Nordic Cochrane Centre

Brussels, 18 November 2013
Joint letter to Member States' Permanent Representatives (CoRePers)

EU Regulation on clinical trials: An urgent call for support to clinical data transparency

At the ENVI Committee's vote on the Clinical Trials Regulation on 29 May 2013, Members of the European Parliament (MEPs) took a clear stance in support of enhanced data transparency. We call upon the Council to also choose transparency.

The current discussions on a **new EU Regulation on Clinical trials** (aimed at repealing Directive 2001/20/EC) offers **an exceptional opportunity to improve the transparency of clinical trials data**.
The current situation of limited access to clinical trial data allows for harmful practices to occur, such as selective publication and the withholding of medicines' safety data, ultimately undermining the protection of public health. It has been widely reported that many adverse drug reactions, including deaths, could have been avoided had the general public known about the undisclosed effects of certain medicines[1,2].

In addition to the many benefits to patients' safety, the **disclosure of full clinical trial data** would allow for **independent analysis** of clinical trials results and enhance the **cost-effectiveness of public health expenditure** by, for example, allowing comparative-effectiveness analysis between therapies. Health Technology Assessment (HTA) agencies strongly rely on this data for their assessments, and they have called for their public release[3]. Beyond doubt, data transparency will lead to improved health decision-making.

In a recent article, European Medicines Agency (EMA) regulators support these arguments and state that, contrary to industry's fears, public access to data sets from clinical trials will **benefit the research-based biopharmaceutical sector** by, amongst other things, increasing

[1] Health Action International (HAI) Europe. Protecting citizens' health: Transparency of clinical trial data on medicines in the EU. Policy paper (October, 2013). Available at: http://haieurope.org/wp-content/uploads/2013/10/HAI_Protecting-citizenshealth-transparency-of-clinical-trial-data-on-medicines-in-the-EU.pdf

[2]- Joint letter by 11 International and European organisations "Clinical trials regulation: protect public health, choose transparency!" Brussels, (April 2013).
Available at: http://english.prescrire.org/en/79/207/46302/2612/2506/SubReportDetails.aspx

[3] Wieseler B., Wolfram N., McGauran N. et al. Completeness of reporting of patient-relevant clinical trial outcomes: comparison of unpublished clinical study reports with publicly available data (2013). *Plos Med* 10(10): e1001526

the efficiency of drug development and reducing duplication of effort amongst trial sponsors[4].

Moreover, transparency of clinical trial data is required for **ethical reasons**. Many patients participate in trials and undertake risks in order to contribute to medical science. Failure to make these results publicly available is a betrayal of their trust. Unnecessary duplication of trials leads to avoidable harm.

For all these reasons, the following European and international organisations - International Society of Drug Bulletins (ISDB), Nordic Cochrane Centre, Medicines in Europe Forum (MiEF), Health Action International (HAI) Europe, Association Internationale de la Mutualité (AIM) and Trans Atlantic Consumer Dialogue (TACD) – have joined to call upon the Council to **support the ENVI Committee's position on data transparency**, in particular:

- **Amendment 30**. The transparency standards of the EMA have to be upheld and reinforced. Once the decision making-process has been completed, the Agency releases documents submitted as part of applications for marketing authorisation, including clinical study reports (CSRs), which are comprehensive documents containing detailed but of course anonymised clinical data[5]. These documents were, until now, made available on request and the EMA is working towards their proactive publication online (scheduled for 2014).
  According to the European Ombudsman, data included in clinical study reports contain no commercially confidential information[6]. This has been confirmed by a recent review of several dozens of clinical study reports[5].

- **Amendment 193.** Clinical study reports offer by far the most comprehensive data on each clinical trial, providing the highest reporting quality on methods and outcomes. It is crucial that these documents are made publicly available, in addition to the summary of the results.
  The disclosure of clinical trial data can safeguard patients' confidentiality. In its previous assessment, the Ombudsman found that "neither the requested documents nor other information in the public domain appeared to allow a link to be made between a given identification number and a particular patient, thus making it possible for him/her to be identified" [6]. In addition, EMA regulators have stressed that "standards for deidentifying personal data are available and continue to evolve to ensure adequate protection" [4].
  Financial penalties must be imposed in the event of non-compliance with disclosure requirements.

[4] Eichler H.G., Pétavy F., Pignatti and Guido R. Access to patient-level trial data- A boon to drug developers (2013). *NEJM* 369:1577-1579. DOI: 10.1056/NEJMp1310771

[5] Doshi P., JeffersonT. et al. Clinical study reports of randomised controlled trials: An explanatory review of previously confidential industry reports. (2013). BMJ Open 3:e002496

[6] European Ombudsman. Decision of the European Ombudsman closing his inquiry into complaint 2560/2007/BEH against the European Medicines Agency. (November 24, 2010).

- **Amendment 194.** The reasons for discontinuing a clinical trial, as well as the obtained results, have to be submitted and published on the EU database. This information could evidence that the investigational medicinal product was not effective or that there were too many adverse drug reactions. This is vital information for patients.

- **Amendment 253.** In order to ensure that the EU database is widely used by the general public, it needs to be available free of charge and set up in a user-friendly way.

In addition to the above listed amendments, the future EU Clinical Trials Regulation has to include the following provisions:

- **Request the publication of clinical study reports within 3 years, at the latest, if the sponsor has not by then applied for marketing authorisation.** This would ensure that these results are not forever lost to science.

- **State that following information is not commercially confidential**: **clinical trial data, the reasons for temporary halt and early termination of a trial as well as regulatory documents** concerning the criteria and decision about the trials' authorisation and granting of drugs' marketing authorisation.

We would be happy to discuss this issue further with you and hope that you will take our recommendations into account.

Cosignatory organisations

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

Nordic Cochrane Centre. The Nordic Cochrane Centre 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

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

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

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.

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