

INTERNSHIP REPORT

Risk assessment of sponsorship in clinical trials

Assigning risks for non-compliance to different sponsor categories in medical clinical trials

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Executive summary

Background: In the Netherlands, the Health and Youth Care Inspectorate (IGJ) supervises clinical research by inspecting compliance with applicable (inter)national legislation. Thereby, IGJ ensures the wellbeing, rights, and safety of participants, and the quality of data during the conduct and after completion of clinical trials. The inspectorate inspects all clinical trial phases that are subject to the Medical Research Involving Human Subjects Act (WMO). Due to the amount of studies that are submitted for ethical review at the competent authorities every year, IGJ must develop an effective and convenient routine inspection approach to prioritise visits. In clinical trials, a sponsor is defined as “an individual, company, institution, or organization which takes responsibility for the initiation, management, and/or financing of a clinical trial.” The inspectorate aims to use a risk-driven approach based on risks for non-compliance with applicable legislation associated with the sponsor type. However, IGJ lacks insight in the current sponsor classification located in the Netherlands and the risks for non-compliance with applicable legislation associated with these sponsors.

Research objective: The research objective of the current study is to offer IGJ recommendations concerning the prioritization of sponsor inspections. Therefore, this study aims to gain insight in 1) the current sponsor classification in clinical research in the Netherlands, 2) the specific risks for non-compliance with applicable legislation associated with this classification according to different stakeholders, and 3) the severity of risks derived from the field according to the inspectorate.

Methods: Methods included an analysis of the Central Committee on Human Research register and European Clinical Trials Database, and a workshop with the inspectorate, to classify different sponsor categories. Additionally, semi-structured interviews with 18 stakeholders and a second workshop with the inspectorate were conducted to identify risks for non-compliance associated with the different sponsor categories. Subsequently, a third workshop with the inspectorate was conducted to rank risks on severity. Finally, a list of risks and scores for each sponsor category was created, to evaluate which sponsor category includes the highest risk for non-compliance.

Results: It was found that eight categories of sponsors can be distinguished in the Netherlands conducting clinical trials with medicines: Large commercial companies, small commercial

companies, contract research organisations (CROs), university medical centres (UMC), hospitals, universities, interest groups, and a remaining group called 'other'. Secondly, it was found that different risks for non-compliance can be assigned to the sponsor categories, which were themed into the following potential risk indicators: Experience, education, interests, combination care and research, man power, sponsor checks, research facilities, and cooperation. Both commercial companies and CROs have financial and commercial interest increasing the chance for non-compliance. Additionally, small commercial companies have a lack of experience, facilities, and knowledge of legislation to conduct clinical trials properly. These three risks were also found for hospitals, interest groups, universities, and 'other' sponsors. UMCs and hospitals showed the highest risks for the combination of healthcare and clinical research, because employees wear many hats and prioritise patients above protocols. Moreover, universities were thought to be at risk for non-compliance due to their interest in outcome, rather than the patient. Finally, hospitals and smaller commercial companies appeared to show the most and most severe risks for non-compliance. Other important study-related risks derived from the interviews for the prioritization of inspection are the amount of participants in the clinical trial, the experience with the investigational medicinal product, and the amount of centres the clinical trial is conducted.

Discussion: Strengths of this study are the involvement of the inspectorate and multiple stakeholders in the study, which increases validity and improves implementation of the results. Limitations of the study include the lack of discussion between interviewees and KO-GCP, the overlap between risks derived from the stakeholders, and the misunderstanding of concepts and the developed classification by the stakeholders.

This study is relevant, because the sponsor landscape and risks regarding non-compliance with legislation had never been studied in the Netherlands. Gaining insight in these risks eventually leads to improved inspections by IGJ, which results in increased quality and safety of clinical trials. Besides, the current study provides a method for risk assessment and potential risk indicators, which is useful for other industries in which compliance with legislation is important.

Conclusion and recommendations: Due to the amount of risks for non-compliance, severity of risks, and study-related risks, smaller companies should be prioritized by IGJ for routine inspection. This sponsor category shows the most risks according to the field and conducts the

studies with the highest impact. Besides, the inspectorate should check which sponsors are assigned as 'other' and decide whether these should be inspected, based on the impact of the clinical trial. Finally, it is of great importance to evaluate the potential risk indicators in future studies.

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