Statement

German Network for Evidence-based Medicine

Berlin, 05 July 2016

The German Network for Evidence-based Medicine endorses the "MoreTrials" initiative (http://moretrials.net/)

The "MoreTrials" initiative aims to diminish bureaucratic hurdles in clinical research so that altogether more clinical trials can be carried out. The main hope is that more clinical trials are once again conducted by physicians – and not solely by the pharmaceutical industry. This is the only way to ensure that medically important questions that are not commercially exploitable are addressed as well.

The current occasion for these considerations is the revision of the international rules governing the conduct of clinical trials. This set of rules, issued by the International Council on Harmonization (ICH) and known as Good Clinical Practice (GCP), also applies to all studies carried out in Germany under the German Medicinal Products Act (Arzneimittelgesetz) or the German Medical Devices Act (Medizinproduktegesetz). The GCP rules notably provide for the detailed and comprehensive documentation of all trial data, on-site data monitoring, expedited reporting of serious adverse events and archiving of all trial documentation for ten years. These and other provisions contribute to an increased reliability of trial results but also lead to a considerable rise in trial costs, with the result that some trials are not carried out at all. Particularly for smaller trials, it can be estimated that the CPG rules more than double trial costs.

These costs must also be covered by German physicians who want to carry out a pharmaceutical clinical trial. The CPG rules have to be observed even when the pharmaceutical in question has been authorized for the investigated indication for ten years. This has repeatedly led to medically important trials not being carried out due to financial constraints. For example, trials intending to investigate the reduction of pharmaceutical dosages or compare two already authorized pharmaceuticals often do not take place because they are not of interest to manufacturers. Even though the risk of severe adverse events in such trials is often minor, they still have to be carried out following GCP standards.

Adapting standards for clinical trials according to risk

Thus, it makes sense to limit regulatory provisions for clinical trials to the necessary extent. The main issue here is maintaining the balance between feasibility and affordability on the one hand and trial quality and safety on the other. Abolishing the GCP rules altogether is not a sensible goal, as they have proven to be very important, particularly in the pre-market authorization stage. Additionally, as pharmaceutical trial results often drive millions in market profits, these trials require meticulous quality control. For example, this became apparent in 2014 and 2015, when numerous trials carried out in India or China turned out to be fabricated. GCP standards are not mandatory in either of the two countries.

However, it is unsatisfactory that academically initiated, less financially equipped trials on already authorized pharmaceuticals are in some cases hampered by the GCP regulation.

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The "MoreTrials" initiative therefore makes the case for more flexible rules. In this context, a distinction could be made between trials carried out before and after the pharmaceutical is authorized to enter the market. Exceptional provisions for academically initiated trials (so-called investigator-initiated trials, IITs) have previously been exploited by the industry, who used clinical "straw men" to circumvent GCP standards. Thus, exact criteria must be set if the GCP rules are to be made more flexible and adapted to the different levels of risk facing trial participants. Moreover, increasing the flexibility of the GCP standards should not interfere with their fundamental principles, such as the on-site monitoring of central trial data.

The "MoreTrials" initiative calls for an open debate on the GCP regulation. How clinical trials are to be conducted should not be decided by a group of experts behind closed doors but rather be determined in an evidence-based, transparent manner. The current version of the GCP regulation has missed important developments, especially the registration of clinical trials, which impedes the concealment of negative results. Therefore, the development of GCP rules must be reformed, so that the focus lies less on obligations regarding validation and documentation and more on study designs of high scientific quality.

The German Network for Evidence-based Medicine wants more trials

The German Network for Evidence-based Medicine considers it appropriate that not all trials under the German Medicines Act need to fulfill every aspect of the GCP rules. Provisions should be simplified when they pertain to clinical trials carried out after the pharmaceutical has received its marketing authorization and on an authorized indication. Further exceptions are conceivable in cases when trial participants are demonstrably not exposed to a relevant risk of adverse events. The German Network for Evidence-based Medicine supports the idea of strengthening non-commercial clinical research, so that all questions that are important to patients can be answered in an evidence-based manner.

References:

„More trials"-Initiative: http://moretrials.net/

Gesetzliche GCP-Verordnung: http://www.gesetze-im-internet.de/gcp-v/

GCP-Guideline E6: http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2015/08/WC500191488.pdf

The **German Network for Evidence-based Medicine (DNEbM)** was founded to spread and further develop the concepts and methods of evidence-based medicine in practice, teaching and research in German-speaking countries. The DNEbM advocates that all citizens receive health care based on best scientific knowledge and informed decision-making.

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