



Brussels, 10 July 2013

Joint letter to Member States' Ministers of Health and Permanent Representatives (CoRePers)

EU Regulation on clinical trials: the Council must further enhance transparency and participants' protection

The draft Regulation on clinical trials prepared by the European Commission is primarily aimed at "fostering EU's attractiveness in clinical research". However, it undermines the protection of trial participants (a).

On 29 May 2013, Members of the European Parliament (MEPs) belonging to the Environment, Public Health and Food Safety (ENVI) Committee adopted their report on the proposal from the European Commission (290 amendments). The plenary vote is scheduled for mid-November 2013.

If the Council confirms the improvements suggested by the ENVI Committee of the European Parliament, the new Regulation could represent an advance in terms of public access to the results of clinical trials. However, if it is to avoid undermining the protection of persons enrolled in clinical trials, the Council must further improve the draft Regulation.

We believe that the following issues need to be urgently addressed:

1. Re-establish the role of Ethics Committees to guarantee the protection of trial participants

With its proposal to disconnect "scientific" assessment (by a reporting Member State, whose findings are binding to the other Member States concerned) from "ethical" assessment (made by each Member State, but limited in practice to verifying compliance with the consent procedure), the European Commission proposes in effect to deprive Member States of their sovereignty over the acceptability of a clinical trial.

► We urge you to:

- Secure ethical improvements put forward by MEPs: **restoring the role of Ethics Committees and also authorising them to comment on the "scientific" assessment** (an ethical assessment also involves an assessment of the methodology and the two issues cannot be assessed separately) (*amendments 2, 64, 77 and 79*); **moreover, the Council must clarify the fact that Ethics Committees' opinion is binding (b)**;
- **Refuse the generalisation of a tacit approval procedure**, to ensure that no trial can be authorised without an Ethics Committee opinion (this would contravene the Charter of Fundamental Rights of the European Union).

2. Strengthen requirements for transparency of clinical trial findings

Selective publication of only those results which favour the drug in question biases both scientific analysis and Medicines Agencies' decisions (c).

Aware of the need for independent analyses, MEPs proposed a compromise based on the 2010 European Medicines Agency's policy on access to documents: MEPs included a provision that clinical data contained in clinical study reports (as defined by *amendment 76*) "should not be considered commercially confidential once a marketing authorisation has been granted or the decision-making process on an application for marketing has been completed" (*amendment 30*, creating a new recital).

a- For more details, read our joint analysis ("[New Proposal for a Regulation on Clinical Trials – Joint analysis](#)" 5 February 2013 : 12 pages.) or Kuhrt N "Unwitting Guinea Pigs: EU Seeks To Reduce Patient Protection in Medical Trials" 24 juin 2013 (www.spiegel.de).

b- According to Article 9(1) of Directive 2001/20/EC, "the sponsor may not start a clinical trial until the ethics committee has issued a favourable opinion and inasmuch as the competent authority of the Member State concerned has not informed the sponsor of any grounds for non-acceptance". Recital 11 of Directive 2001/20/EC confirms that a "tacit" administrative authorisation by the Member States' competent authority [often the drug regulatory agencies] is only possible "if there has been a vote in favour by the ethics committee".

c- Thus, in Europe, in 2009, several EU governments stockpiled millions of doses of Tamiflu® to combat A/H1N1 influenza, even though the effectiveness of Tamiflu® in the prevention of influenza complications was unproven and even unlikely, so wasting billions of euros. Health authorities made decisions without seeing the full data set (more examples are presented in the BMJ campaign for access to data at <http://www.bmj.com/open-data>).

This demand is perfectly reasonable, and is in line with what the European Medicines Agency intends to implement in the review of its policy on access to documents (d).

- ▶ We therefore ask you to **support Amendment 30**, and also to **add this requirement to the Regulation, in the form of an article**. A clear stance by the Council in favour of freedom of information for European citizens and of public access to the results of clinical trials is needed to enable the European Medicines Agency to defend itself in the procedure brought before the EU Court of Justice by two companies challenging its 2010 policy on access to documents.
- ▶ We also ask you to further **strengthen transparency requirements by demanding the publication of clinical study reports within 5 years from the end of the clinical trial when the company has not by then applied for marketing authorisation**, to ensure that these results are not forever lost to science should the company decide in the end not to seek marketing authorisation.

3. Clarification of definitions, including "low-risk clinical trials"

MEPs wish to support the Commission's proposal to create a new category of "low-intervention trials" for drugs already on the market. However, MEPs understand the dangers of the recent trend to accelerate marketing authorisation procedures before gathering sufficient data on the efficacy and safety of the drugs concerned (e). MEPs therefore supported only "low-risk trials", which differ from "low-intervention trials" because post-approval efficacy and safety studies of medicinal products authorised within the previous 10 years are excluded from "low-risk trials" (*amendment 57* explicitly included trials involving recent medicinal products in the definition of "standard" clinical trials, so they cannot be categorized as "low-risk").

- ▶ **We urge you to support the clarification of definitions requested by MEPs**, particularly to avoid the risk that some clinical trials will be considered, by default, "non-interventional studies";
- ▶ **We call on you to be particularly cautious with "low-risk trials"**, particularly in order to ensure that:
 - **participants in "low-risk clinical trials" will be eligible for compensation** in case of damages as requested by MEPs (*amendment 235*) (f);
 - **"low-risk trials" cannot cover off-label indications**, even if they are based on "*sufficient published evidence and/or standard treatment guidelines*" (refuse *amendments 56 and 60*), **and cannot be conducted without seeking patients' informed consent** (refuse *amendments 17, 34 and 167*).

4. Strengthening the study of adverse drug reactions (ADRs) before granting a marketing authorisation

Clinical trials should also aim to determine how well patients tolerate new medicines. The Regulation only requires reporting of serious adverse drug reactions by the trial sponsor to the Agency if they are "*unexpected*". Yet recent evidence underlines the fact that companies are reluctant to report adverse reactions of their drugs to health authorities. Indeed, being both "judge and defendant", they have a tendency to present adverse reactions as unrelated to their products, or even to hide them for as long as possible (g).

- ▶ **We urge you to demand reporting by the investigator (the clinician) of all serious adverse reactions, whether "expected" or not, via the centralised portal**, in order to avoid harmful delays in the decision-making process, especially when urgent measures are needed to protect participants.

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International Society of Drug Bulletins (ISDB)

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d- In addition, this requirement is consistent with the position of the European Ombudsman, who found that clinical study reports do not contain commercially confidential information or personal data (participants' clinical data are previously anonymised) (*BMJ* 2011, **342**:d2686). This was confirmed by an in-depth analysis of 78 clinical trials by two researchers from the Cochrane Collaboration in early 2013 (*BMJ Open* 2013;3:e 002496).

e- In such cases, the authorities ask companies to perform post-approval efficacy and safety studies (PAES and PASS studies).

f- Directive 2001/20/EC made it obligatory to take out insurance for all human trials.

g- There are many examples, well documented, e.g.:

- Healy D "Let them eat Prozac" New York: New York University Press, 2004.

- "GlaxoSmithKline to plead guilty and pay \$3 billion to resolve fraud allegations and failure to report safety data". July 2012. www.justice.gov: 3 pages.

- "European Medicines Agency acts on deficiencies in Roche medicine-safety reporting". July 2012. www.ema.europa.eu: 2 pages.

Cosignatory organisations

AIM. The Association Internationale de la Mutualité (AIM) is a grouping of autonomous health insurance and social protection bodies operating according to the principles of solidarity and non-profit-making orientation. Currently, AIM's membership consists of 41 national federations representing 29 countries. In Europe, they provide social coverage against sickness and other risks to more than 150 million people. AIM strives via its network to make an active contribution to the preservation and improvement of access to health care for everyone. More info: www.aim-mutual.org. Contact: corinna.hartrampf@aim-mutual.org.

Nordic Cochrane Center. The Nordic Cochrane Center is part of the Cochrane Collaboration. The Cochrane Collaboration is an international not-for-profit international network of more than 28,000 dedicated people from over 100 countries preparing, maintaining and promoting the accessibility of systematic reviews of the effects of health care. More information: www.cochrane.org. Contact: pcg@cochrane.dk

HAI Europe. Health Action International (HAI) Europe is a non-profit, European network of consumers, public interest NGOs, health care providers, academics, media and individuals working to increase access to essential medicines and improve their rational use through research excellence and evidence-based advocacy. More info: www.haieurope.org. Contact: ancel.la@haieurope.org

ISDB. The International Society of Drug Bulletins (ISDB), founded in 1986, is a worldwide Network of bulletins and journals on drugs and therapeutics that are financially and intellectually independent of pharmaceutical industry. Currently ISDB has around 80 members in 41 countries around the world. More info: www.isdbweb.org. Contact: press@isdbweb.org

MiEF. The Medicines in Europe Forum (MiEF) was launched in March 2002 and reaches 12 European Member States. It includes more than 70 member organizations representing the four key players on the health field, i.e. patients groups, family and consumer bodies, social security systems, and health professionals. Such a grouping is unique in the history of the European Union and is testament of the importance of European medicines policy. Contact: pierrechirac@aol.com

TACD. The Transatlantic Consumer Dialogue (TACD) is a forum of US and EU consumer organisations which develops and agrees on joint consumer policy recommendations to the US government and European Union to promote the consumer interest in EU and US policy making. More information: www.tacd.org. Contact: tacd@consint.org or hammerstein.david3@gmail.com

Wemos. Wemos influences international policy in such a way that the right to health is respected, protected and promoted. In doing so, Wemos devotes special attention to vulnerable sections of society. Wemos advocates ethical conduct, coherent policy and equal access to care. Its lobbying work focuses on lasting improvements in Dutch, European and global policy. More information: www.wemos.nl. Contact: annelies.den.boer@wemos.nl