areas where use of placebo is deemed ethical and one or more established medicines are available" Committee for Medicinal Products for Human Use - Draft November 2010 EMA/759784/2010. www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2011/01/WC500100710.pdf.

2- World Medical Association "Declaration of Helsinki - Ethical Principles for Medical Research Involving Human Subjects" www.wma.net/en/30publications/10policies/b3/.

3- International Conference on Harmonisation "ICH Topic E 10 - Choice of Control Group in Clinical Trials" www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500002925.pdf.

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
		Comment: Proposed change (if any):	
		Comment: Proposed change (if any):	
		Comment: Proposed change (if any):	

Please add more rows if needed.