Clinical trial investigators violate EU regulations—entries in EU Register are incomplete

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According to EU legislation, clinical trials must be prospectively registered in the European Union Clinical Trials Register (EUCTR) and the main results must be reported there one year after completion of the

trial. The information is thus publicly available. But in fact, results are only reported for half of drug trials (49.5 percent). According to an analysis recently published in the *British Medical Journal* (*BMJ*), pharmaceutical companies were relatively compliant with a rate of 68.1 percent, but the result was very poor for non-commercial research organizations, with a rate of 11.0 percent,.

Jürgen Windeler, the director of the German Institute for Quality and Efficiency in Health Care (IQWiG) notes: "The fact that tax-funded universities are not fulfilling their legal obligations is particularly regrettable. But the *BMJ* article does not surprise us. On several previous occasions, the institute experienced that clinical trial investigators at universities withheld data."

Transparency is relatively high for drug trials

In general, data transparency is higher for drug trials than for trials of non-drug interventions, in which medical devices are often used. This is because the EU regulation has been effective for drugs since 2012. A comparable regulation for medical devices was only concluded in 2017, and will be effective from 2020 onward.

Moreover, since 2011, according to the Act on the Reform of the Market for Medicinal Products (AMNOG), pharmaceutical companies in Germany must provide all relevant data on new drugs, which as a rule can be published. After initial resistance, the companies now accept these transparency requirements. This corresponds to the *BMJ* finding that 11 large commercial sponsors of trials reported all results in EUCTR within the one-year deadline.

University research groups withhold data

According to the *BMJ*, compliance is particularly lacking at universities

conducting drug trials. These also include German universities such as Berlin (Charité), Heidelberg and Cologne (0 percent). In contrast, a British university, Dundee, reached the highest rate of registry entries (82 percent).

IQWiG's negative experiences with university research groups primarily refer to medical device trials. At the end of August 2018, in its preliminary report on negative pressure wound therapy, the institute found that the device manufacturer and the clinical trial investigators at universities answered the institute's requests only incompletely or not at all.

This was not an exceptional case. The institute could not draw a conclusion on the benefit or harm of stem cell transplantation for multiple myeloma because even more than 10 years after their completion, three large trials had still not been fully published. Two of these trials were under German supervision (universities of Heidelberg and Würzburg). An Australian research group has shown that things can be handled differently. They provided all individual patient data from a trial to IQWiG. This enabled IQWiG to perform additional analyses that ultimately led to a positive conclusion in the benefit assessment (corneal collagen cross-linking in patients with keratoconus).

Increase pressure on clinical trial investigators

Jürgen Windeler says, "There are substantial deficits in investigator-initiated trials with regard to data transparency—and sanctions are seemingly required to quickly change this." One option could be that research funders impose specific requirements. They should check whether an applicant has completely reported its previously funded project in the EU Register and, if applicable, refuse further funding.

As trials are also conducted without public funding, ethics committees

should also monitor whether legal regulations such as inclusion of a trial in the EU Register are being followed, because these committees know all trials conducted in a certain region or university.

The fact that clinical trials are not registered and their results are not reported is not a trivial offence. Rather, ethical and scientific standards are being violated because the benefit and harm of medical interventions can only be correctly assessed on the basis of complete data. Only then can physicians and patients decide on the best-possible alternative.

More information: Ben Goldacre et al, Compliance with requirement to report results on the EU Clinical Trials Register: cohort study and web resource, *BMJ* (2018). DOI: 10.1136/bmj.k3218

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