

EAHP STATEMENT ON CLINICAL TRIALS

JUNE 2012

What needs to improve with the current regulation of Clinical Trials in Europe?

Clinical Trials are critical in achieving continuous improvement in patient outcomes and improving survival rates for patients with acute illnesses. Such advances are key to European health systems successfully meeting the demographic and disease challenges of the future.

However, according to European Commission figures, between 2007 and 2010 there has been a 15% decline in both the number of clinical trial studies within EU sites and the number of EU subjects participating in these studies¹. Although other issues are involved as well, there is a consensus within the health sector that a major factor attributed to this decline in trial activity relates to the EU Clinical Trials Directive² (2001/20/EC), including:

- differing interpretations of requirements in different member states;
- separate definitions of key terms across Europe; and,
- a lack of guidance in implementing and complying with the Directive.

Indeed, it is estimated by some organisations that the Directive has contributed to a 65 per cent increase in the time it takes researchers to get approval for their studies, and a 75 per cent increase in administrative costs³. Another assessment undertaken by the Impact on Clinical Research of European Legislation (ICREL) found that non-commercial sponsors required an increase from 1.5 to 2.8 FTE (full-time equivalent) staff to manage administrative tasks associated with a Clinical Trial Authorisation, and that there was an increase in time between finalisation of protocol and first patient recruited from 144 to 178 days⁴.

Europe's 21,000 Hospital Pharmacists, as the secondary and tertiary care sector's experts in medicines, pharmacotherapy and pharmacokinetics, play a key role in the implementation and conduct of clinical trials in all European countries.

The European Association of Hospital Pharmacists (EAHP), as the representative organisation for the hospital pharmacy profession across Europe, recognises the need to reform the EU Clinical Trials Directive (2001/20/EC) in order to provide a more favourable regulatory environment for clinical research in pharmaceuticals.

Furthermore, EAHP makes the below statement of areas for trial regulation improvement, as approved by its June 2012 General Assembly.

¹ http://ec.europa.eu/commission_2010-2014/dalli/docs/speech_07032012_en.pdf

²

http://info.cancerresearchuk.org/prod_consump/groups/cr_common/@nre/@pol/documents/generalcontent/cr_077460.pdf

³ <http://www.theparliament.com/latest-news/article/newsarticle/eu-urged-to-revamp-clinical-trials-directive/>

⁴ http://www.efgcp.be/downloads/icrel_docs/Final_report_ICREL.pdf

EAHP's Call for Action

1) Application and Assessment of Trials

EAHP support the suggestion of a single electronic portal for submission when proposing a new clinical trial, and look forward to examining forthcoming proposals for improving national level cooperation in relation to assessment. Implementing such measures should reduce complexity and bureaucracy, reduce costs for applicant parties and should facilitate standardisation of application processes and definitions. EAHP member experience from Italy⁵ suggests electronic portal processes for clinical trial applications can work well and facilitate processes.

EAHP furthermore support the Commission's intention of keeping ethical assessments of trials at a national level.

2) Distinction between high risk and low risk trials

EAHP support the Clinical Trials Directive making a greater distinction between high risk and low risk trials. This should permit a more proportionate regulatory approach and facilitate trials for extending the terms of use for medicines already holding marketing authorisation e.g. off-label and off-licence trials.

Distinction between non-profit and for-profit trials

EAHP support efforts to decrease regulatory burden where possible and proportionate, and in particular for non-profit organisations leading trial activity. Whilst standards of Good Ethics and Good Clinical Practice need to be maintained in all trial activity, EAHP considers there is scope to reduce areas of administrative regulatory burden.

Multi sponsor trials

EAHP support further examination of whether a process can be put in place for multi-sponsor trials. In a period of constrained budgets in both private and public sectors, it occurs to the Association that multi-sponsor trials could reduce cost burdens of research and more generally serve to consolidate research activity.

3) Clinical Trials and Patient Groups

There is a recognised need to improve the participation rates of older people in clinical trials. Medicines are not only most commonly used in older patients, but there are important elements of understanding required by prescribers and other health professionals related to:

- the increased susceptibility for medicines to have side effects in older persons due to the physical effects of ageing;
- the trend for older persons to have multimorbidity and take multiple medications⁶; and,

⁵ <http://oss-sper-clin.agenziafarmaco.it/>

⁶ The more medications a patient uses, the greater the risk of interactions between these medicines and the risk of adverse reactions.

- potential medicines adherence difficulties for patients with failing eyesight, memory and dementia.

Information from trials on efficacy in this patient group is therefore of high importance. **The EAHP recommends that in the context of forthcoming revisions to clinical trial regulation the European Commission, European Medicines Agency and national agencies give due consideration to how the regulation and requirements for trials could be improved in order to achieve more robust information on treatment effects in older people. This includes examination of how to achieve greater participation in trials by older persons.**

In a similar fashion, children are a separate patient group that require distinct consideration in relation to the improvement of the European clinical trial environment. The use of unlicensed and off-label medicines in children is widespread, and yet it has been reported that in the EU 50% or more of medicines used in children have never actually been studied in this population, but only in adults, and not necessarily in the same indication (or the same disease)⁷.

The introduction of the EU Pediatric Regulation in 2007 appears to have led to some improvements in this area, with earlier discussion of pediatric development within pharmaceutical companies now taking place when developing new products⁸. However in order to realise continuous improvement EAHP considers that the Regulation's impact and operation need to be kept under ongoing review with the aim of ensuring the Pediatric Investigation Plan (PIP) process, and other elements of the regulation, operate to optimum effect.

Finally, another evidenced under-represented group in trials are females⁹. As with older people and children, ongoing efforts must be made within the review of clinical trials regulation of how to improve participation from this patient group.

4) Publication of Clinical Trial Data

In relation to the publication of clinical trial information, EAHP supports further opening up of access. Open access can benefit public health by allowing independent analysis¹⁰ and the development of predictive models. EAHP therefore consider that the information within EMA's EudraCT database, which contains full drug trial results on all approved drugs, should be made more accessible.

⁷ Conroy S et al. Br Med J. 2000;320:79-82

Chalumeau M et al., Arch. Dis. Child. 2000;83: 502-5.

⁸

http://www.ema.europa.eu/docs/en_GB/document_library/Presentation/2011/05/WC500106718.pdf

⁹ *Under-representation of women in high-impact published clinical cancer research.* Jaggi R, Motomura AR, Amarnath S, Jankovic A, Sheets N, Ubel PA. Cancer. 2009 Jul 15;115(14):3293-301.

See also EMA reflection paper on gender differences in cardiovascular diseases: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/09/WC500003289.pdf

¹⁰ Including independent re-analysis of a medicine's benefits and risks

Also in relation to Clinical Trial databases, and increased globalisation of trial activity, EAHP calls for further efforts by relevant international regulatory bodies, in Europe and beyond, to coordinate the holding and accessibility of international trial information for the purposes of:

- global research coordination;
- transparency; and,
- prevention of duplication.

The extent to which current coordination efforts by regulators is achieving this should be subject to a form of independent monitoring.

Finally, to improve transparency and enable independent assessment, EAHP considers it should be a condition on licence applicants to publish all available trial data provided to the European Medicines Agency in peer-reviewed Journals.

5) Protecting Patient Safety

EAHP identify a need for further harmonisation in the management of adverse reactions in Trials. It should be a standard requirement that Ethics Committees assure the presence of a Data Safety Monitoring Board in the trial when they approve a study and periodical reports to the Ethics Committees should contain all the relevant information required for a thorough evaluation (e.g., number and type of adverse reactions by type of treated population, the total number of treated patients (denominator) etc).

In Conclusion

As the Commission, EMA and national governments and agencies address the issue of improving European trial regulation over the next 18 months, EAHP urge that decision-makers are mindful that:

- clinical trials are essential to the future health and well being of all EU citizens and should therefore be addressed as a priority political issue;
- for the protection of patient safety however, there is a need to ensure research is of the highest clinical and ethical standards and that regulation supports this;
- there is a need to ensure participation of older people and those with multiple pathologies, often the same, to ensure trial outcomes are well reflected in respect of future general use; and.
- ongoing efforts are made to ensure clinical trial regulation is fit for purpose in relation to the participation of, and evidence provided, in relation to children and gender.

Within all this there is a continued need to reduce bureaucracy and achieve better standardisation in requirements and assessment criteria between national competent authorities.

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The European Association of Hospital Pharmacists (EAHP) is a Federation of national associations of hospital pharmacists. EAHP represents and develops the hospital pharmacy profession within Europe in order to ensure the continuous improvement of care and outcomes for patients in the hospital setting. This is achieved through science, research, education, practice, as well as sharing best-practice and responsibility with other healthcare professionals.