

A Study of Clinical Trials in a Nordic Arena

Spring 2010

Contents

Executive summary:.....	4
A Study of Clinical Trials on a Nordic Arena	9
1. Main findings and summary	9
Summary	9
Main challenges	9
2. Recommendations.....	9
A drafted model for implementation of a common Nordic platform.....	10
Estimated business case for common Nordic trial platform can give up to a 50% time and hence cost reduction	11
3. Background.....	13
4. Main findings from the interviews in the Nordic region.....	14
This report focuses on interventional clinical trials due to large preference in the Nordic countries .	14
5. Existing Nordic clinical trials collaboration	15
European Clinical Research Infrastructure Network	15
Nordic University Hospital Research Conference	15
Other Nordic networks, more loosely coupled	16
An option is to go beyond Nordic by including the ScanBalt region	16
6. Status of clinical trials in the Nordic region.....	16
The Nordic region as a whole	17
Norway.....	18
Sweden.....	20
Denmark.....	21
Finland	22
Iceland.....	23
7. Data and method	24
Interviews.....	24
8. Literature review	25
9. Discussion.....	27
Nordic coordination unit – suggested platform for organization of Nordic collaboration.....	28
Harmonization of application processes and trial administration	33
Information – the basis for feasibility studies.....	36
Appendix.....	40
List of interviewees:.....	40
Reference group	41
References.....	41

Title: A Study of Clinical Trials in a Nordic Arena		
Nordic Innovation Centre project number:		
Author(s): Ida Iren Eriksen and Kirsti Kierulf		
Institutions: Accenture		
Abstract: <p>The number of clinical trials conducted in the Nordic countries is showing a decline. This trend can be reversed through increased Nordic collaboration. This study looks at how such Nordic collaboration could be structured.</p> <p>The study uses qualitative interview data, literature references and quantitative data on trial characteristics from the clinicaltrials.gov trial database.</p> <p>Interviews revealed that the Nordic clinical trial community is ready for more formalized collaboration across borders. Interviewees gave their opinions on how this collaboration could be facilitated. Based on this, discussions with the project's reference group, and a review of the literature in the field, this report recommends the establishment of a platform for Nordic collaboration on clinical trials. Its main elements are:</p> <ul style="list-style-type: none"> - harmonizing application and government approval processes - a coordinating unit that manages a Web site - public access to databases containing relevant information on trial centres, contact details, and ongoing and completed clinical trials 		
Topic/NICe Focus Area: Life sciences		
ISSN:	Language: English	Pages: 45
Key words: Clinical trials, Nordic cooperation		
Distributed by: Nordic Innovation Centre Stensberggata 25 NO-0170 Oslo Norway		Contact person:

Executive summary:

Main objectives:

Each Nordic country has limited patient populations, but if they join resources, the region will become more attractive and easier to operate in for institutions that wish to conduct clinical trials. The aim of this study is to propose models and make recommendations which will enhance cooperation on clinical trials in the Nordic region.

Method/implementation:

The report gives an overview of the current status of clinical trial activity in the five countries, and the level of collaboration between them. Clinicaltrials.gov was used to supply data to this overview from the database, and was supported by other available data like annual reports from ethics committees and research councils and statistics from national pharmaceutical industry organizations.

Interview data was used to understand challenges and obstacles, generate ideas for solutions and to find out if the stakeholders see the potential and need for increased Nordic collaboration. A total of 39 people were interviewed in every country, originating from hospitals, government agencies, industry and the public sector.

Discussions within the reference group were used to further develop solutions, and look at how existing infrastructure initiatives like the European Research Infrastructures Network (ECRIN) could be brought into the further development of the collaboration.

Results and conclusions:

Clinical trial activity in the Nordic countries is levelling out or decreasing. In 2005–2008, this trend was most evident in Norway. Sweden was the most stable country during the same period. Analysis of figures from clinicaltrials.gov indicates that multinational studies are driven by industrial institutions, while investigator-driven and publicly-driven studies are mostly restricted to one country. Sweden is the country that participates in trials that include one or more of the other Nordic countries most frequently, and Sweden and Denmark appear in the highest number of common trials (156).

The interviews revealed comprehensive support for increased Nordic collaboration in every sector. The need for an infrastructure differed between the group of university/hospital researchers (investigators) and industrial companies. The investigators expressed a greater need for help and support in the application process – the process in which the researcher has to explain the project and its implications for the humans involved to government agencies to obtain authorization to proceed with the project. This process is characterized by strict regulation and investigators want more help and support during this process.

The industry, on the other hand, has much experience and good internal support functions, and thus sees no major problems with the application process, but has difficulty finding enough patients, researchers and locations quickly enough when approached by international organizations to host a trial.

Recommendations:

The recommendations have been made to answer the challenges put forth by interviewees, and have been discussed by the reference group. The discussions are presented to some extent in the main section of the report, bringing in references from other reports and written material

discussing the same topics. The figure below is a proposed model for the stakeholders the platform should serve and the services that should be provided.

Recommendation	Benefit	Implementation	Challenges
Overall coordination – unit, portal and data warehouse	Investigators, industry and the authorities in every country have a single point of entry for seeking information and services.	Governments must cooperate to channel resources to the unit, and efforts must be made to make this the primary point of entry for anyone with questions regarding clinical trials in the Nordic region	All existing networks and current initiatives should be included in the work and encouraged to continue their work.
Easy access to database information	Primarily a solution to the challenge of a quicker start to trials put forward by the industry, but the authorities will benefit by getting easy access to strategic information and investigators will have more options and the possibility of acquiring new knowledge.	Development of data warehouse, connecting the best data. Important to have a good architecture with fast access to relevant information.	Ethical issues concerning patient rights and protection of patient data must be taken into consideration and data security – information must be used in accordance with the legislation that protects patients.
Communication plan to increase international awareness about high-quality data in the Nordic countries	This will stimulate international companies to choose the Nordic region as their study location and will benefit all parties engaged in clinical trials by increasing the number of trials conducted.	The responsibility of elaborating such a communication plan should be placed with the coordination unit.	
Single point of entry for applications for approval to conduct clinical trials in the Nordic countries	A single point of entry will make the application processes less time-consuming for actors applying to test treatments on humans.	There are different levels for a single point of entry. Changes to legislation and a single physical point of entry may lie in the future, but the preparations for this absolute single point, like pilots and discussions, will yield benefits today and prepare the ground for such a solution in the	A complete single point of entry to all of the Nordic countries is a long-term goal, which is not expected to be achieved in the near future. Still some actions could be taken to move in the right direction and provide benefits immediately by e.g.

		future.	implementing the same application form in every country.
Common understanding and interpretation of laws	It is important for investigators as well as the industry to have stable and predictable case review in the region. This will speed up the process and avoid misunderstandings and duplication of work.	The executors of laws – case officers and medicines agency executives, ethics committees, and other relevant government agencies – should discuss, analyze and define common definitions of concepts and interpretation of common laws.	
Common guidelines	Actors applying to government authorities for permission to conduct clinical trials have common guidelines for all of the Nordic countries, which will help make the process more stable and predictable. An application written for one country can be reused more easily in other Nordic countries, and there is less need for time-consuming tailoring of applications for the different countries' agencies.	Investigate whether existing guidelines are adequate or whether some areas are yet to be covered.	Common guidelines already exist through GCP. The challenge is that they are implemented and interpreted differently.
Courses in good clinical practice (GCP), ethics and effective case review for personnel employed to manage applications on ethics committees	If all personnel working on review of clinical trial applications attended GCP courses, they would harmonize their view of how to review cases.	Courses already exist. Some could be recommended by the coordination unit and some travel expense reimbursement could be given.	
English language in applications to government	The use of the English language in every section of an application will make	The informed consent material and the participant information	For example, in Sweden applications to

authorities	it easier to reuse material from country to country, and it will be easier for international companies without local knowledge to choose to file an application with the Nordic countries. If all applications could be submitted in English, this would help harmonize the process and make it easier, especially for pharmaceutical companies with loose connections and knowledge about the Nordic countries and their languages.	should still be in the native tongue.	ethics committees have to be submitted in Swedish. Translation technology could be evaluated as a tool.
Risk assessment of trials	Trials imposing little risk on patients and other participants should be reviewed more quickly and have a less strict case review process, including GCP monitoring, than trials which impose a higher level of risk to the people involved.	This should be coordinated with work being done in the EU.	Requires changes to national legislation.
Common education for Nordic study nurses	A common educational programme for study nurses could help build a strong professional affiliation and network in clinical studies. Nurses with common education will also have the same starting-point and this in turn will help harmonize clinical trials.	As a start, a list of existing courses in the Nordic countries could be recommended, and some reimbursement of travel expenses could be offered. As a next step, the NORDEN association already has some experience with offering a common Nordic education, and in time could start offering total educational programmes.	

Figure 1 below illustrates the tasks the Nordic coordination unit could offer the different stakeholders in the clinical trial community. The unit would take care of all issues shared by the specialized medical professional organizations and serve them by making it easier for them to collaborate across Nordic borders. It would also give information to patients and authorities and connect people and institutions across the borders.

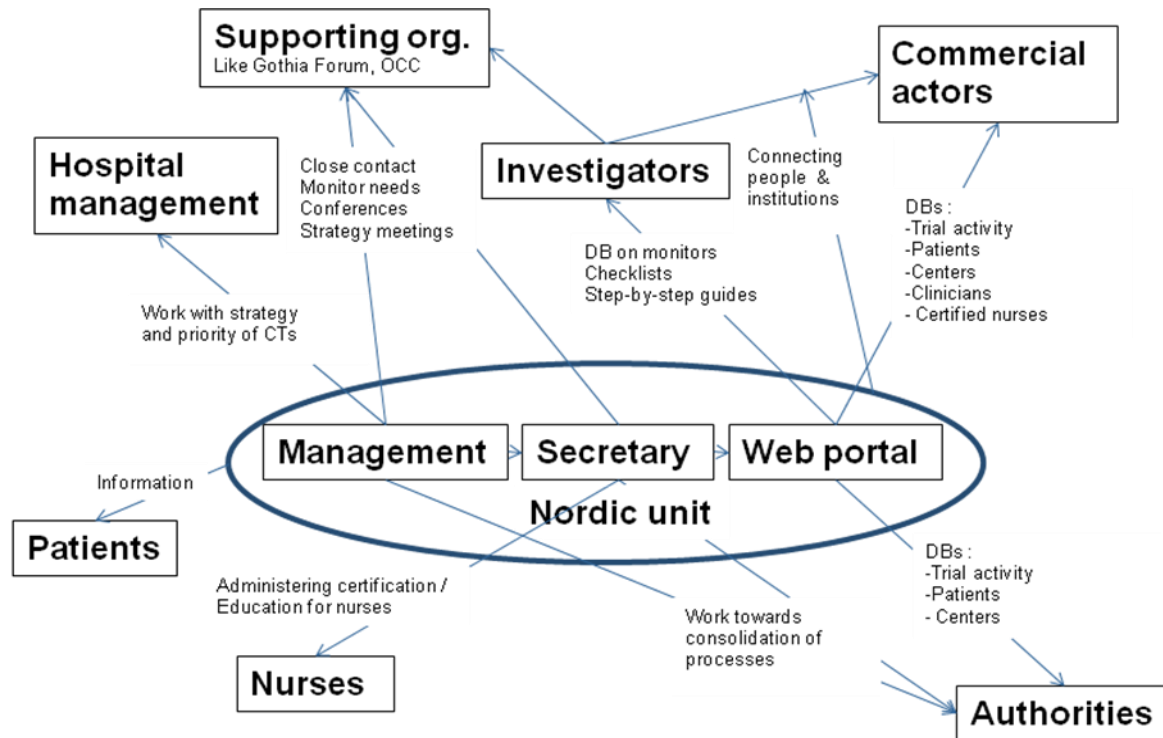


Figure 1: Nordic unit and services offered to stakeholders in the clinical trial community. DB=Database

A Study of Clinical Trials in a Nordic Arena

1. Main findings and summary

Summary

The number of clinical trials conducted in the Nordic countries is showing a decline. This trend can be reversed through increased Nordic collaboration. This study looks at how such Nordic collaboration could be structured.

The study uses qualitative interview data, literature references and quantitative data on trial characteristics from the international clinicaltrials.gov trial database.

Interviews revealed that the Nordic clinical trial community is ready for more formalized collaboration across borders. Interviewees gave their opinions on how this collaboration could be facilitated. Based on this, discussions with the projects' reference group, and a review of the literature in the field, this report recommends the establishment of a platform for Nordic collaboration on clinical trials. Its main elements are:

- harmonizing application and government approval processes
- a coordinating unit that manages a Web site
- public access to databases containing relevant information on trial centres, contact details, and ongoing and completed clinical trials

Main challenges

- 1) For investigators conducting clinical trials: the application process and the administrative aspects of the trial.
- 2) For commercial actors conducting clinical trials: the speed of which a trial can be established and completed, e.g. contract negotiations, employment of nurses and clinicians, locations and identification of the patient base, patient recruitment speed and cost of the study.
- 3) For governments: achievement of additional treatment options beyond conventional medicine through clinical trials.
- 4) For inhabitants: to make the Nordic region attractive to pharmaceutical and medical companies.

A number of solutions are recommended, targeting a common platform for Nordic trials to overcome these challenges in the field of clinical trials.

2. Recommendations

This table gives an overview of the recommendations. The recommendations are spelled out more thoroughly in the list below, and are discussed in depth later in this report.

- 1) Improving the application process
 - i. Single point of entry for applications in the Nordic region
 - i. Approaching a solution where government agencies' approval of a study in one country gives automatic approval in all Nordic countries. Discussions,

meetings and pilots. Medical agencies, ethics committees and bio-bank agreements.

- ii. Work towards common application forms – one form for applying to Nordic medical agencies, one for applying to Nordic ethics committees, and one for Nordic bio-bank agreements.
 - ii. Courses in good clinical practice (GCP), ethics and effective case review for personnel employed to manage applications on ethics committees.
- 2) Common Nordic understanding and interpretation of laws and rules, especially common EU regulation, but also discussion of national issues to learn from each other and strive to align practice with each other. Preferably four workshops a year. Strive for consolidation of every aspect of the application process, also technical support mechanisms like case review solutions.
- 3) Common Nordic guidelines for the criteria by which applications are judged within ethics committees and bio-banks. Common requirements and guidelines for quality assurance and monitoring.
- 4) Evaluation to reach a Nordic solution for clinical trials without a Nordic language requirement. Evaluate available language tools for automated inclusion of the Nordic language capability. It should be possible to deliver the information required by authorities in English.
- 5) Trials imposing a low risk on participants should have less strict requirements regarding delivery of information in the application process, and should be sent through the process on a fast track.
- 6) Providing possibilities to utilize database information
 - i. All trials need to be approved by an ethics committee. Ethics committees in every country are encouraged to make available *all* information in the applications they approve, excluding the information which is strictly confidential for commercial reasons.
 - ii. A voluntary database of clinical research should be established with clinical trial sites and contact details.
 - iii. Efforts should be made to find out how we can use patient data and electronic health records to support faster identification of participants within an ethical and legal framework.
 - iv. There should be a database of all centres that work with clinical trials and the patient bases the centres cover.
 - v. All of the above-mentioned information should be collected and made accessible through a meta-database or data warehouse.

A drafted model for implementation of a common Nordic platform

- 1) Overall coordination of the clinical trials field in the Nordic region.
 - i. The data warehouse should be accessible through a Web portal. This Web portal should also contain collaboration tools like user-driven meeting-places for

discussions and forums. It should also contain step-by-step guides and checklists to support new and inexperienced researchers.

ii. Coordination units should be responsible for all above-mentioned initiatives. In addition to the above-mentioned measures, the unit could act as a consultant, helping investigators with additional information and consult in application processes.

2) A focus on clinical trials requiring higher quality of data as a competitive advantage, compared to other alternatives and a communication plan for industry supporting this message. Investing in a Nordic coordination unit and a database with a data information solution would support this advantage.

The recommended model for the coordination unit is depicted in figure 1:

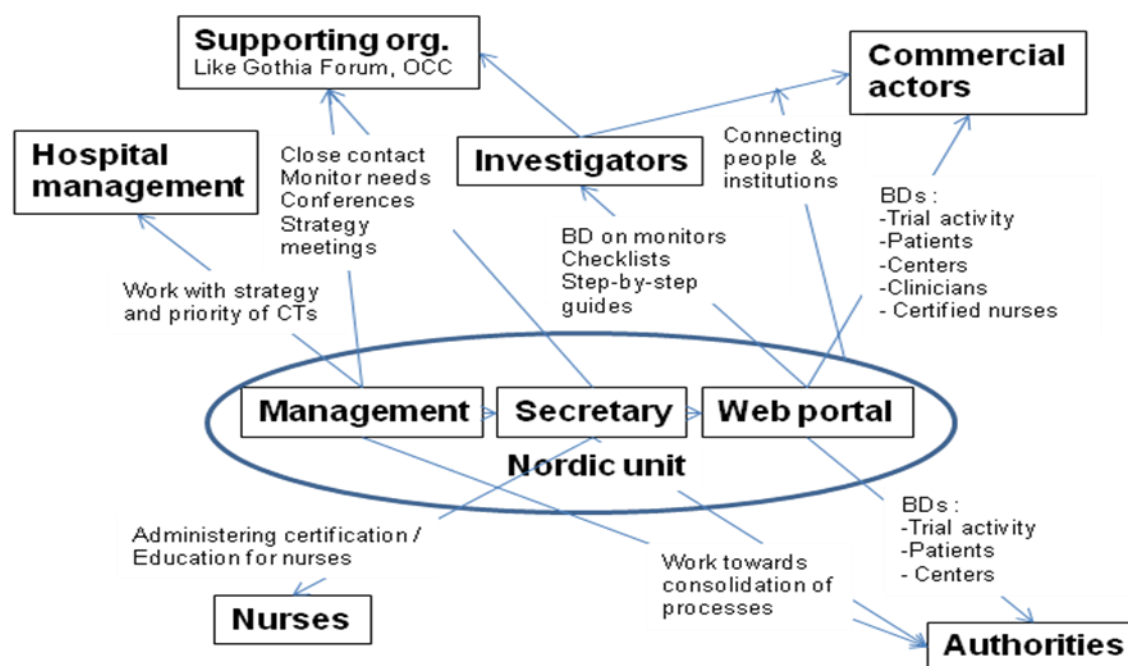


Figure 1: Recommended model of Nordic coordination unit with services and stakeholders

The estimated business case for a common Nordic trial platform is an increase of up to 50 % and hence a cost reduction

By establishing a common Nordic unit for coordination, one can assume that the unit in time will be able to take on the work of processing the applications that are aimed at two or more Nordic countries.

Table 2: Number of open interventional trials, July 2010, clinicaltrials.gov

The table gives a picture of how many trials include Nordic collaboration and need approval from the competent national authorities and ethics committees.

Nordic countries included in studies	Number of trials

Sweden, Finland, Denmark, Norway, Iceland	7
Sweden, Finland, Denmark, Norway	38
Sweden, Finland, Denmark	62
Sweden, Finland, Norway	45
Sweden, Denmark	156
Sweden, Norway	105
Sweden, Finland	98
Sweden, Iceland	11
Finland, Denmark	73
Finland, Norway	52
Finland, Iceland	11
Norway, Denmark	84
Norway, Iceland	9
Iceland, Denmark	11

The trials listed in the table are by and large industry-driven and also include several other countries. The goal of the coordination efforts presented in this report is to make it easier for all institutions to consider the Nordic region as one large trial infrastructure – we want those who perform clinical trials to fully benefit from the resources we have to offer, without being hampered by a fragmented administration. We want all actors to feel that the region can be accessed as one unit, even if it is just the Nordic region the clients are interested in or if our region is seen as one of several larger units in a large trial that includes many countries. Two scenarios are the main likely outcomes of the establishment of a Nordic platform for coordination of clinical trials. One is that the activity stays at current levels, averting a decline in Nordic trial activity. The other scenario is that the level of activity increases.

At present there are about 300 ongoing trials that include collaboration between two or more Nordic countries. Most of them are industry-driven. Let us assume that the studies are conducted over a period of 2–3 years. Drawing on this, we can assume that 150 studies are submitted for assessment each year. Let us also assume that 100 of these studies include collaboration between two Nordic countries and 50 include three countries. As seen in table 1, these assumptions are sound and moderate. As we will see later in this report, the maximum number of days allowed for an ethics committee to review a case is 60, although some Nordic ethics committees are on average faster. Let us assume that each national ethics committee takes 40 days to review each case. Without a coordinated Nordic single point of entry, the number of days needed to review the yearly intake of trials including more than one Nordic country is: $(100 \times 40) \times 2 + (50 \times 40) \times 3 = 14000$ hours or 1867 days. If the cases are reviewed by just one Nordic unit it will take $(100 \times 45) + (50 \times 45) = 6750$ hours and 900 days. Even though 5 hours are added to the review time for the Nordic unit due to extra complexity in the cases, it will review the cases in 50 % of the time taken by national units.

This estimate is based on available information and assumptions to show potential savings. Pilots and experiments should be carried out to make more accurate estimates.

3. Background

The Nordic Innovation Centre (NICE)¹ initiated and funded this study. Reports and papers clearly identified an urgent need for a better Nordic solution. The mandate for this study was to identify the next steps to achieve a Nordic solution through interviews and reference group discussions, as well as to remove any obstacles. The hypothesis was made that Nordic collaboration would introduce better conditions for conducting clinical trials for investigators and sponsors in the Nordic region. The need to enhance collaboration between the Nordic countries was identified as a result of the strong competition faced from Asia, USA and Eastern Europe². In the Terms of Reference drawn up by NICE for this study, the content should be outlined as follows:

The scope of the study should be to

- (i) investigate the potential and possible outcomes of establishing a formalized Nordic collaboration
- (ii) address and propose solutions to possible challenges (e.g. regulations, intellectual property rights (IPR)) for a Nordic collaboration
- (iii) propose models and recommendations for a Nordic collaboration on clinical trials.

The study should take into account the preliminary study that looks at the opportunities and challenges of a Nordic cooperation within clinical trials, in particular the suggestion to build a Nordic collaboration based on existing national networks for clinical trials, of which three are linked to the European Clinical Research Infrastructures Network (ECRIN).

We would like the study to answer the following questions:

- What existing Nordic clinical trials collaboration exist and how formalized are the collaborations? What are the results of the collaborations?
- How many clinical trials are undertaken in the Nordic countries, medical areas, types of studies as well as number of patients and centres involved and the financing structure?
- What is the current status for infrastructure for clinical trials (staff, facilities, ICT, good clinical practice guidelines, strategic operating procedures, enabling technologies, ethics committees, and medical agencies etc)? How could the Nordic infrastructure for clinical trials be streamlined and improved?
- Is it possible to establish a strong Nordic network for clinical trials based on the Nordic Clinical Research Infrastructure Networks that have been established in Sweden, Denmark and Finland as part to the European Clinical Research Infrastructure Network (ECRIN) supplied with further members similar networks in Norway and Iceland.
- What legal, ethical and administrative obstacles are there for establishing a joint Nordic clinical trial infrastructure?

¹ <http://www.nordicinnovation.net/>

² Karlberg, J. (2008): "Development of Sponsored Clinical Trials in Asia" http://www.cro-mediport.co.jp/data/news/9_2.pdf

- Do the stakeholders (at different levels) see the potential and need for an increased Nordic collaboration? What partners should and need to be engaged in a Nordic collaboration?
- What areas (diseases, phases?) are most suitable for Nordic collaboration? Do we need unique networks per disease area, or is it better to establish area-independent networks.

This report will submit its recommendations to the Nordic Innovation Centre (NICE), which is an agency of the Nordic Council of Ministers. Its objective is to promote innovation and competence development in the Nordic business sector. NICE aims to develop and strengthen the Nordic business sector³. One of the tools available to achieve this goal is harmonization of regulation. In the interviews that provide the basis for this report, many challenges and solutions were discussed where implementation is the task of national governments. Matters categorized as national matters are not addressed in this report. An example of such a national matter is the fact that a perceived major barrier by all actors is the low priority given by hospital management, hospital owners and payers, and society as a whole to the execution of clinical trials.

4. Main findings from the interviews in the Nordic region

The results of the interview study makes it clear that the clinical trial community in the Nordic region is ready to enter into a more formalized and structured form of collaboration. Almost everyone agreed that something should be done to enhance the conditions for Nordic collaboration and that the results of such an effort would be more and better clinical trials in our region. However, there are barriers against Nordic cooperation that need to be overcome, based on the fact that institutions compete with each other for scarce resources and assignments, and that all cooperation involves transaction costs. The establishment of trust, incentives, an infrastructure to ease information-sharing, common ways of operating and a sense of common mentality appear to be necessary for the parties to collaborate successfully. This list indicates the complexity of the field by showing that political, cultural, practical, and economic aspects are at play.

This report focuses on interventional clinical trials due to a great preference in the Nordic countries

Clinical trials are just one part of the wide field of clinical research. Clinical research also includes basic science and epidemiology which is not defined as clinical trials. Clinical trials are “generally considered to be biomedical or health-related research studies in human beings that follow a pre-defined protocol”⁴. They are translational in the sense that they aim to make discoveries and innovations developed by basic science applicable to clinical practice. In a phase I clinical trial, small doses of a drug are tested in healthy participants to find out how the human body tolerates the agent. Phase II tests the drug in a larger group of patients to evaluate dose response, adverse events and efficacy. Phase III tests the drug in a heterogeneous patient population, to collect further information on efficacy and adverse events⁵. The comparison of two established drugs targeting the same condition to determine guidelines for preferred

³ <http://www.nordicinnovation.net/article.cfm?id=1-834-914>

⁴ <http://clinicaltrials.gov/ct2/info/understand>

⁵ http://www.clinicalresearch.pitt.edu/docs/comparison_of_clinical_trial_phases.pdf

treatments is an example of a phase IV study. Clinical trials can be interventional or observational, but the interventional study design called randomized clinical trials (RCT) is often preferred and thought of as the gold standard because of its alleged capacity to eliminate selection bias⁶. Interventional trials are those in which the research participants are assigned by the investigator to an intervention which can be treatment by drug, a procedure, diagnostic tests or preventive measures, and its outcomes are measured⁷. This report focuses on interventional trials, but stakeholders conducting observational studies will also benefit from the recommendations in this report.

The literature has established a distinction between investigator-driven and industry-driven trials. Our interviews have confirmed the view that trials mainly managed and driven by investigators meet other challenges, and the clinical trial process is often a bit different than clinical trials driven and administered by the industry. Investigators are often clinicians or researchers working in hospitals or universities. They mainly do not have the same economic resources or the administrative support and experience as industry. On the other hand, they often have easier access to their own patients. We will come back to the distinction between investigator-driven and industry-driven trials throughout this report.

5. Existing Nordic clinical trials collaboration

The European Clinical Research Infrastructure Network (ECRIN)

ECRIN⁸ was funded to bridge fragmented organization of clinical research in Europe and to improve its quality and efficiency⁹. It offers consultancy and practical information during the preparation of clinical research projects and services during the execution of the project, such as interaction with competent authorities and ethics committees and adverse event reporting, data management and statistical analysis¹⁰. ECRIN has national networks in Denmark (DCRIN), coordinated by the Copenhagen Trial Unit, Sweden (SweCRIN¹¹), coordinated by the Karolinska Trial Alliance, and Finland (FinnCRIN), coordinated by FinnMedi Oy. Norway is in the process of establishing such a network. There are also individuals on Iceland working towards closer links with the ECRIN organization. ECRIN is supported by the 6th and 7th EU Framework Programmes.

Nordic University Hospital Research Conference (NRC network)¹²

The NRC network's board of directors has six members, and its faculty has 11 members representing all of the Nordic countries. The faculty has members from the industry, universities, hospitals, local governments, clinics and administration. The network is industry-independent and funded by Innovest AS, Bergen Teknologioverføring (Technology Transfer), Nordea Bank Norway and Norwegian Holberg Fondene. Its aims are as stated on its Web site: "to challenge,

⁶ <http://www.contentnejmorg.zuom.info/cgi/content/full/342/25/1887>

⁷ <http://clinicaltrials.gov/ct2/info/understand>

⁸ <http://www.ecriin.org/>

⁹ "European Clinical Research Infrastructures Network: promoting harmonisation and quality in European clinical research": http://www.sciencedirect.com/lancetnorway?_ob=ArticleURL&_udi=B6T1B-4F6CG40-9&_user=6468133&_coverDate=01%2F14%2F2005&_rdoc=1&_fmt=high&_orig=search&_sort=d&_docanchor=&_view=c&_acct=C000069886&_version=1&_urlVersion=0&_userid=6468133&md5=192202c0847c1fa5392c4bd52b87e1ee

¹⁰ <http://www.ecriin.org/index.php?id=103>

¹¹ <http://www.swecrin.se/eng/index.php?menyval=2>

¹² <http://www.nrcnetwork.com/>

stimulate and inspire researchers and administrators at University Hospitals throughout the Nordic countries in order to increase the rate of success in medical research.” It was created in 2006 “to create a network of professionals at University Hospitals in the Nordic countries. An arena where researchers and administrators can meet, share their experiences and learn from the best.” The initiative came from the Strategic Research Program at Haukeland University Hospital, Helse Bergen HF and Innovest AS. The NRC network targets clinical research and is not restricted to clinical trials, although the last conference focused specifically on clinical trials. Its main activity is the conference held every year in May.

Other Nordic networks, more loosely coupled

In addition to these two general initiatives, there are also many more specific networks within the medical specialties listed in the report by Stina Gestrelus¹³. These networks are often informal and loosely-coupled connections between professionals which meet to discuss trends in their professions and sometimes initiate and collaborate on clinical trials.

Another Nordic initiative is the Nordic committee on bioethics: <http://ncbio.org/english/>

There is also biotechnology collaboration between Sweden and Norway:

<http://www.medcoast.org/vanstermeny/scienceresearch.4.16939cde10b7130fe2e800023326.html>

For a tabular overview of laws, ethics committees and consent in the Nordic countries see the publication from the Norden association: “Legislation on Biotechnology in the Nordic Countries and overview”¹⁴

One option is to go beyond Nordic by including the ScanBalt region

The ScanBalt bio-region, which is a Baltic Sea Region life science community, serves as a service provider for its members, and promotes the ScanBalt BioRegion as a globally competitive green valley and health region. It consists of the Nordic region, the Baltic states, northern Germany, Poland and western Russia¹⁵. This region is said to have a history of economic collaboration. Many of the pharmaceutical companies we have spoken with also tend to see the Nordic and the Baltic countries as a single region when planning clinical trials. As there already appears to be some contact and collaboration between the countries in this larger region, there might also be an opportunity to expand the Nordic collaboration on clinical trials to include the Baltic states and possibly even Poland, northern Germany and western Russia.

6. The status of clinical trials in the Nordic region

In this section, the current clinical trial activity for both each single country and trials which include collaboration between the countries in the Nordic region will be reported. The figures reported are cited from various sources, and due to a variation in the information available from the different countries, the information will vary somewhat between countries. Still, all of the figures have been collected to give a picture of the current situation. The main picture is that the clinical trial activity levels off or decreases slightly, and that it is mainly the industry which conducts trials involving more than one country.

¹³ Stina Gestrelus, “Nordic Cooperation in Clinical Research - Opportunities and Challenges” (Nordic Forum for Innovation in Health Care and Medicine, February 18, 2010).

¹⁴ <http://www.norden.org/da/publikationer/publikationer/2006-506>

¹⁵ <http://www.scanbalt.org/the+region>

The Nordic region as a whole

We can capture a picture of trials conducted in more of the Nordic countries by looking at the data available at clinicaltrials.gov. The figures reported below include *all* trials in which the Nordic countries have participated. If nothing else is stated, other countries might be included in the collaboration.

For some insight on what characterizes the trials on which Nordic countries collaborate, a short analysis will be given of the 62 trials¹⁶ in which Sweden, Finland and Denmark all are engaged: Six of the trials are not funded by industry at all and another six are funded by a mix of industrial and public institutions. All the other studies are funded by the industry. Companies Bristol-Myers Squibb, Eli Lilly and Company, Hoffmann-La Roche, Novartis, Pfizer, and Wyeth are sponsoring 27 of the 62 trials and there are about 39 different sponsoring institutions on whole. There are 17 cancer trials, 14 on cardiovascular diseases, 5 on diabetes, and 5 on arthritis. Just 7 of the studies only included Nordic countries; one funded by the industry and the other six publicly-funded. A conclusion to be drawn from this is that the industry mostly sponsors studies that include many countries, and mostly more countries than just in the Nordic region. Public or investigator-driven studies, on the other hand, mainly are not ventures between countries. This conclusion is supported by the analysis of the Norwegian studies that will be reported further down.

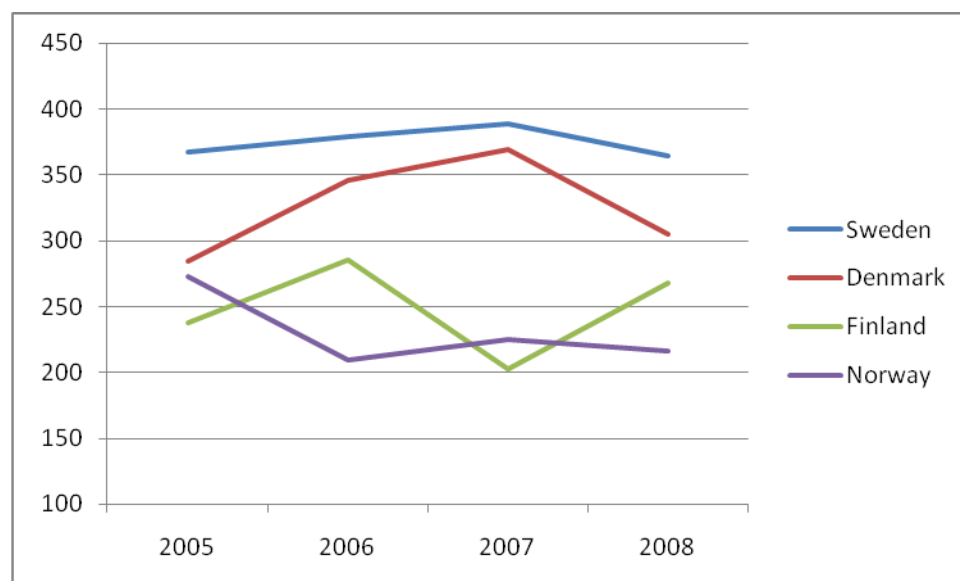


Figure 1: Number of trials conducted in 2005–2008 by country

The figures in table 2 are not consistent between countries, but are consistent within countries,¹⁷ which means that they can show the trend over time, but do not give a valid picture of the

¹⁶ As reported in table 2

¹⁷ Different data sources between countries. The figures do not depict exactly the same variables, but still show the trend.

Finish data: clinicaltrials.gov – Investigator and industry – only those who aim at publishing

Swedish data: Annual reports of the ethics committees

Danish data: Klinisk forsk i Danmark – tid for handling (EudraCT data) – opstartede studier – Kilde Lægemiddelstyrelsen – appears to be both public and private sector

Norwegian data: LMI – figures and facts – ongoing studies – only industry-driven.

distribution of activity between countries. See figure 1 for a more valid picture of the distribution between countries. Table 2 shows that there was a small decline in activity from 2005 to 2008. The declining trend is more evident in Norway than in the other countries.

	2005	2006	2007	2008
Phase I	97	92	115	113
Phase II	190	216	197	163
Phase III	495	517	531	515
Phase IV	214	230	198	166

Table 3: Number of trials conducted in the Nordic area in 2005–2008 per phase

The sources for the figures in table 3 are the same as for table 2, except for the Swedish figures. The figures from ethics committees' annual reports, which are used in table 2 for Sweden are more accurate, but they were not broken down into phases. The Swedish figures for table 3 are gathered from LIF Fakta 2010¹⁸ which contains only a sample of the industry trials. We should still be able to see a valid time trend. The Nordic countries conduct more late-phase trials than early-phase trials.

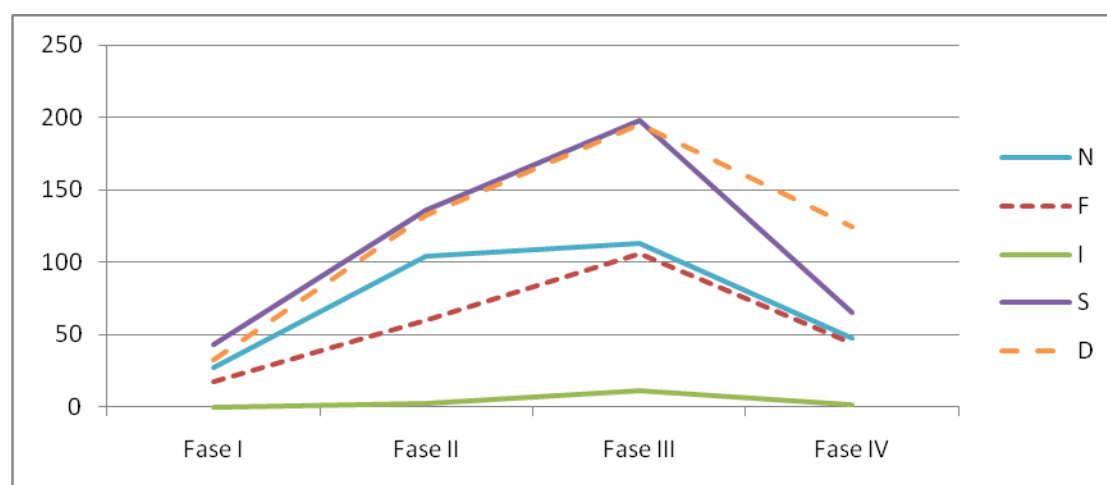


Figure 2: Open studies registered in each country on clinicaltrials.gov in April 2010.

Norway

In Norway, phase III trials were reduced in 2005–2008.

¹⁸ LIF Fakta 2010 – started clinical trials – survey to members of LIF – only part of industry

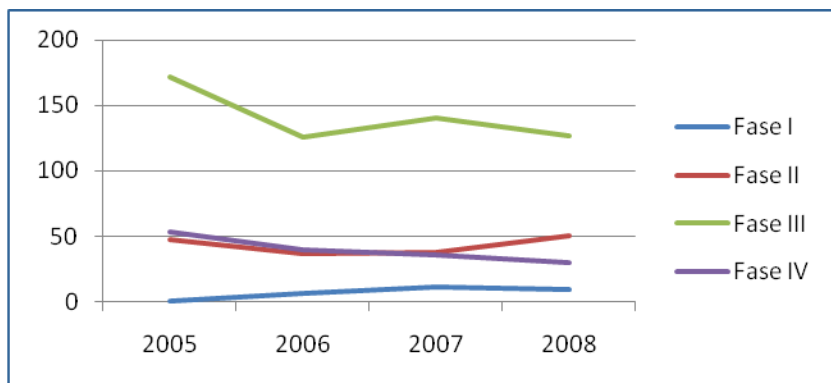


Figure 3: Norway's production of clinical trials, 2005–2008¹⁹

Norway has seven regional ethics committees²⁰.

Public financing of clinical trials in Norway is mainly provided by the Research Council of Norway, which covers larger national or international trials, while the regional health authorities cover trials conducted in their region.

In 2009, the Research Council of Norway spent NOK 23.5 million on clinical research²¹. This amount funded 23 research projects, 1 Postdoc fellowship, and institutional support for 2 institutions. Among the 40 projects which have been or are totally or partly funded by the Research Council, 18 are randomized clinical trials (RCTs), and 6 of those 18 include collaboration across regional health authorities or across countries²². The RCTs have mainly been conducted within the fields of cardiovascular diseases and diabetes. The Research Council funds 18 PhD candidates within the field of clinical research. It reports that the number of PhDs increased from 2006 to 2009.

We conducted a more thorough analysis of ongoing trials including Norway registered at clinicaltrials.gov. When analyzing the data collected in April 2010 (investigator-driven studies) and in July 2010 (industry-driven studies) we found the following:

- 288 trials are driven by universities, hospitals or other public institutions, while 119 are driven by the industry.
- There are 7 industry-driven trials testing devices while 104 are testing drugs. None are testing procedures or behavioural interventions.
- Among the investigator-driven trials, 67 are testing behavioural interventions like diet restrictions and cognitive therapy, and 63 are testing devices and procedures.
- Investigator-driven interventional trials (n=232) have or plan to enrol a total of 131,000 patients.
- 16 of the 232 investigator-driven interventional trials report international collaboration.

¹⁹ LMI – Numbers and facts – ongoing studies – only industry-driven studies:

<http://www.lmi.no/91/Legemiddelstatistikk/146.html>

²⁰ <http://helseforskning.etikkom.no/ikbViewer/page/forside?lan=2>

²¹ Annual report 2009 The Research Council of Norway, Clinical research:

<http://skattefunn.no/servlet/Satellite?c=Page&cid=1228296189455&pagename=kliniskforskning%2FHovedsidemal>

²² Annual report 2009 The Research Council of Norway, Clinical research:

<http://skattefunn.no/servlet/Satellite?c=Page&cid=1228296189455&pagename=kliniskforskning%2FHovedsidemal>

- 4 of the 119 industry-driven trials only include Norway.

Sponsor/Phase	I	II	III	IV
Investigator	13 (203)	44 (152)	37 (2,080)	28 (402)
Industry	5 (92)	34 (405)	66 (2,733)	13 (1,551)

Table 4: Number of ongoing interventional trials in July 2010, average patient enrolment in parentheses

As a comment to table 4, it is important to note that as most of the investigator-driven trials are only being conducted in Norway, the patients enrolled in these studies are Norwegian. The industry-driven trials include patients from all over the world, and just a fraction of the patients enrolled in these studies are Norwegian. Thus, even though it seems as if the industry-driven trials include more patients, this is not necessarily true from a national point of view.

Sweden

Sweden is the country that produces most of the clinical trials in the Nordic region.

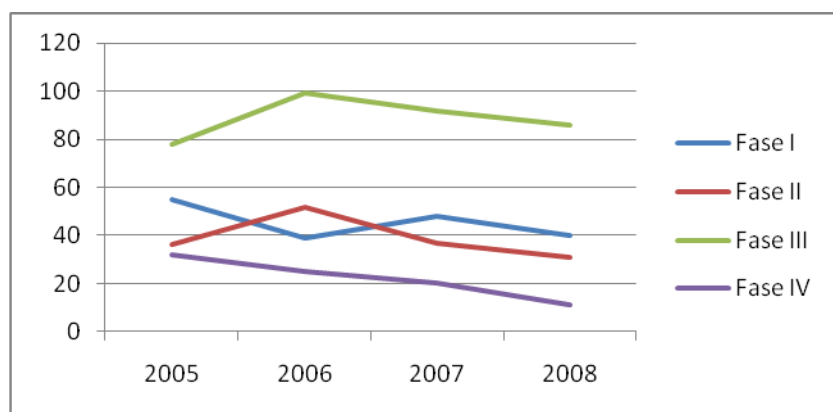


Figure 4: Sweden's production of clinical trials in 2005–2008²³

Sweden reports more phase I trials than the other Nordic countries, and is the only country that conducts more phase I trials than phase II and IV trials. Sweden is also the country that conducts fewer phase IV trials than any other phases.

There are six regional ethics committees in Sweden²⁴.

Looking at the annual reports from the regional ethics committees in Sweden, the number of clinical trial applications received are summarized in the following table:

Region	2004	2005	2006	2007	2008	2009
Gothenburg	75	83	69	70	69	47
Linköping	23	24	33	23	22	n/a
Lund	n/a	53	59	72	69	n/a
Stockholm	133	122	129	140	121	n/a

²³ LIF report 2010:1 – started clinical trials – survey to members of LIF – only part of industry: www.lif.se/cs/default.asp?id=50097

²⁴ <http://www.epn.se/centrala-etikproevningsnaemnden/om-naemnden.aspx>

Umea	n/a	9	15	11	14	n/a
Uppsala	n/a	76	74	73	69	n/a
Total	n/a	367	379	389	364	n/a

Table 5: Figures can be found in the first table in each of the annual reports in the column for clinical trials ("klinisk läkemedelsprövning"):

Gothenburg: <http://www.epn.se/goeteborg/om-naemnden.aspx> Linköping: <http://www.epn.se/linkoeeping/om-naemnden.aspx> Lund:

<http://www.epn.se/lund/om-naemnden.aspx> Stockholm: <http://www.epn.se/stockholm/om-naemnden.aspx> Umea: <http://www.epn.se/umeea/om-naemnden.aspx> Uppsala: <http://www.epn.se/uppsala/om-naemnden.aspx>

According to the table, the number of trials in Sweden appears to be stable to decreasing during the period in question.

The Swedish Clinical Research Infrastructure Network (SweCRIN²⁵), is a national network established in 2003 which is a member of ECRIN.

Denmark

Denmark is the country that produces the most phase III trials in the Nordic region. The number of phase III trials in Denmark increased in 2005–2008. However, activity in the other phases appears to have dropped.

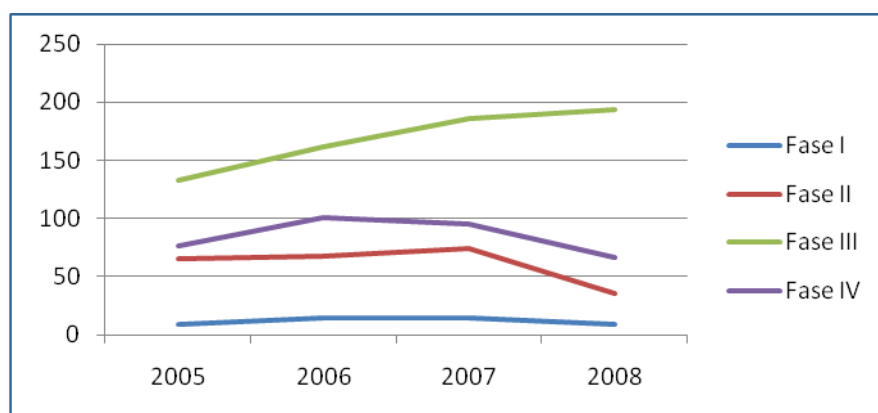


Figure 5: Denmark's production of clinical trials in 2005–2008 26

A research article published in the *BMJ* studied the applications submitted to the Danish Medicines Agency in 1993–2006 and found that there had been a steady decline in clinical trials, from 417 applications in 1993 to 260 applications in 2005, and an increase to 336 in 2006²⁷.

There are 11 regional and 1 central Danish ethics committee²⁸. The Web site includes guidance and information on how to apply, how to submit a complaint and the review process after the application is submitted.

²⁵ <http://www.swecrin.se/eng/index.php?menyval=2>

²⁶ "Klinisk forskning i Danmark – tid for handling" (EudraCT data) – ongoing studies – Source Medicines Authority – seems to be both private and public

²⁷ Berendt, L. et al (2008): "Effect of European Clinical Trials Directive on academic drug trials in Denmark: retrospective study of applications to the Danish Medicines Agency 1993-2006" in the *BMJ*:

<http://www.bmj.com/cgi/content/abstract/336/7634/33>

²⁸ <http://www.cvk.sum.dk/>

In the autumn of 2010, it will be possible to submit all applications to the Medicines Agency electronically.

The Danish Clinical Research Infrastructure Network (DCRIN), is a national network which was established in 2003, and is a member of ECRIN.

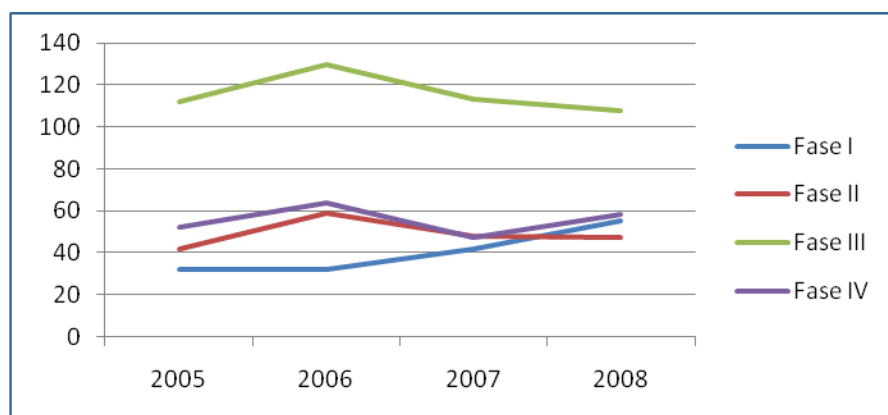
European Union Standards and Training in the Inspection of Tissue Establishments (EUSTITE) Denmark is a partner in this European project²⁹ and established a Nordic fraction of this project called NORDic Partnership of the EUSTITE Project (NORPEP)³⁰, focusing on “transposing the Tissue Establishment Directives into national regulations”.

Research support units³¹:

- The Copenhagen Trial Unit (CTU), Centre for Clinical Intervention Research, Rigshospitalet – Copenhagen University Hospital is a general academic research centre that was established in 1995. The CTU designs, conducts and analyzes clinical trials and systematic reviews of such trials.
- The GCP units consult investigators on compliance with the EU directive and monitor drug trials.
- TechTrans units consult researchers on intellectual property rights, patents, contracts, etc.
- Centres of excellence offer services within statistical analysis and make available data from the Danish clinical databases.
- The regional committees on science ethics secretaries guide researchers on scientific ethics.
- The university units for research support guide researchers on the writing of applications for funding from the national research council, private funds and the EU.

Finland

The production of clinical trials in Finland in 2005–2008 was relatively stable.



²⁹ http://www.eustite.org/index.php?option=com_content&task=view&id=24&Itemid=118

³⁰ http://www.eustite.org/index.php?option=com_content&task=view&id=844&Itemid=117
<http://www.eustite.org/>

³¹ This list is taken from the NSS 2010 report:

<http://www.sum.dk/Aktuelt/Nyheder/Forskning/2010/April/patient.aspx>

Figure 6: Finland's production of clinical trials in 2005–2008 ³²

Finland has 21 ethics committees, but according to the new Medical Research Act, which will enter into force in late 2010, there will be 5 regional ethics committees for multinational trials and approximately 20 for research in general.

Medicines agency: National Agency for Medicines

Disease database:

http://findis.org/molgenis_findis/molgenis.do?_target=Diseases&_action=select_disease&item=COH1

The Finnish participant in ECRIN is FinnMedi Oy³³, a biotechnology and healthcare technology development company which is owned by the Hospital District of Pirkanmaa, City of Tampere, Tampere University of Technology Foundation, Tampere University Foundation and the Finnish Red Cross. They cover “different phases of the research process, from research planning to practical arrangements and project management.”

The Finish Agency for Technology and Innovation is funding the national initiative FinnTrials in order to strengthen national cooperation and procedures.

Iceland

Iceland has two regional ethics committees³⁴.

Medicines agency: Icelandic Medicines Control Agency (Lyfjastofnun)

According to clinicaltrials.gov, 3 phase I, 8 phase II, 37 phase III and 5 phase IV interventional trials are or have been conducted as of July 2010. The conditions targeted by the treatments tested in the Icelandic trials are:

Conditions targeted by Icelandic trials:	
Arthritis/osteoporosis	4
Asthma/COPD	6
Cancer	12
Cardiovascular	10
Gastrointestinal	2
Skin-related conditions	6
Other	13
Total	53

Table 6: Conditions targeted by Icelandic trials

³² clinicaltrials.gov – Investigator and industry – only those who aim to publish

³³ http://www.finnmedi.com/in_english/

³⁴ <http://www.visindasidanefnd.is/Default.aspx?id=64&cmd=menu>

7. Data and methods

Interviews

A total of 39 people were interviewed for the study, including representatives of all five countries, government agencies, industry, hospital and the university environment (see the Appendix for a list of interviewees). An Accenture team consisting of one team member in each Nordic country conducted the interviews, interviewing people from their own country.

As a starting-point, we sought to interview at least 3 people from the industry, 3 people from the hospital/university sector and one person from the authorities in each country. This aim was set to ensure that all sectors of the field were covered. The project group started by contacting the people listed as relevant contributors by Stina Gestrelus, the author of a report on the same topic. The people interviewed also made recommendations as to whom to contact, and the reference group also made some recommendations. Some interview participants were also identified at random by contacting hospitals, pharmaceutical firms and other relevant institutions. We continued contacting new interview participants until we reached a point of saturation – new participants repeated the points already made and little new information was added. We also tried to focus on senior people with relevant decision-making power and good knowledge of the field.

Questions have been raised regarding the validity of the findings in this study. There are two issues in particular. The first one addresses the validity of interview data in general. What is the personal agenda of the individuals who get to voice their opinions through interviews? There should be quantitative data to support the issues raised. We have summarized the main points of the existing literature as an effort to address this weakness. We have also analyzed public data from clinicaltrials.gov for Finland and Norway, and we have looked into the trials conducted in two or more Nordic countries. Also this data was collected from the clinicaltrials.gov Web site. The data we have collected from clinicaltrials.gov is not really adequate to give a total overview of trial activity in the Nordic region, because only projects that seek to publish results need to register there. We have thus supplemented the data with figures from other reports available. This makes the data in this report a bit fragmented and not perfectly comparable between countries. This has also been noted by the interviewees, and one of the problems raised in this report was thus the lack of publicly-available data. One of the recommendations was to support the building of public databases or applications which can withdraw information from existing databases, to share information on the activities undertaken in the field.

The second question is in regards to the selection of individuals to be interviewed. Are they the right people to voice the opinion of the entire community of individuals and institutions involved with clinical trials? The problem of introducing bias through the selection of interview participants is a problem in any project which aims at to study human beings. We could have made a list of all individuals working within the field and have a computer program generate a random sample to contact. However, those who would answer the request to join would still be those who are interested in the topic of Nordic collaboration and have something, most likely negative, to communicate³⁵.

³⁵ Ref Melberg and Humphreys on this
<http://www3.interscience.wiley.com/journal/122539708/abstract?CRETRY=1&SRETRY=0>

8. Literature review

There are some other studies of relevance to this field. Some challenges, opportunities and solutions to improve conditions for collaboration on clinical trials across countries have already been suggested. Some of the studies referred to here target clinical research in general, but we find the result of these studies to be interesting, as clinical trials are a part of this larger field of research and different aspects of clinical research are confronted by many of the same challenges.

In 2010, Stina Gestrelus³⁶ suggested that the ECRIN networks in Denmark, Finland and Sweden and representatives from Norway and Iceland form a network which could be funded by NICE and Nordforsk and work together with national authorities and ethics committees. In 2003, the Academy of Science in the UK³⁷ published a report on how to strengthen clinical research. Its recommendations were to create a national network to create and support clinical trials, funding through the Medical Research Council, improved career structures and incentives, an improved regulatory environment and that the NHS would support clinical research with 1.5 % of its turnover. A Danish working group reviewed the existing literature and analysis of clinical research in Denmark³⁸. It made many recommendations based on the review, and some of them are that public funding of public clinical research be increased, support functions are strengthened, legislation is optimized so as to not create barriers towards research, more dedicated time for research and a better-defined career path for clinical research, other professionals like pharmacists are brought into clinical research, encouragement of research networks and better use of registered patient data in clinical research. The Academy of Finland published an evaluation report³⁹ that looked more closely at the relationship between Sweden and Finland. It also focused on engineering of research careers for health care professionals and improvement of the research funding portfolio for clinical research. In addition, it wanted to mount a clear uniform strategy for governance of academic hospitals from executive management to daily operations.

As of now the large multicentre and multinational trials are driven by the big industrial companies, but people interviewed for this report also see the need for trials sponsored by investigators which cooperate across the borders, driven without the help of pharmaceutical companies. The big industrial companies have their own funding and a large support network around them. The regulatory environment can be considered a deterrent for individual investigators and smaller research groups who do not have this support. This pattern was also seen in the analysis of the 62 trials conducted in Denmark, Finland and Sweden. Only six of the trials are investigator-driven and they were restricted to centres in the Nordic countries, while the 48 purely industry-driven trials were conducted at an average of 220 locations each. The EU report on investigator-driven trials makes many recommendations to help balance the relationship between publicly-funded investigators and the industry⁴⁰. Improvement of

³⁶ Stina Gestrelus, "Nordic Cooperation in Clinical Research - Opportunities and Challenges" (Nordic Forum for Innovation in Health Care and Medicine, February 18, 2010).

³⁷ Working group of the Academy of Medical Sciences, Strengthening Clinical Research (The Academy of Medical Sciences, October 2003).

³⁸ Working group Peter Schwartz and others: "Klinisk forskning i Danmark – tid til handling" 2 December 2009

³⁹ Evaluation Panel, Clinical Research in Finland and Sweden Evaluation Report (Publication of the Academy of Finland 5/09).

⁴⁰ Jurgen Scholmerich, Roger Bouillon, og Håkan Billig, Investigator-Driven Clinical Trials, Forward look (European Science Foundation, 2009).

education, training and the career structure for scientists involved in clinical research was emphasized also in the EU. Again, as in UK and in the Nordic region, they recommend increased levels of funding for investigator-driven clinical trials. An interesting contribution by this report in particular is the recommendation to adopt a risk-based approach to regulation of investigator-driven clinical trials. As also discussed in this current report, the EU report recommends streamlining procedures for obtaining authorization of investigator-driven clinical trials and to ensure that there are patients for trials for statistically reliable results.

The industry can conduct its clinical trials anywhere in the world, and the attractiveness of the Nordic countries is declining very quickly⁴¹. If nothing is done, this decline might become permanent. As the Swedish advisory board for collaboration on clinical research put it: “If clinical research is mistaken to be a sideline to care and not a prerequisite for it, there is a risk that huge sums of money will be spent on ineffective and unnecessary expensive treatments that do not generate any increased value for neither the individual patient nor society as a whole.”⁴²

The Nordic countries have a good tradition of clinical research and are well-known for quality research. Comparing the publication output of the different EU countries after adjusting for population size, the top countries were Denmark, Finland and Sweden⁴³. They should advertise their **comparative advantages**, which especially lie in the fact that the region has a relatively stable settlement pattern and excellent health registries, which provides a good foundation for implementing clinical trials that require historic information on patients and trials in which the patients have to be followed over time. The use of electronic health records (EHR) in feasibility studies so that centres with patients can be found and accurately estimated, as well as used for recruiting patients, is a unique possibility for the Nordic countries that should be investigated (compare with Innovative Medicines Initiative call 2 topic 9)⁴⁴.

Some studies have been conducted in Sweden and the recommendations are consistent with the international studies mentioned above. For example, SOU report 2009:43⁴⁵ made recommendations that fall within these four areas:

- 1) Recruitment: Strengthen links with research in education and create more services where research and clinical work can be combined in a clear manner.
- 2) University hospitals: Integrate research on health care at university hospitals and convert them to university medical centres with states and counties in a common direction.
- 3) Use of research results: Establish a fund for research and treatment; a national liaison group. This is useful for making new discoveries on care.
- 4) Infrastructure: Provide support for infrastructure in the form of bio-banks and quality and patient data files.

⁴¹ Wallenbeck, Läkemedelsverket, Competent Authority statistics on clinical trials with medicines

⁴² “Everybody wins through collaboration in clinical research!” Final report of the Advisory Board for collaboration in clinical research, N2007:4: <http://www.sou.gov.se/samverkanklinforsk/>

⁴³ Impact on Clinical Research of European Legislation (ICREL), Final report: <http://www.efgcp.be/ICREL/>

⁴⁴ http://imi.europa.eu/docs/imi-ju-2009-call-topics-14092009_en.pdf

⁴⁵ ”Klinisk forskning – Ett lyft för sjukvården, Slutbetänkande av Utredningen av den kliniska forskningen” *Statens Offentliga Utredningar* 2009:43, Stockholm 2009

9. Discussion

The discussion consists of three main sections. The first main section, “Nordic coordination unit – suggested platform for organization of Nordic collaboration”, discusses the overall coordination of the clinical trial initiatives recommended. The solution suggested involves a coordination unit based in existing networks. It recommends holding an open competition where interested parties can suggest how to solve the task of coordinating clinical trial collaboration in the Nordic region. A short discussion on therapeutic areas and financing and findings from another report by Accenture on Nordic cooperation applied to the clinical trial setting is also included.

The second main section discusses in detail the “Harmonization of application processes and trial administration”. Topics are ethics committees and competent authorities, and it recommends that those authorities develop common Nordic guidelines and discuss how common policies should be adhered to and how compliance to guidelines and regulation is assessed.

The third main section, “Information – the basis for feasibility studies”, discusses in detail the need for information to facilitate clinical trial activity and how existing data can be better exploited to the advantage of more and better clinical trials in the Nordic region.

One of the main reasons given by interviewees from the industry as to why the Nordic countries lose out in the competition for clinical trials is our **high costs**. There is little we can do to change the high wages and cost level of the Nordic countries, but we can find new ways to organize and work to streamline processes so that we can be faster, smarter and better than our competitors. In the execution of clinical trials, time is a major resource and cutting down on it can to some extent reduce the high cost levels. From the investigators' point of view, the most time-consuming part of the clinical trial process is the application process and the most time-consuming part for the industry is the period before the application process, the period of identifying the feasibility of the study, like where centres with enough patients and clinicians willing to participate in the trial can be found. For example, this process can be made easier and more cost-efficient by using electronic health records (EHR) to identify centres where there are enough patients for recruitment within a given time frame and enough to lower the cost per patient (certain fixed costs are so high that they require many patients to reduce the cost per patient).

Some of the solutions discussed in the following are easy, concrete and straightforward, but many of them stress the need for a changed mindset and mentality. Such changes are slow to implement and require continuous and systematic work over time. We believe that the quick and easy solutions will yield much more value if the hard and slow work to change mindsets, mentality and priority are implemented in parallel.

Some conditions must be secured for the implementation of new solution to be constructive.

- 1) There are already many well-functioning support units for coordinating established clinical trials. Some units focus on facilitating specific kinds such as cancer, like the Oslo Cancer Cluster or on a specific geographical area like the Gothia Forum, which focuses on the region of Västra Götaland in Sweden. Any new measures should support the continued development of successful existing initiatives and as far as possible learn and build on that which is already established.
- 2) Actors express concern that the field will become more bureaucratic and complex. More complexity will also be introduced by introducing new measures. Before introducing any

new measures, it must be ensured that they will not add bureaucracy or unnecessary complexity.

Trials are usually initiated and driven by the international or national industry, often referred to as industry-driven trials or researchers based in hospitals or universities, also called investigator-driven trials. These main types of actors have somewhat different problems and different needs regarding their barriers and the measures that would be constructive for them to be able to conduct more and better clinical trials. The solutions discussed aim to make it easier for the actors involved in clinical trials to conduct them in the Nordic region according to the barriers and needs identified through interviews. Investigators from the hospital/university sector need help with administration and understanding regulation and laws and help to locate possible collaboration partners in other countries.

Speed is crucial for the companies. They need quick decisions as to whether studies can be carried out (feasibility studies), and they need to locate patients, clinicians, nurses and locations and get them up and running as fast as possible.

Nordic coordination unit – suggested platform for organization of Nordic collaboration

Many of the interviewees have suggested a **Nordic unit for coordination** of clinical research. As discussed in the literature review, other countries and groups of countries have experience with such common collaborating units. Many of our recommendations are steps to be managed by the Nordic coordination unit.

If it is decided that the coordination unit is a measure that the Nordic Innovation Centre wants to pursue, we recommend that this be done by supporting and developing the initiatives that have already been established, like ECRIN, the NRC network, competent authorities, ethics committees and patient organizations required for a successful result and in order to change the current situation. An alternative is to create a totally new unit or organization, but we would then be unable to take advantage of many years of experience and work already performed by the existing initiatives. Moreover, this new organization would add to the complexity of the current environment. Two of the conditions we have chosen as crucial for new measures to be helpful and constructive are that the existing initiatives are used as much as possible to take advantage of experience and knowledge built up over time, and that any new initiatives do not add to the bureaucracy and complexity of the sector already perceived as a barrier towards collaboration.

There are several existing initiatives which can serve as a basis for further development of a Nordic coordination unit.

One of them is the ECRIN organization or a collaboration between the Nordic countries' national networks of the ECRIN (European Clinical Research Infrastructure Network) organization. They could create a unit that focuses on Nordic issues. Another way the Nordic ECRIN networks could offer better support to Nordic cooperation is that they be strengthened to the extent that they are able to perform their designated tasks. The ECRIN organization has a European scope and its network is multinational. The organization is also formalized and linked to regional and national levels in every country in which it is established. However, certain issues need to be dealt with. It must work on behalf of the whole Nordic region, not only a smaller region. It must also employ people who are dedicated to serving those in need, the investigators and the industry. Most interviewees claim that the national ECRIN organizations do not function as intended or that they have not heard of them at all. It has been mentioned that FinnMedi Oy, located in the Tampere region, and SweCRIN, located at the Karolinska Institutet, have adopted

an overly-narrow regional approach, although they should be acting on behalf of the national clinical trial community. One of the reasons why ECRIN is not commonly known by researchers is that the organization has spent much time on less visible tasks, preparing the ground for easier execution of clinical trials in Europe. For example, it has conducted studies on how directives and laws can be harmonized^{46, 47}. There is no plan for further EU funds to the SweCrim, DCRIN or FinnMedi Oy after 2011.

ECRIN offers a much broader range of activities and services than the NRC network, and it might be easier to reach out to a broader group of people with a more compact mission, such as the conference annually hosted by the NRC network. It may take longer to successfully establish the broad range of services and activities offered by ECRIN.

The operating staff of the organization should be somewhat larger but only so large that it manages to perform the tasks desired by the actors in the field. The unit should have good Web sites which cover the services required for successful Nordic collaboration in the field of clinical trials (will be elaborated on below).

An alternative to ECRIN is the NRC network (Nordic University Hospital Research Conference). Although this network does not have any formal links to any authorities, **the NRC network** is perceived by some interviewees as an organization with the potential to become a Nordic unit for collaboration on clinical trials. So far the NRC network is perceived as being interested and open towards both the academic/clinical environment, as well as the industry and private sector. This unit is also in the process of building a reputation and has managed to obtain a certain degree of visibility in the Nordic region. The NRC network is encouraged to maintain and continue developing these positive and open attitudes towards every sector of the field. Also the NRC network has to address some challenges. One of the most important aspects of a Nordic unit for collaboration on clinical trials is that it is Nordic. The NRC network has organized and hosted 5 Nordic conferences; all in Bergen, Norway. If the NRC network is going to be a Nordic organization, it must rotate the conference venue to all Nordic countries, to secure legitimacy and participation from all relevant actors. There should also be some rules (statutes) that ensure that there will be a Nordic organization in the future, tending to the needs of all of the Nordic countries. Another point is that the NRC network organization is composed of people who have other jobs and responsibilities. They have many other points on their agenda and do not have the time for daily operation of the functions that the unit here is suggested to be responsible for. Thus (depending on the final scope of the functions for which the organization is responsible) the organization must be extended with people who can dedicate their time to perform those activities. Its work is now mostly internal, but it should also gain an external surface as the door opens into the Nordic clinical trial community for actors coming from other areas.

⁴⁶Common definition of categories of clinical research: a prerequisite for a survey on regulatory requirements by the European Clinical Research Infrastructures Network (ECRIN):

http://www.ecrin.org/fileadmin/user_upload/public_documents/About_ecrin/downloads/1745-6215-10-95.pdf

⁴⁷Harmonization of ethics committees' practice in 10 European countries:

<http://jme.bmj.com/content/35/11/696.html>

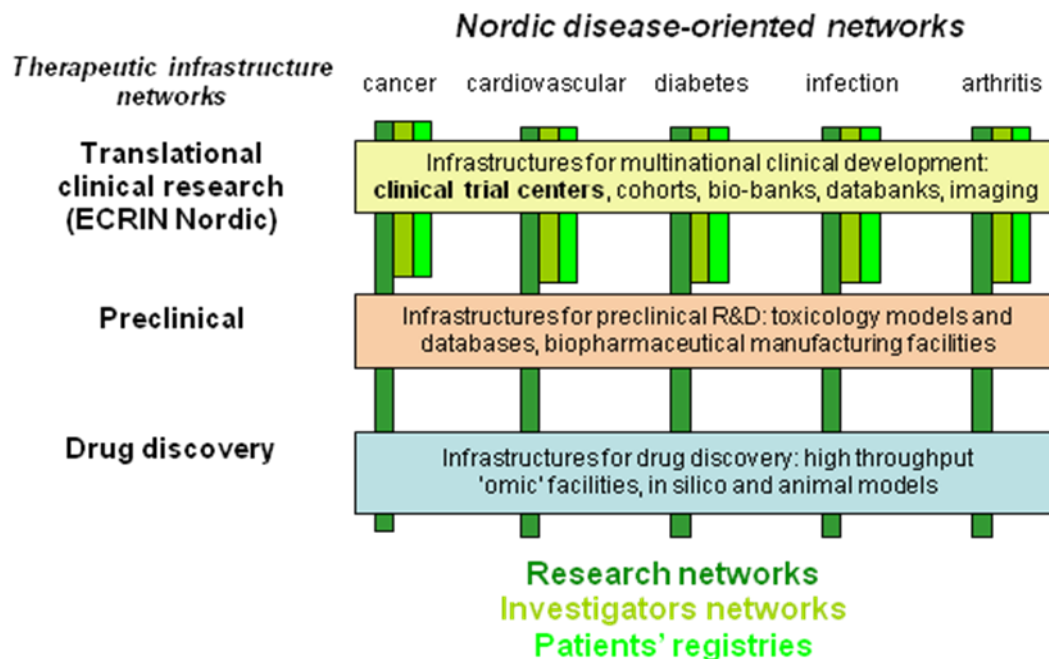


Figure 7: Nordic disease-oriented networks

The coordination unit secretariat in the UK has been mentioned by many as a pioneering organization which should be used as an example to follow.

Any unit working on behalf of the field of Nordic clinical trials should be independent, and consist of representatives from both industry, hospitals, universities and authorities.

As an alternative to ECRIN and the NRC network, it should also be possible to develop organizations which so far have been working only with one therapeutic area or a smaller geographic area. The downside to that is that most of the existing organizations are working very well and there will still be need for the work those organizations perform today, even if we get a generic organization. They will be valuable parts of a larger network, but they need an umbrella organization, or some generic organization which can tend to the common needs of all of those units which have a narrower scope.

Yet another possibility is for the NRC network and ECRIN to join forces in a merger. If they decide to join forces, they would become a stronger organization with better opportunities to achieve their common goals.

Recommendation:

The task of coordinating Nordic cooperation should be given to the unit with the best basis for managing such a task. There should be an open competition where all interested parties can submit their offer and explain how they intend to solve the task and at what price.

If the unit is established and in the end is not comprised of ECRIN or any other existing initiatives, the unit should maintain a close link to the Nordic ECRIN network, as well as other units working towards the same goals, like the Gothia Forum. In fact the Nordic coordination organization should be the common Nordic meeting place for all of those organizations and units. The Web portal of the Nordic unit should be linked to all of the Web sites of units working towards the same goal.

Many of the services requested to conduct clinical trials can easily be solved through a **Web portal**. The Swedish Medical Agency already has much information available for researchers like FAQs, collection of laws and guidelines, step-by step-guides and information on GPC⁴⁸. There is experience with such a portal in the UK⁴⁹. Another example of a portal for coordinating clinical trial collaboration is the one at the Gothia Forum⁵⁰. A final example of how such a portal can be designed is the [IFPMA Clinical Trials Portal](#).

The portal can offer access to the database information listed above, there may be checklists and step-by-step guides for researchers on the application processes for ethics committees, bio-banks and medical agencies for all countries. There may be user-driven networking opportunities, contact details for trial units, announcements of conferences and relevant meetings, discussion forums, etc.

Another measure that can be taken to achieve more general coordination of the field is to encourage the establishment of the profession of trial nurse. The NRC network has probed the idea of setting up such an education for nurses. This would be a new profession which to some extent can take over coordination of the field and secure the development of relevant networks and activities. It would be of importance that this education cover topics of managing the application process and how to successfully conduct a trial. Depending on the curriculum and topics to be covered by this education, we **recommend** that the Nordic Innovation Centre and the Norden association determine what assistance it can provide regarding their Nordic college and experience with offering Nordic education.

Therapy areas

In relation to specific **therapy areas**, there are some areas in which the Nordic countries have a comparative edge, and it will be easier for our region to obtain assignments within those fields. We believe that the coordination unit should be a unit for trials within every therapeutic area, but the strategic discussions should identify areas where activity should be encouraged like:

- Diabetes
- Cardiovascular diseases
- Kidney transplants
- Vaccines
- Osteoporosis
- Cancer
- Orphan diseases, diseases with small patient volumes

The field of clinical trials in UK is organized by therapeutic areas, but in retrospect representatives from UK decision-makers have recommended that other countries should primarily organize their systems in a generic way. The alternative should nevertheless be explored in the Nordic arena. The overarching coordination unit should be a generic unit, but the professional networks should continue to be concentrated around specific therapeutic areas.

⁴⁸ <http://www.lakemedelsverket.se/malgrupp/Foretag/Lakemedel/Kliniska-provningar/>

⁴⁹ <http://www.ukcrc.org/>

⁵⁰ <http://www.gothiaforum.com/sv/Ovriga-sidor/Gothia-Forum1/Om-Gothia-Forum/>

When asked for examples of good collaboration across the borders today, collaboration within certain **therapeutic areas** like oncology are mentioned as **successful**. The successful networks should be further supported and should be in close contact with any new unit or organization which aims at more overall coordination. Such therapeutic networks are often more loosely organized without much formal structures. This gives these forums and networks the opportunity to work fast and without bureaucratic aspects to slow them down. The importance of such networks lies within its efficiency in sharing information and discussing narrow field specific topics. The forums are often very narrow, like the society for breast cancer.

Within certain therapeutic areas, like oncology, the patient base in each country is too small to run an entire trial in one of the countries alone. In such cases in particular, the collaboration on finding patients suitable for the trial across borders should be established. We strongly recommend that there be some kind of information-sharing between the countries on incidence and prevalence rates, so that patients can be located more easily. Prevalence and incidence figures are a substitute for actual individual patient information, and can be used in the case where the law prohibits the sharing of personal data (though an actual patient database would be preferred for this mean). The preferred case is that a good Nordic patient database can be established, making the need for information-sharing on incidence and prevalence rates redundant.

The Oslo Cancer Cluster⁵¹ is a “non-profit member organization dedicated to accelerate the development of new cancer diagnostics and medicines.” Its vision as stated on its Web site is: “We are committed to improving the lives of cancer patients by accelerating the development of new cancer diagnostics and medicines. We will be one of the world leading cancer clusters by 2013.”

It was mentioned at the inaugural seminar to mark the merger of Medinnova and Birkeland Innovasjon⁵² that a neurology cluster created in the image of the Oslo Cancer Cluster had been established and opened. It may be possible for NICE to finance such Nordic networks within therapeutic areas and access the challenges towards clinical trial activity in the Nordic region discussed above through such specialized networks.

A group of Nordic researchers are planning to establish Nordic collaboration on phase I and IIa trials within the field of cancer. Their first meeting was in May 2010 in Kastrup. Steinar Aamdal of the Norwegian Radium Hospital in Oslo is a driving force behind this work.

Financing

Funding of clinical trial projects: According to one of the interviewees, some of the trial centres in Norway are cooperating with other centres more now than just a few years ago. In the past, there was more competition between different centres in the country. The change came with a new condition attached to funding from the EU and some of the funding from the Norwegian Research Council. A condition for funding was that the project contain collaboration between different centres and institutions in Norway. One of the centres interviewed explained that the effects of stronger collaboration with European countries have had very positive effects for the centre. Those positive effects include insight into the research and thoughts of other networks and groups working in the same field, a more international environment at the centre, a higher

⁵¹ <http://www.oslocancercluster.no/Default.aspx>

⁵² <http://www.medinnova.no/English/>

degree of exchange – both own employees on sabbatical to other institutions and researchers from other institutions coming in. It is suggested that some of the funding available for clinical research in the Nordic countries should set as a condition for applications that they involve an aspect of Nordic collaboration. The interviews have shown that common Nordic funding is desirable. This funding should only be offered to projects that include cooperation between countries, and supplement national and private funding.

Funding of the Nordic coordination unit: Funding should come from every country and every stakeholder. This way, every actor on whose behalf the unit acts has some kind of stake and the possibility to legitimately voice its wishes and influence. The unit should act as a body that represents all clinical trial activity and the whole Nordic field of clinical trials.

It must be discussed whether or not the services offered by the coordination unit should be chargeable. They may be free of charge, there may be a fixed membership fee or charges for each service performed. They may be free of charge for both the industry and public users, they may be fully chargeable for industry and free of charge for investigators or there may be a mixed version where some functions are free of charge for everyone and some functions have to be paid for by the user. As this initiative is based on a desire to make it easier to perform clinical trials across the Nordic countries, and a high cost level is identified as one of the main barriers to performing trials in the Nordic countries, we recommend that any charges be low so as to not deter potential users from using the services. The UK, France, Spain, Italy and Germany already have coordination units that offer services to commercial and non-commercial investigators, and if the Nordic Innovation Centre decides to go ahead with this plan, the experiences of those countries' systems should be reviewed.

Different investigators request different types of services. Referring to the discussion of charges above, it might be an idea for charges to be adapted to the demand for services. This must be analyzed in greater detail once a decision has been made to create such a service that offers coordination unit.

Harmonization of application processes and trial administration

For investigators in academia and hospitals, one of the major barriers toward the effective and successful conduct of clinical trials is the **application process**, which is viewed as the most time-consuming part of the trial. It was stated by an interviewee that if a trial is to be carried out without an industrial partner, the researcher must take weeks off work at the clinic to prepare the applications and papers. Investigators themselves mostly do not have support, education or knowledge of the legal aspects of, and the practical requirements towards the application process. In interviews, medicines agencies note that applications from the industry are more complete than those from academic institutions. For example, many investigator-initiated project applications do not contain any monitoring plan. The consequence will either be that the researchers' applications are returned for revision, which incurs delays and extra work for both the researcher and the authority handling the application, or they will encounter problems during their project.

The industry has more resources and better routines for developing applications and coping with the application process. However, the industry *does* need applications to be reviewed by the authorities as fast as possible, which means that the discussion in this section is relevant to both parties.

Ethics committees' case review routines are perceived as a barrier by some of the investigators interviewed. Some of the interviewees claim that decisions on applications vary to a great extent both between countries and within countries (Sweden, Norway, Finland). They also claim that the case review process is too time-consuming. The Swedish ethics committees publish average days used by the committee from the day they receive the complete application to the day before they announce their decision to the applicant. In 2006 on average they took 26 days, in 2007 they took 25 days and in 2008 they took 26 days⁵³. In the US, applications are reviewed within a median of 15 days⁵⁴. The maximum number of days ethics committees in the EU are allowed to spend on reviewing an application is 60 days, indicating that the Swedish committees are on average faster than required, but still slower than committees in the US. Nevertheless it has been **recommended** that common Nordic **training for ethics committee personnel** be established on topics like GCP, ethics and efficient case review to help harmonize practices across borders and make ethics committees judgment more predictive across borders for applicants. Training has also been suggested by others as a means to achieve ethical cohesion between countries⁵⁵.

Many of the people interviewed have been asked about their views on the possibility of achieving **a single point of entry** for the Nordic region for applications to authorities – medicines agencies, ethics committees and possibly bio-banks. The issue of changes to legislation has been raised in the discussion around a single point of entry and alignment of the countries' application processes. Most of the people interviewed for this report responded that the issue is not so much the need for changes to legislation, but rather their interpretation of them and also the achievement of alignment through more effective administration and management through the legislation. As expressed by an interviewee, “The need for a change in laws is not as urgent as the need for a change in processes.” Regulation is fairly similar in the Nordic countries through the EU's Clinical Trials Directive 2001/20/EC, but the interpretation of laws and practice diverges greatly, according to interviewees. They also claim that the principles for monitoring and quality control differ between countries. The interviewees do not perceive that the countries are ready to agree to on single access to the whole Nordic region through just one of the countries. However, there are many measures which could bring the Nordic countries closer and prepare the ground for a single point of entry to be established in the future, such as working with culture, mentality and mindsets which provide the foundation of actual practice, and the application processes in the Nordic countries can be made more similar, streamlined and coordinated without amending legislation.

We recommend that relevant authorities like medicines agencies and ethics committees **meet and discuss the interpretations and the process around the application process and the regulation involved**. They should strive to learn from each other, establish common best practices and make their processes as similar as possible. Investigator and industry representatives should take part in these discussions, as only they know where the problems lay and how they should be fixed in order to improve the research environment. This will provide a foundation for a possible single point of entry in the future and will bring the regulators closer to

⁵³ <http://www.epn.se/start/startside.aspx> The aggregated average review time for Sweden was calculated by the author on the basis of each of the region's annual reports.

⁵⁴ Hiddo J. et al (2008): “Does the European Clinical Trials Directive really improve clinical trial approval time?” in the British Journal of Clinical Pharmacology:

<http://www3.interscience.wiley.com/journal/120081980/abstract?CRETRY=1&SRETRY=0>

⁵⁵ “Harmonization of ethics committees’ practice in 10 European countries”:

<http://www.swecrin.se/filer/ethics696.full.pdf>

each other concerning the way they judge applications which will provide a more stable and predictable environment for the actors that seek to conduct clinical trials. For example, we recommend that the Nordic countries agree on a common definition of an “interventional” trial. Although this has been defined by the EU directive, it is a problem that many European countries differ in their interpretations^{56, 57}. Also other problematic terms and areas where the interpretations diverge should be identified and a common definition should be elaborated. Not only should the authorities meet between themselves, they should also meet to listen together to the investigators and the industry.

A second recommendation to help streamline the application processes is clear and common **guidelines** for the criteria by which applications are judged and for monitoring and quality control. Common practice can only be achieved through discussions and by respecting the other partners. Such common guidelines should be decided on in meetings between national authorities and representatives from industry and investigators as outlined above.

Data handling and **bio-banks** are also mentioned as areas with potential for more effective application processes. An agreement with a bio-bank will be needed if a trial entails collaboration across Nordic countries, and biological material is sent across borders. The best-known bio-banks in the Nordic region are DeCode in Iceland and Swegene in Sweden. The application process to obtain such an agreement is complicated and time-consuming, because the laws and regulations are different in every country. This should be a topic in the meetings outlined above.

Another barrier concerning the application process is the fact that many of the application papers must be in **the country’s own language**. The system should be changed so that most of the paperwork is submitted in English.

It is also important that when there is an **opportunity** to harmonize systems, they should strive to do so. For example, when one of the countries' ethics committees plans to change its electronic application system or change the mandatory data fields on an application form, there should be a discussion with the other countries about what they are doing, and what they can learn from other organizations that have experienced the same changes. The views of users should be taken into account, as well as what the users think of the existing systems and how they think the systems should be changed and developed, and not the least how the changes can contribute to harmonization of processes.

Some comments regarding the enhancement and cross-national alignment of laws have surfaced. When there is an **opportunity** to do so, the laws can be coordinated. An opportunity may be that one of the countries decides to change its laws.

Under the auspices of EU, there have been efforts to harmonize the application process to the medicines agencies. If a trial is to be carried out in three or more member states, a single application submitted to the Clinical Trials Facilitation Group (CTFG) in English will be evaluated in a single process together with the competent authorities of those member states where the clinical trial will be carried out. Scientific questions on the protocol and the

⁵⁶ http://www.ecriin.org/fileadmin/user_upload/public_documents/About_ecriin/downloads/1745-6215-10-95.pdf

⁵⁷ Impact on Clinical Research of European Legislation (ICREL), Final report: <http://www.efgcp.be/ICREL/>

investigational medicinal product will then be clarified together. The clinical trial authorization by each competent authority involved will subsequently be generally provided within 10 days⁵⁸.

The question has been raised as to whether commercial and non-commercial trials or sponsors should be treated differently by the law. According to the reference panel, there should be no differences in the regulatory requirements of the two types of trials, because the quality should be equally high for both types, and because the perception could be established that non-commercial trials have lower quality because they are treated more easily by the authorities. High quality is for the safety of the patient, and to guarantee reproducible research results. Differences in laws that govern trials conducted by different types of sponsors are not recommended, but it should be investigated whether there should be differences in laws that govern trials exposing trial participants to a lower level of risk, compared to a higher level of risk. The Forward Look report on investigator-driven clinical trials from the European Science Foundation⁵⁹ looked into the idea of assigning **different risk profiles** to trials and tailoring the review of the trial according to the risk to the patients involved in the trial. Strict regulation of clinical trials is important to protect participants who are willing to try experimental medications and treatments in trials from unnecessary harm. There is a large difference in the risk taken by a person participating in a phase I trial that is testing a new agent in humans for the first time and a person participating in a phase IV trial that aims to establish the equivalent dosages of two well-established drugs. The application process for the latter type of trial could be less strict and subject to less control than the first type of trial. This is something which could be considered in the Nordic region as well, while it would make the application process shorter for studies that do not involve a high degree of risk to the patients.

Information – the basis for feasibility studies

Although the application process is seen as the most critical point of the process for investigator-initiated trials, the stage before the application process is seen as the most critical one by the industry, according to interviewees. It is of importance to the industry trials that **feasibility studies** are performed quickly in order to answer an international company that is looking for trial locations as quickly as possible. For the Nordic region to be competitive despite the high level of costs, we need to ensure that we are as effective as possible in finding out whether or not a trial can be carried out by pinpointing the need for resources, locating those resources, and employing personnel for rapid start to recruiting patients. This is essential due to the competitive nature of the decision of where to locate a trial. Today, a firm that wants carry out a trial sends a request to all of its local divisions around the world, and the departments which answer first and have solutions that will yield quality trials at an acceptable price will be chosen to start the trial process. The local divisions in the Nordic region have to contact every single clinic to find out if they have available researchers/clinicians, what their patient base is, and whether they are interested in being involved in the trial. This information could be available in a public **database**, aggregated disease statistics on the patient base (incidence and prevalence statistics), from the personnel who perform research at the centre and possibly even whether they will have available capacity during the next few months or not. A site is under development in Sweden

⁵⁸ http://www.pei.de/nn_163516/EN/infos-en/pu-en/02-clinical-trials-pu-en/vhp-trials/vhp-trials-node-en.html?_nnn=true

⁵⁹ See: <http://www.esf.org/activities/forward-looks/medical-sciences-emrc/fl-07-001-investigator-driven-clinical-trials.html>

where registry data is used to create value for patients, physicians and scientists⁶⁰. A site for both patients and doctors to register interest in taking part in study could be useful and the use of electronic health records to identify patients should be investigated in greater depth. Interviewees have pointed at some problems with the current system. One is that individuals at the different companies develop certain relationships and networks, and when a new trial is coming up they call the same people they have worked with before. One consequence of this is that it is difficult to increase the group of clinicians who have industry trial experience and the work is kept to certain clinics and environments. It could be suggested that a more accessible and visible overview of available clinicians would be a way to introduce more clinicians to the work on clinical trials and make it easier for new generations to gain relevant experience. Another major problem is that a direct consequence of this time-consuming activity is that we as a region cannot compete with other parts of the world that manage to receive quicker clarifications as to whether, where and how the trial can be conducted.

A database for sharing information on cancer clinical trials has been implemented in Denmark, where a Web site that is open to the public allows searches for trials, based on different search criteria⁶¹. The material in the Danish list is based on reported information from the oncological clinical research units. The Norwegian Council for Quality Improvement and Priority Setting in Health Care (Priority Council) has recommended the establishment of a Web site that publishes an **overview of ongoing, planned and completed clinical experimental treatment projects** in the field of cancer⁶². The motivation for this recommendation is the need for patients that have not been successfully treated with conventional medicine to have an alternative treatment option. In the contract documents from the Norwegian government, the Norwegian regional health authorities are given the assignment, in collaboration with the national ethics committees, to establish a national database with information on ongoing clinical trials within all areas⁶³. The presentation of the case by the Priority Council states that such a Web site should be based on existing databases like the EudraCT clinical trials database⁶⁴ which is not publicly accessible. Such a database serves many functions. One has already been mentioned; that patients can orient themselves on existing trials. More relevant to our setting is a positive effect for researchers and CT sponsors by making information which can be used in literature reviews and reviews of projects testing the same or similar medicines easily available, where it can be used in pre-studies and as a way to avoid double work. If the database is designed intelligently, it can also be used to identify centres and researchers with experience in different CT areas, which again can help identify collaboration partners and trial locations. Last but not least, this database can be used by politicians and other decision-makers to gain an overview of the actual clinical trial activity, which can provide important information for strategic decisions. Many sites already exist that collect data about clinical trial projects. For example, the WHO has made a platform that collects information on trials from many countries into one searchable clinical trial database⁶⁵. CenterWatch is a US-based organization that offers Web-based services to patients,

⁶⁰ <http://www.kurnet.se/english/>

⁶¹ <http://www.skaccd.org/abc%20catalog/index.asp>

⁶² <http://195.159.251.11/binary?id=3711>

⁶³ <http://www.regjeringen.no/nb/dep/hod/tema/sykehus/styringsdokumenter/oppdragsdokument.html?id=535564>

⁶⁴ <https://eudract.emea.europa.eu/>

⁶⁵ <http://apps.who.int/trialsearch/>

investigators, sponsors, CROs and companies⁶⁶. The US department of Health and Human Services has this option for browsing trials⁶⁷.

The Norwegian ethics committee is going to make public the content of the applications it receives⁶⁸, only exempting commercial secrets from publication, and there are separate databases for all of the Nordic countries. All projects which seek to publish in an international journal also have to register in the clinicaltrials.gov database or a similar database. As all of the Nordic project databases already exist, we do not have to reregister all of the information. This is an example of a meta-database created from several original databases: <http://www.controlled-trials.com/mrct/>. A similar Web site should be established in the Nordic region. It was mentioned in interviews that several institutions or organizations have looked into the possibility of establishing **databases** of volunteers which can be used in feasibility studies.

We thus **recommend** that good databases are developed which can be used actively in both the more overall strategy development and for feasibility studies in the preparation of every trial. Most of the information already exists in databases. It is crucial that it is structured, made visible and usable. One way to do this is through meta-databases or data warehouses. We recommend that the option of creating such a data warehouse is considered before duplicating existing databases. The duplication of databases will also duplicate the workload of updating and maintenance and will increase the risk of introducing mistakes and flaws.

The database should include information on the following units:

- Trials
 - Centres involved
 - Indications treated
 - Interventions on trial (medicine, procedure, device, etc.)
 - Other units of information as covered by clinicaltrials.gov and the WHO platform
- Centres
 - Patient base covered by the centre
 - Incidence rates and prevalence (if individual patient data is not possible)
 - Overview of number of patients in treatment for each diagnostic group
 - Interest in research – phases, therapeutic areas
 - Technical facilities (medical and administrative)
 - Capacity
 - Availability
- Clinicians and nurses (voluntary)
 - Interest

⁶⁶ <http://www.centerwatch.com/about-centerwatch/index.htm>

⁶⁷ <http://clinicalstudies.info.nih.gov/>

⁶⁸ http://helseforskning.etikkom.no/ikbViewer/page/sakerogtema/prosjekter?p_dim=34977&lan=2

- Specialty
- Availability

As shown by the list above, the information units are closely interconnected and the architecture should be worked out to reflect and exploit this as best possible.

The advantages of good databases on projects, patient and investigators are:

- Shorter time from idea to practice.
- Credibility from international companies by making visible what we have to offer
- Background data for government decisions
- It is easier for researchers to consult previous research⁶⁹
- Easier to locate collaboration partners for investigators
- Clinicians who are interested in working with trials are more easily recruited, which makes the field more attractive as a career path

Patients will be able to locate projects and voice their interest in participating

Conditions for value:

- Databases are up-to-date
- They are legal
- Good architecture based on actual needs
- Visibility and usability
- Good application for withdrawal of information
- Self-service

⁶⁹ For the importance of this, see Chalmers: <http://www.trialsjournal.com/content/1/1/3>

Appendix

List of interviewees:

Institution	Name	Institution	Name
GlaxoSmithKline (GSK) (Swe)	Cecilia Omning	Smerud Medical Research International AS (Nor)	Knut T. Smerud
Lund University Hospital (Swe)	Mats Jerkeman	Research Council of Norway (Nor)	Mari Kristine Nes and Henrietta Blankson
Lund University Hospital (Swe)	Ulf Malmqvist	Anonymous pharmaceutical company (Nor)	Anonymous
Medical Products Agency (Swe)	Ingrid Wallenbeck	Regional ethics committee (Nor)	Knut Reuter
LIF (Industry Organization for Researching Pharmaceutical Companies) (Swe)	Karin Eriksson	Nordic Bioscience A/S (Dan)	Bente Juel Friis
Active Biotech (Swe)	Tore Nederman	Danish Medicines Agency (Dan)	Karina Markersen
Novartis (Swe)	Torsten Rydman	The Danish Association of the Pharmaceutical Industry (Dan)	Jakob Bjerg Larsen
AstraZeneca (Swe)	Carin Fellenius	CCBR-Synarc A/S (Dan)	Jeppe Ragnar Andersen
Sahlgrenska University Hospital & Gothia Forum (Swe)	Kaj Stenlöf	Rigshospitalet – Copenhagen University Hospital (Dan)	Gedske Daugaard
Karolinska Institutet (Swe)	Peter Westerling	Pharma Industry Finland	Mia Bengtström
GlaxoSmithKline (GSK) (Nor)	Olav Flaten	Fimea (Finnish Medicines Agency) (Fin)	Esko Nuotto
Sanofi Aventis (Nor)	Gabriel Johannesen	HYKS-Instituutti (HUCS Institute Ltd) (Fin)	Seppo Pakkala
Ahus (Nor)	Torbjørn Omland	Turku University (Fin)	Mika Sheinin
Rikshospitalet University Hospital (Nor)	Erik Fosse	GSK (Fin)	Petteri Knudsen
HOD (Nor)	Maiken Engelstad	Novartis (Fin)	Maari Hillilä
Innovest (Nor)	Arne Godal and Tone Skår	Orion Pharma (Fin)	Taru Blom
Oslo Cancer Cluster (Nor)	Marthe Løberg and Jutta Heix	ENCODE (Ice)	Johanna F. Sigurjonsdottir and Birna Bjornsdottir
Ullevål University Hospital (Nor)	Tormod Guren	Landspítali University Hospital (Ice)	Pétur Gunnarsson

Reference group

The reference groups already existed at the time the Accenture team was brought into the study. Two workshops were held. See table 1 for a list of people who attended one or both of the workshops. One workshop was carried out 11 May 2010 in Stockholm, Sweden. The other one was held on 25 May 2010 in Copenhagen, Denmark.

An early draft of the report containing preliminary recommendations was discussed during a teleconference on 2 July. The discussion focused on determining which measures were most relevant and important to implement.

Name	Institution
Maiken Engelstad	Ministry of Health, Norway (1)
Marcus Zackrisson	Nordic Innovation Centre, Norway (2)
Johan Englund	Nordic Innovation Centre, Norway (1)
Stina Gestrelus	Sigridscience, Sweden (1)
Merja Kurkinen	FinnMedi Oy, Finland (2)
Christian Gluud	Copenhagen Trial Unit, DCRIN, Denmark (2)
Sigríður Ólafsdóttir	SOL consultancy, Board of NICE, Iceland (2)
Steinar Aamdal	Norwegian Radium Hospital, Norway (1)
Fredrik Melander	Nordic Council of Ministers, Sweden (2)
Hanna Johansson	Karolinska Trial Alliance, SweCRIN, Sweden (1)
Karolina Andersson	Nordic School of Public Health, Sweden (1)
Kirsti Kierulf	Accenture, Norway (1)
Ida Iren Eriksen	Accenture, Norway (2)

Table 7: List of workshop attendees, and number of workshops attended in parentheses

References

1. Peter Schwarz mfl, *Klinisk forskning i Danmark – tid til handling*, 2 December 2009.

2. The Norwegian Research Council, *Annual report 2009 Clinical research* (in Norwegian): <http://www.forskningsradet.no/servlet/Satellite?blobcol=urldata&blobheader=application%2Fpdf&blobheadername1=Content-Disposition%3A&blobheadervalue1=+attachment%3B+filename%3DAarsrapport2009.pdf&blobkey=id&blobtable=MungoBlobs&blobwhere=1253968210050&ssbinary=true>
3. The Norwegian Research Council, Foreløpig programplan Klinisk 2011–2015 (in Norwegian): <http://www.forskningsradet.no/servlet/Satellite?c=Page&cid=1228296189455&pagename=kliniskforskning%2FHovedsidemal>

Relevant Web sites:

All health projects supported by the European Commission. This gives access to projects' results which, together with search devices, will facilitate the identification of potential collaboration partners and between academia and industry in health research.

<http://www.healthcompetence.eu/converis/publicweb/area/1>

List of relevant links: <http://www.cvk.sum.dk/links.aspx>

The Danish Medicines agency: <http://www.dkma.dk/1024/visUKLSForside.asp?artikelID=728>