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Competences of the Clinical Trials Site in the Assessment of Sponsors and Cro Companies

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Abstract

Introduction: *The study, the results of which are presented in this article, describes the relationship between the structures of the Clinical Trials Site and representatives of the CRO (Contract Research Organization) and Sponsors.*

Objectives: *The aim of the study is to determine which factors of these relationships have the greatest impact on the positive or negative assessment of the Clinical Trials Site in the opinion of Sponsor and CRO companies.*

Material and methods: *The study, using a questionnaire, was conducted on a randomly selected sample of 270 clinical trials of Clinical Research Sponsors present on the Polish market, CRO companies and entrepreneurs conducting clinical trials commissioned (freelancers).*

Results: *Based on the analysis of the survey results and suggestions of people who cooperate with the Clinical Trials Site on a permanent basis, it should be stated that while the Clinical Trials Site is a fairly highly rated health care facility, the main advantage is the qualified medical staff working on modern diagnostic equipment.*

Conclusions: *The analysis of the answers given by 189 respondents clearly showed that the hypothesis about the equal participation of the Site's technological aspects and the education and qualification of staff in relation to the share of aspects of the business approach to the contracting relationship was incorrect.*

Key words: *clinical studies, trials, registries, accounts of centers participating in clinical trials*

Introduction

Clinical trials are one of the indicators of the efforts to improve human existence on the plane of the most important factor conditioning human life. This work is to assess the importance of relations between the companies commissioning and financing clinical trials and the site where the research is conducted. The results of the study showed whether the innovative approach to pharmaceutical premium innovative approach in contacts between contractors, and rapid adaptation lead to an increase in the relative value of the site and, as a result, increase the possibility of conducting clinical trials.

According to the Pharmaceutical Law "a clinical trial is any trial involving humans to discover or confirm clinical, pharmacological, including pharmacodynamic, effects of one or more investigated medicinal products, or to identify adverse effects of one or more investigated medicinal products, or tracking the absorption, distribution, metabolism and excretion of one or more investigated medicinal products, with a view to their safety and efficacy" [1]. In this understanding, patient treatment is not the main purpose of the clinical trial, but only one of the options [2]. Participation in a clinical trial is also associated with the risk of the patient not responding to therapy or the risk of deterioration of health. Clinical trials are carried out in particular to determine the therapeutic benefit or lack thereof, to prove the safety and tolerance of the test substance, as well as to objectively observe the safety and efficacy of the medicinal product in a given health situation [3]. The long-term goal is to reduce the cost of treatment and improve the patient's quality of life [4,5]. It happens that the clinical trial is the only method of comparing existing therapy methods to determine the most effective and also the safest treatment regimen [6,7].

Pursuant to the provisions of the Regulation of the European Parliament and of the Council of the European Union, a clinical trial must meet any of the conditions [8]:

- the therapeutic strategy is not a standard of clinical practice and the participant's allocation is determined in advance,

- the decision to include a participant in the biomedical study is the same as the decision to prescribe the investigated medicinal product,
- the participant – in addition to standard clinical practice – is subject to additional diagnostic/monitoring procedures.

The need to conduct clinical trials is explained by the provisions of the Helsinki Declaration, according to which: "Medical progress is based on scientific research, which in the final stages must include research involving humans. (...) The basic goal of medical research conducted with the participation of people is to understand the causes, development and effects of diseases and to improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatment)" [9].

For patients suffering from diseases whose previous treatment, which exhausts all available therapies as standard, has not given results, the clinical trial is the last chance – if not for a complete cure, than a significant improvement in the quality of life, especially in the case of terminal diseases. Clinical trials are one of the most important elements of creating a new drug – over 60% of financial resources on the development of a given drug are the costs of clinical trials [7]. This share is constantly growing, mainly due to the increasingly higher, and thus increasingly more expensive, safety standards for the use of medicinal products and increasingly advanced medical technologies used in modern therapies. Due to demographic, epidemiological and technological prognosis, it should be presumed that this trend will continue [6].

Not only the costs of conducting clinical trials are increasing. With the development of medicine and technology and the growing number of so-called "civilization diseases" also the number of clinical trials increases at an exponential rate. In the last 19 years, the number of registered trials has increased more than 123 times – Table 1 [10].

Table 1. Number of clinical trials registered in the years 2000-2017

Year:	Number of clinical trials registered
2000	2119
2001	3892
2002	5270
2003	8858
2004	12024
2005	24824
2006	35741
2007	48295
2008	65868
2009	82887
2010	100240
2011	118063
2012	137535
2013	157984
2014	181306
2015	205437
2016	233246
2017	262446

Source: own study based on the list of registers [10].

Material and methods

The aim of the study, the results of which are presented in this article, is to assess the relationship between the structures of the Clinical Trials Site and representatives of the CRO (Contract Research Organisation) and Sponsors. Particular emphasis was placed on examining which factors of these relationships have the greatest impact on the positive or negative assessment of the Clinical Trials Site in the opinion of Sponsor and CRO companies.

As part of the work, the following research questions were formulated:

1. Does the assessment of the Clinical Research Site depend on the territorial scope of the unit conducting the clinical trial?
2. Do the soft competences of employees of Clinical Research Sites and additional components manifested during service and

availability/contact options have a greater impact on the overall image of the Site among Sponsors/CRO than their substantive knowledge?

3. How does the Sponsor/CRO assess the Site from the angle of courtesy and personal culture of its employees?
4. What is the significance of the availability and readability of information about clinical trials and the Site itself (its strengths and weaknesses) in this assessment?
5. Which of the elements – qualifications of the medical staff or availability of the latest diagnostic technologies – is more important in the Site's assessment?

The tool used in the study was a survey conducted in October 2018 – February 2019 among randomly selected 270[1] Clinical Research Sponsors, CRO companies and entrepreneurs present on the Polish clinical trials market conducting commissioned clinical trials (freelancers). The study was conducted by e-mail (162 questionnaires were distributed this way), on paper (92 questionnaires were distributed this way) and by telephone interview (interviews were conducted for14 questionnaires). A feedback response was obtained from 189 respondents, achieving a 70% response rate.

[1] The sample size (262 representatives of the population) was calculated according to the formula:

$$n = \frac{N\left(Z^2 \times P(1-P)\right)}{N \times e^2 + Z^2 \times P(1-P)}$$

where:
n – sample size
N – population size (assumed was 2878 – the number of business entities registered in Poland with 72.19.Z PKD subclass)
Z – confidence level value in the normal distribution for the assumed significance level: 1.96
P – he predicted size of the population fraction (it was assumed that about 20% of all enterprises with 72.19.Z PKD subclass carry out clinical trials, by type of research in individual branches of the subclass)
e – standard estimation error of 5%

Results

The vast majority of respondents were CRO companies – 67% of all respondents, followed by Sponsors – 29% of respondents, and persons offering on-demand clinical trials – 4% of respondents. The territory of operation of the assessment units is presented in Diagram 1.

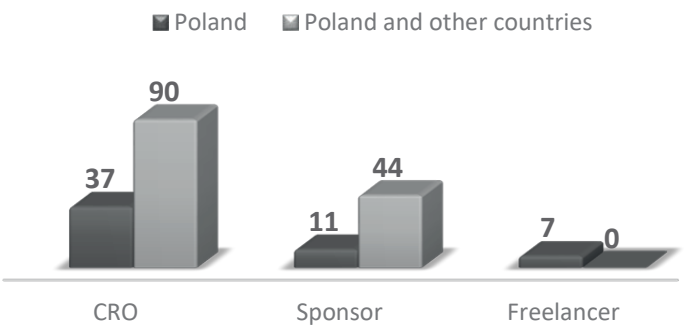
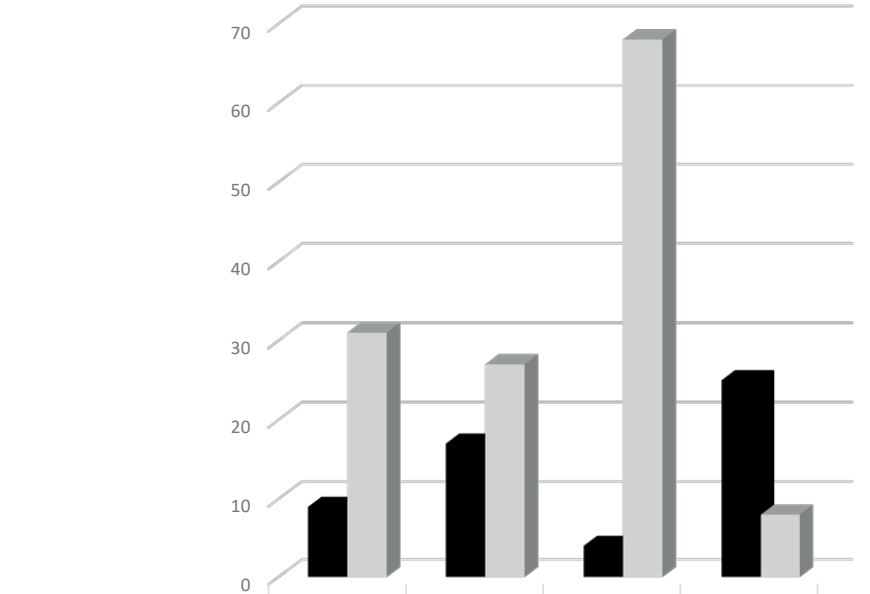


Diagram 1. Territory of operation of assessment units

In the case of units operating internationally out of 134 examined, almost 70% of respondents gave the Site an overall rating of 4 (on a scale of 1-5, where 1 is the lowest and 5 the highest). Over a half of the respondents considered that Polish Sites are competently weaker than foreign Sites, while every fifth respondent rated Polish Sites as good as Sites in other countries. Among the remaining answers, there were 27 claims that national Sites are better organised than those of international reach.

Among the 55 respondents whose facilities conduct clinical trials only on the territory of the Republic of Poland, the highest possible overall rating prevailed, i.e. 5 (85% of respondents in this group). The vast majority of respondents assessd Polish Sites as better organised than the international ones – Diagram 2.



	Just as good organization	Polish centers rated better	Foreign Centers rated better	No opinion
Units operating only in Poland	9	17	4	25
Units operating also in other countries	31	27	68	8

Diagram 2. Site evaluation depending on the operating range of the assessment unit

The list of scores obtained for each of the components of the Clinical Research Site assessment is presented in Table 1. The highest number of maximum ratings – 10 points – from respondents (137 maximum ratings) were obtained by managerial staff qualifications, while the lowest the time of service of the trial – only 13 maximum ratings. The average rating of both components is 9 and 6, respectively – tables 1 and 2 and Diagram 3 present the detailed distribution of scores.

Table 1. Average grade received for each component of the Site's rating

FACTOR	AVERAGE GRADE
Service time	6
Professionalism	8
Staff knowledge level	8
Kindness and personal culture of staff	8
Readability and availability of information on clinical trials in the Site	7
Contact availability	8
Technological capabilities (apparatus, possibility of performing procedures)	9
Qualifications of medical staff	9
Site organisation	8

Table 2. Summary list of scores obtained by individual elements affecting the evaluation of the Clinical Research Site

GRADE	SERVICE TIME	PROFESSIONALISM	STAFF KNOWLEDGE LEVEL	KINDNESS AND PERSONAL CULTURE OF STAFF	READABILITY AND AVAILABILITY OF INFORMATION ABOUT THE SITE	CONTACT AVAILABILITY	TECHNOLOGICAL CAPABILITIES (APPARATUS, POSSIBILITY OF PERFORMING PROCEDURES)	QUALIFICATIONS OF MEDICAL STAFF	SITE ORGANISATION
1	9	2	2	1	3	2	0	0	0
2	4	0	5	1	2	1	0	0	3
3	12	1	5	0	13	2	0	1	2
4	33	0	10	5	12	3	1	3	5
5	7	6	15	16	12	10	4	6	15
6	11	5	17	29	20	14	8	8	19
7	34	43	24	14	26	18	10	9	19
8	38	35	20	22	28	29	11	11	38
9	28	34	43	43	34	33	34	14	42
10	13	63	48	58	39	77	121	137	46

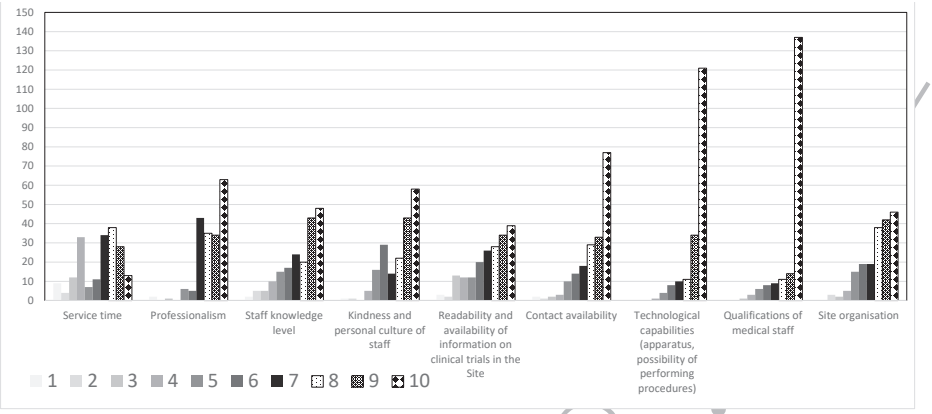


Diagram 3. Scoring of individual components of the Centre's assessment

Discussion and Conclusions

Based on the results of the survey, it should be stated that the majority of clinical trials are conducted by international units. The main determinant of this situation is the universal and multiple-site nature of most clinical trials. Therefore, it can be assumed that the assessment of the Clinical Research Site largely depends on the scope of activity of the company conducting the given research. Negative assessment of the site conducting the survey on a national scale is primarily related to the unfavourable result of comparing it to other facilities of this type outside Poland. On this basis, it can be concluded that the national Sites are still imperfect: they need to be systematised and finally unified in organisational terms – both on the part of the sites themselves and the legal regulations. Without these changes, they will still be rated worse than the international ones.

The impact of the soft competences of the employees of Clinical Research Sites on the assessment of cooperation with the Site

According to the results of the study, the professionalism and all soft skills of the employees of Clinical Research Sites are important and af-

fect its overall assessment. However, the substantive knowledge of employees is still rated the highest. In addition, the results of the study showed that the knowledge of medical staff and administrative employees of the surveyed Sites is at a high level and is positively assessed by respondents. Therefore, it should be concluded that the most accurate way to improve the overall assessment of the Site is to focus efforts and training on education, raising technical and technological qualifications and competences.

Assessment of the Site by the Sponsor/CRO in terms of the personal culture of the site's employees

The broadly understood personal culture in the presented study was defined as the ability to act adequately to the situation in accordance with the principles of savoir-vivre, generally accepted social norms and respect for other people. It consists not only of intellectual values and emotional intelligence, but also: morality, learned behaviour patterns, personality, communication skills, self-control, as well as care for personal hygiene and health [11]. Given the high prestige of clinical trials, the results of the study are surprising. The respondents assessed the importance of the personal culture of the employees of the Site (with whom they often have contact only by phone) on average at 8/10. This means that it is still not a priority aspect not only for the Site itself, but also for its employees.

The impact of the availability and readability of information on clinical trials and the Site itself on its overall assessment

Clinical trials are a highly innovative field. It is even more surprising that the use of new technologies and communication routes is uneven at individual stages of the research. While conducting the research itself, medical and information technologies are used (diagnostics, documentation), in the research administration, knowledge about the Site and broadly

understood marketing, the average rating of information accessibility is only 7. The solution to the problem may be the introduction of appropriate software, as well as a review of the number of people employed to handle the research. Often, a dozen or so years pass from the Sponsor's search for information about a potential Site until the closure of the research, so the most advisable is the proportionality of employment growth to the number of opened projects. This is confirmed by the results of international studies in the field of „tracking clinical trials" [12]. To facilitate the availability and readability of information on clinical trials, followed by a comparative analysis of the frequency of publication of clinical trial results by academic institutions and private companies, two solutions are recommended: improving the links between registration and publication, for example through institutional policies for academic institutions and private companies, and comprehensive and transparent research reporting [13,14].

Strengths and weaknesses of the Sites

The results of the study clearly show that the weakest element of handling a clinical trial at the Site is the long time it took to carry out administrative procedures. It is true that the decision to start the trial, sign a contract or prepare appropriate documentation are highly complex and legally bound processes, but appropriate technological solutions and modification of the work organisation system can have a positive impact on this aspect of the trial. Similar results are presented in the study recommending the use of outsourcing strategies and IT technologies in clinical trials [15].

In turn, the strongest side of the Clinical Research Site is the perfectly educated medical staff with appropriate knowledge, experience and qualifications, enabling impeccable performance of the examination, compliance with the law, protocol, and out of concern for patient safety. The Site is likewise highly rated in terms of medical technologies, i.e. availability of diagnostic equipment and readiness to introduce further innovative solutions.

Because international research results show that well-educated clinical trial staff often rotate between the Sites, The Clinical Trials Transformation Initiative (CTTI) was created due to the need to understand the causes of high migration rates among researchers who conduct clinical trials regulated by American Food and Drug administration in research sites. Because the researcher's knowledge and experience directly affect the quality and ultimate success of clinical trials, researcher marketing has important implications for the research company as well as patients and other stakeholders who depend on the results of clinical trials. The CTTI team used the findings from quantitative and qualitative research, as well as input from an expert meeting with many stakeholders to outline key researchers' concerns and recommend practical action-based solutions. The recommendations focus on strengthening four key categories of on-site research activities: developing research infrastructure and on-site staff, optimising research performance and research, improving site budget development and contract negotiations, and discovering additional testing opportunities [16].

Impact of qualifications of medical staff and availability of new diagnostic technologies on assessment of the Site

The results of the conducted surveys clearly indicate an even distribution of the assessment of the qualifications of the medical staff and the technological capabilities of the Site. Both aspects received high scores – average evaluation of 9. Undoubtedly, these are the two most important factors for the Sponsor/CRO which build a positive image of the Clinical Research Site.

Possibilities of Sponsors/CRO participation as equal partners in remodelling of the Clinical Research Site

The proposed changes, unfortunately submitted only in 6 cases, concerned:

- waiting time for administrative activities ("would significantly improve the terms of cooperation if the conclusion of the contract for the examination did not last so long", "please reduce the waiting time for decisions of the legal department", "my proposal – more people to work"),
- the possibility of contacting representatives of the Site (" (...) on-call duty of the person responsible after the hospital administration's working hours"), and
- the possibility of performing diagnostic procedures and the scope of health services provided ("I suggest considering making PETA[2] available for examinations, because separate contracting and transport of the patient increases costs and causes logistic difficulties" "We also conduct phase II-IV clinical research in allergology: is it possible to conduct such a study at your place?")[3]. Unfortunately, the results of the study indicate that only slightly more than 3% of the respondents decided to propose solutions leading to improvement in the functioning of the Clinical Research Site. This is an alarmingly low result, taking into account the potential benefits of dialogue between the parties, which proves that the model of joint work of different organisations while modernising the area of clinical trials on many levels is still in the theoretical phase.

International research in this area shows the need to create an academic research organisation in each country in order to efficiently design, conduct, coordinate and analyse clinical research, the so-called centre for clinical trials and data coordination [17].

The attempt to answer the research questions asked on the basis of the collected survey results and suggestions of people who cooperate with the Clinical Trials Site on a permanent basis, it should be stated that

[2] Refers to the possibility of performing the Positron Emission Tomography on Site.
[3] Quotes from questionnaires received, the original spelling was retained.

while the Clinical Trials Site is a fairly highly rated health care facility, the main advantage is the qualified medical staff working on modern diagnostic equipment. The business approach to the Sponsor/CRO and the Site as contractors and business partners is only in the initial phase – one can be sure that, as in other sectors of the economy, this area will change too, but at present it should be stated that the value of the Clinical Trial Site is defined by the level of education of the scientific staff and technological advancement of the diagnostic equipment possessed, with a less significant impact on the quality of mutual contractual relations.

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