

**The establishment of a national clinical research infrastructure:**

**the Danish Clinical Research Consortium  
(DCRC)**

**- unlocking Denmark's clinical research potential**

The Danish Clinical Research Consortium (DCRC)

- unlocking Denmark's clinical research potential.

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DCRC

## List of abbreviations

<b>BBMRI</b>	Biobanking and Biomolecular Resources Research Infrastructure
<b>DCRC</b>	Danish Clinical Research Consortium
<b>DCRIN</b>	Danish Clinical Research Infrastructures Network
<b>EATRIS</b>	European Advanced Translational Research Infrastructure in Medicine
<b>ECRIN</b>	European Clinical Research Infrastructures Network
<b>ECRIN-I (RKP)</b>	European Clinical Research Infrastructures Network – reciprocal knowledge programme (phase I)
<b>ECRIN-II (TWG)</b>	European Clinical Research Infrastructures Network – transnational working groups (phase II)
<b>ECRIN-III (PPI)</b>	European Clinical Research Infrastructures Network – preparation phase for the infrastructure (phase III)
<b>EFGCP</b>	European Forum for Good Clinical Practice
<b>EFMRI-BMS</b>	European Strategy Forum on Research Infrastructures – Biological and Medical Sciences
<b>EORTC</b>	European Organisation for Research and Treatment of Cancer
<b>EU</b>	European Union
<b>FP-6</b>	EU framework program 6
<b>FP-7</b>	EU framework program 7
<b>GCP</b>	Good clinical practice
<b>GMP</b>	Good manufacturing practice
<b>IT</b>	Information Technology
<b>Lif</b>	Danish Association of the Pharmaceutical Industry
<b>NASTRA</b>	Det nationale strategiudvalg for sundhedsvidenskab
<b>Ph.D.</b>	Philosophiae Doctor (doctor of philosophy)
<b>SMEs</b>	Small to medium sized enterprises
<b>SOP</b>	Standard operating procedure
<b>TMF</b>	Telematikplattform

## English abstract

Denmark has a leading international position in clinical research. This is due to the high number of well-educated clinical researchers; the many resources put into clinical research from the industry among others; and the excellent opportunities presented by the unique Civil Registration System.

The national network of the three good clinical research practices (GCP) units were established in 1996. These GCP-units have been immensely successful in quality control (monitoring) of clinical trials on medicinal products. Following the GCP-units, a need for a more extensive national infrastructure for clinical research has been uncovered. Despite the fact that Danish researchers are very well-educated, they are facing burdensome administrative, logistical, financial, and regulatory barriers. These barriers hampers research and the limited knowledge-sharing across Denmark leave great resources unused. In 2008, investment in Danish clinical research dropped sharply. Denmark now is conducting fewer trials and employing fewer clinical research professionals. The general financial situation is also causing the pharmaceutical industry to close branches in Denmark, and withdrawing their clinical trial activity from Scandinavian countries altogether. As a consequence, stakeholders in research activities have expressed a wish for an improved research infrastructure.

At the international level, Denmark was, in 2004, one of the first four countries to join the Framework Programme funded European Clinical Research Infrastructures Network (ECRIN, [www.ecrin.org](http://www.ecrin.org)). ECRIN facilitates multinational clinical trials among its 14 member nations in Europe. By establishing a strong national infrastructure, Denmark will boost its attractiveness as a participating country in the multinational clinical trials facilitated by ECRIN, and reap the benefits of this valuable international partnership.

**The Danish Clinical Research Consortium** is a national clinical research infrastructure established in 2008. The DCRC is a not-for-profit organisation providing independent and comprehensive consultancy and services in clinical research – from phase I to phase IV trials, encompassing drug trials as well as trials involving other types of interventions, in all disease areas.

**The mission** of the DCRC is to improve the health of all patients and citizens by facilitating patient-centred transparent clinical intervention research of high quality according to the best international standards.

**The objectives** of the DCRC are:

- to be a 'one-stop-shop', a single contact point for researchers conducting (local, regional, national and multinational) clinical trials in Denmark;
- to be accessible for investigator-initiated clinical trials and clinical trials initiated by industry;
- to develop, implement and maintain national instruction documents – 'standard operating procedures' (SOPs) that will be free of charge and available for all;
- to strengthen the Danish research environment nationally and internationally with a commitment to international collaboration (i.e., ECRIN).

The DCRC objectives will be carried out by offering a number of **services** to researchers:

- support in trial design and collection of current evidence (e.g., systematic reviewing including meta-analyses and trial sequential analyses);
- support in interacting with ethics committees and regulatory authorities (e.g., Danish Medicines Agency);
- support in site selection, recruitment and investigation of healthy participants and patients;
- support in sample size estimation, interim analyses, and statistical analyses;
- support in drug dispensing;
- support in circulation and storage of blood and tissue samples;
- support in data management;
- support in adverse event reporting;
- support in medical reporting and archiving.

The DCRC shall function as a **one-stop-shop**. Researchers access the DCRC through a website and/or one of the institutions involved in the DCRC.

The DCRC will offer consultancy and services from concept, to conduct to completion of clinical trials according to Danish national law, the ethical principles in the Helsinki Declaration, the methodological guidelines of The Cochrane Collaboration, the good clinical research practice (GCP) guidelines, and the CONSORT statement.

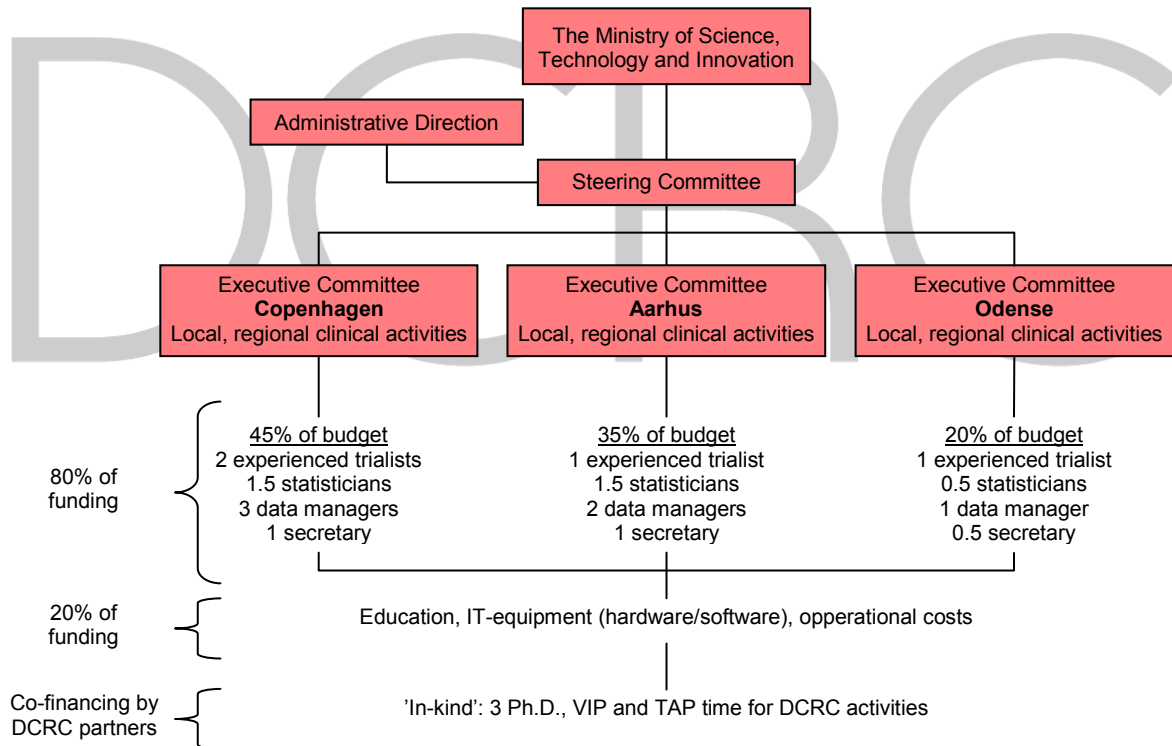
The DCRC standard operation procedures (SOPs) will reflect the above-mentioned high standards. All researchers conducting clinical trials in collaboration with the DCRC will be offered access to these quality assurance documents. The SOPs will not be imposed,

but will merely serve as a guideline for researchers. The high standards of the DCRC will secure an overall high level of quality for clinical trials in Denmark.

The DCRC will through its partnership with ECRIN (DCRIN – the Danish Clinical Research Infrastructures Network) offer a single contact point for this European network. In the DCRC institution in Copenhagen resides the national Network Coordinator as well as the European Correspondent of Denmark.

The DCRC will build on the existing partnering institutions and people by adding further resources and personnel to them. The DCRC organisational diagram is illustrated below

### DCRC organisational diagram





## Dansk resumé

Danmark er en af de førende nationer i verden, når det kommer til klinisk forskning. Dette skyldes et højt antal veluddannede kliniske forskere, de mange ressourcer investeret i kliniske forskning af bl.a. medicinalindustrien, og de fantastiske muligheder CPR-nummer systemet giver for forskning.

Det nationale netværk af de tre 'god klinisk forskningspraksis' (GCP) enheder blev etableret i 1996. GCP-enhederne har haft stor succes med kvalitetskontrol (monitorering) af kliniske forsøg på lægemidler. I kølvandet på dette netværk, er det blevet afdækket nye hidtil udækkede behov for en mere omfattende national infrastruktur for klinisk forskning. For selvom danske kliniske forskere er meget veluddannede, står de overfor stadig større administrative, logistiske, finansielle og regulatoriske barrierer. Disse barrierer vanskeliggør forskningen, og den begrænsede vidensdeling på tværs af landet medfører en begrænset ressourceudnyttelse. I 2008 faldt investeringerne i dansk klinisk forskning voldsomt. Der bliver nu gennemført færre kliniske forsøg, og der er ansat færre ansat i kliniske forskningsjob. Grundet den nuværende finansielle situation lukker medicinalindustrien ligeledes filialer i Danmark, samt trækker klinisk forskningsvirksomhed ud af de skandinaviske lande. Som en konsekvens heraf, har forskellige interessenter på området givet udtryk for et ønske om en forbedret forskningsinfrastruktur.

På det internationale plan, blev Danmark i 2004 som en et de første fire lande, medlem af det 'Framework Programme' finansierede 'European Clinical Research Infrastructures Network' (ECRIN, [www.ecrin.org](http://www.ecrin.org)). ECRIN faciliterer multinationale kliniske forsøg blandt de 14 europæiske medlemslande. Ved at etableringen af en stærk national infrastruktur, bliver Danmark attraktiv som deltagende land i de multinationale kliniske forsøg, der faciliteres af ECRIN, and dansk klinisk forskning kan høste frugterne af dette værdifulde internationale partnerskab.

**Danish Clinical Research Consortium** er en national infrastruktur for klinisk forskning, der blev etableret i 2008. DCRC er en 'not-for-profit' organisation, der tilbyder uafhængig og omfattende konsultation og støtte i klinisk forskning – fra fase I til fase IV forsøg, i såvel lægemiddelforsøg som forsøg med andre typer interventioner i alle sygdomme.

**DCRCs mission** er at forbedre sundheden for alle patienter og borgere ved at facilitere patientfokuseret gennemsigtig klinisk interventionsforskning af høj kvalitet i henhold til de bedste internationale standarder.

### DCRCs formål er:

- at fungere som en 'one-stop-shop', en enkelt indgang for forskere, der gennemfører (lokal, regional, national og multinational) klinisk forskning i Danmark;
- at stå til råde for såvel investigator-initierede forsøg som forsøg, der er initierede af industrien;
- at udvikle, implementere og vedligeholde nationale procedure dokumenter – 'standard operating procedures' (SOPs), der vil være gratis og tilgængelige for alle;
- at styrke det danske forskningsmiljø nationalt og internationalt med et forpligtende internationalt samarbejde (ECRIN).

DCRCs formål vil blive udført ved at tilbyde en række **services** til kliniske forskere:

- støtte i forsøgsdesign og indsamling af aktuel evidens på området (fx systematisk litteraturgennemgang inkl. metanalyse og 'trial sequential analyses');
- støtte til forsøgsanmeldelse mv. til etiske komitéer og regulatoriske myndigheder, fx Lægemiddelstyrelsen;
- støtte til udvælgelse af deltagende hospitalsafdelinger, samt til rekruttering og undersøgelse af raske borgere og patienter;
- støtte til materialestørrelsesberegning, interim analyser og statistiske analyser;
- støtte til distribution af forsøgslægemidler;
- støtte til opbevaring af blod- og vævsprøver;
- støtte til data management;
- støtte til rapportering af utilsigtede hændelser;
- støtte til rapportering af resultater samt arkivering.

DCRC vil fungere som en '**one-stop-shop**'. Forskere får adgang til DCRC gennem en hjemmeside og/eller ved en af de involverede institutioner i DCRC.

DCRC vil tilbyde konsultationer og services fra idé, til udførelse og afslutning af forsøg i henhold til dansk lovgivning, de etiske principper beskrevet i Helsinki Deklarationen, de metodiske retningslinier fra Cochrane Collaboration, de gode klinisk forskningspraksis (GCP) retningslinier og 'CONSORT statement'.

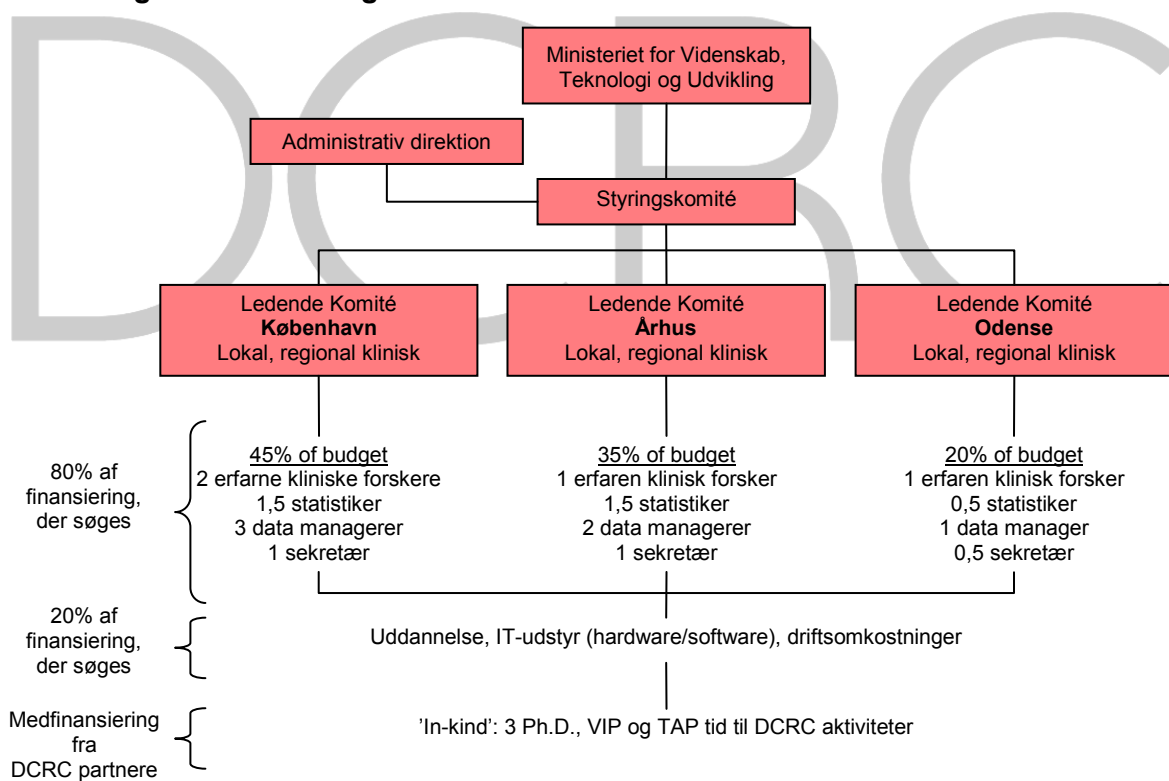
DCRC SOPs vil reflektere de ovennævnte høje standarder. Alle forskere der gennemfører kliniske forsøg i samarbejde med DCRC vil blive tilbudt adgang til disse kvalitetssikringsdokumenter. SOP'erne vil ikke blive pålagt nogen, men skal blot ses som

et tilbud og en guide for forskere. DCRCs høje standarder vil sikre en overordnet høj kvalitet af kliniske forsøg i Danmark.

DCRC vil gennem dets partnerskab med ECRIN (DCRIN – the Danish Clinical Research Infrastructures Network) tilbyde et enkelt kontaktpunkt til dette europæiske netværk af nationale infrastrukturer. I den københavnske DCRC institution findes den nationale netværkskoordinator samt den 'European Correspondent' fra Danmark.

DCRC vil bygge videre på de eksisterende partnerinstitutioner og personale ved at tilføje yderligere ressourcer og personale til dem. Det organisatoriske diagram for DCRC ses nedenfor.

### DCRC organisatorisk diagram



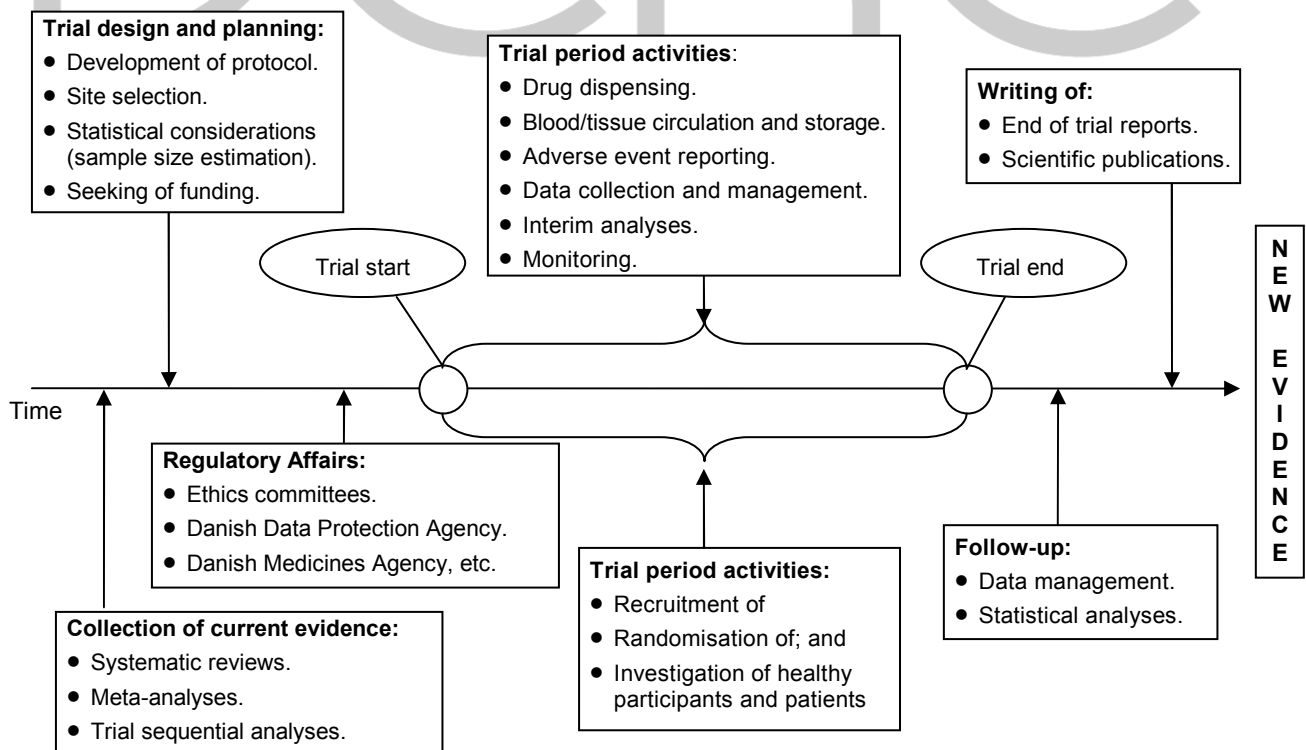
# 1. Evidence-based clinical practice

For patients and their relatives it is of utmost importance to get the best and safest treatment in case of illness. In order to give such treatment, doctors need to base their decision and choice of treatment on the best and most up-to-date evidence. On top of the evidence hierarchy are randomised clinical trials and systematic reviews of such trials.

A randomised clinical trial is a comparison between a new intervention and a placebo (non active intervention) or the best available treatment to date. Interventions can be a pharmaceutical drug, a surgical procedure, a medical device, or a psychological treatment, etc. The element of randomisation is a key element in a trial, as it makes the groups of trial participants even in terms of known and unknown prognostic factors and therefore comparable. The risks and benefits of all types of intervention should be assessed in a clinical trial before the treatment is introduced into the health-care system.

Clinical trials are complex, it takes a lot of planning and interaction with different regulatory authorities, experts and clinical trial sites in order to set up and execute a clinical trial. A simplified outline of a clinical trial, with its most fundamental steps, is figured below.

**Figure 1: Clinical trial outline**



## 2. Project description

### 2.1 Background for establishing the DCRC

Denmark has traditionally been conducting a high amount of clinical intervention research of a high quality. This is due to the high proportion of well-educated clinical researchers, our unique Civil Registration System that makes it easy to conduct and follow up both short and long time effects of interventions, and due to a successful pharmaceutical industry that have been funding and conducting a large amount of research in medicinal products. DCRC aims for Denmark to stay on the top, maximise resource efficiency, and continue to produce a large amount of high quality clinical research.

Denmark has shown itself capable of organising itself into infrastructures to meet the demands of clinical research, as seen by the establishment of the network of three good clinical research practice (GCP) units.<sup>2,3</sup> These units have been very successful in conducting quality control, i.e., monitoring of clinical trials on medicinal products. However, in doing so, the units have revealed a further need for national collaboration in clinical research. As the law is getting more complex there is a need for a national collaboration that involves the conduct of clinical research on all types of interventions. Currently, other clinical trial units, clinical research centres and centres of competence remain working alone, according to their own traditions, procedures, and usual practice. This means that resources are left unused and some efforts are doubled. When combining and uniforming these efforts, the output will be greater than the sum of the parts. This is what the DCRC will achieve.

National networks work.<sup>6</sup> National networks benefit the clinical investigators by offering a comprehensive set of services through a single contact point, benefit patients by enabling them to access clinical research projects which affects their health-care, and benefits the clinical research professionals through knowledge sharing and competence strengthening.

Traditionally the pharmaceutical industry has contributed greatly to clinical research on medicinal products in Denmark. However, investment in Danish clinical research is currently dropping sharply. A body representing the Danish pharmaceutical industry (Lif) have published data showing a sharp drop in investment and employment in the clinical research sector in 2008.<sup>4</sup> Denmark is conducting fewer trials and employing fewer clinical research professionals than ever before. To re-boost Danish clinical research Denmark needs the right investment. The IRIS Groups suggests a biotech cluster in the Capital Region.<sup>5</sup> The partners behind the DCRC supports this idea, however, there is no doubt that a *national* clinical research infrastructure is needed to conduct cost-efficient research, releasing the latent expertise.

Public investment in biomedical research leads to a perpetual return on investment of about 40% per year<sup>1</sup>. Three mechanisms account for this outstanding value, and they are particularly relevant to clinical research: development of innovative health products, healthcare cost containment, and a healthy more productive population.

- The clinical proof of concept is a prerequisite for the transfer of discovery and preventive, diagnostic or therapeutic applications (medicines, medical devices, biotherapy, vaccines, diagnostics), generating value and wealth for the public and private bodies who developed the concept when reaching the market.
- Investing in clinical trials represents a major element in the cost containment strategy for national health services, allowing the assessment of the real advantage of healthcare interventions, and to set evidence-based standards of care. More generally evidence-based medicine and assessment of diagnostic, preventative, and treatment strategies through clinical trials ensures optimisation of healthcare strategies, therefore contributes to the country's health and wealth.
- Finally, improved productivity of a healthy population is also a strong determinant of economic growth.

Denmark needs a national infrastructure, the DCRC, if we are going to participate and benefit from the opportunities arising from European clinical research in the European Research Area. The DCRC follows the European Union's (EU) definition of 'Research Infrastructure': it will centre the competences which provides a service for the wider research community based on assembly of techniques and 'know how'.<sup>7</sup>

Participation in DCRC will provide the capacity to easily initiate local, regional and national clinical research projects, allowing the conduct of large-scale clinical trials, genetic studies, or studies on rare diseases and personalised treatments. It also allows easy collaboration across Denmark, initiated in all regions of Denmark. This capacity to initiate, or to collaborate in local, regional and national trials is critical to the number of Danish trials, the quality of these trials, and their ability to be published in the best medical journals.

The DCRC will develop, implement and maintain national procedure documents – standard operating procedures (SOPs). The SOPs will contain and reflect up-to-date and accurate information on the Danish law, the Declaration of Helsinki, guidelines of The Cochrane Collaboration and good clinical research practice (GCP) guidelines. The SOPs will be available to all researchers. This harmonised approach will lead to resource efficiency and ultimately even better and safer randomised clinical trials in Denmark.

The DCRC will mean greater output of highest quality clinical research, leading to evidence-based health care in Denmark.

## **2.2 Added value of the DCRC**

The DCRC will unlock the latent potential in Denmark and make the best use of existing expertise. Through capacity building, the DCRC will help retain those experts in Denmark, through knowledge sharing and career development, thus quality assuring and protecting future Danish research.

By linking the clinical research centres, clinical trial units, and centres of competence in Denmark, the DCRC will improve access to more clinical trial participants. Thus, facilitating for clinical investigators to reach the required population size of a given clinical trial, and meeting the expectations of Danish patients of having the opportunity to take an active part in the research which affects them.

The DCRC will enable necessary multi-site clinical trials in Denmark at the local, regional, national, and international level. National clinical trials involving a broad population are more relevant in terms of benefits, harms and generalisability, and better in order to inform national health-care policies and guidelines.

The DCRC will co-develop and co-maintain standardised procedural documents (standard operating procedures (SOPs)), which will mean no more duplication of efforts, and efficient and cost-effective clinical trials with a uniformity of quality.

There are six main components which make it timely and relevant to establish a single major national clinical research infrastructure – the DCRC:

1. Multi-site, multi-expert, and multi-participant.
2. Cost effective clinical research in Denmark.
3. The range of legislation and regulatory requirements in clinical research in Denmark.
4. The golden opportunities presented by ECRIN.
5. The establishment and experience of DCRIN.
6. The poor quality of most clinical research.

### **2.2.1 Multi-site, multi-expert, and multi-participant**

Clinical research from ‘bench to bedside’ is a multi-step process. The expertise, resources, and number of trial participants involved are multiple. The range of professionals encompasses:

- Health: research nurses, pharmacists, clinical investigators including, physicians, dentists, physiotherapists, etc.
- Science: methodologists, pharmacologists, cell biologist, bio-medics, biochemists.
- Statistics: data analysts, biostatisticians.
- Information technology (IT): data managers, programmers.
- Management: project managers, coordinators, financial managers.

Getting reliable results from clinical trials means enrolling sufficient numbers of trial participants, i.e., getting the right population size. The best way to do this is through multi-site trials. Furthermore, for rare diseases this is the only way to conduct research. Results from national, multi-site clinical trials are more reliable and generalisable and can be used directly to develop Danish health-care guidelines. Multi-site, multi-expert and multi-participant clinical research can only be conducted when the latent potential throughout Denmark is unlocked in a formal national clinical research network.

### **2.2.2. Cost effective clinical research in Denmark**

The DCRC will allow the best use of expertise in Denmark. Linking expertise, knowledge and experience share and spread these skills, making best use of the investment in Danish researchers, best use of these skills, and retains these skills in Denmark. The DCRC will allow clinical trials to be conducted in Denmark with improved efficiency, reducing duplication of efforts, and saving money. A further cost benefit is that of health-care research itself. National health-care policy and guidelines needs to be based on the best available evidence from national or multinational clinical research. Current use of ineffective health-care interventions is expensive, wasteful, and unethical.

### **2.2.3. The range of legislation and regulatory requirements in clinical research**

It is right and necessary that clinical research involving humans is highly regulated. In Denmark regulatory authorities must approve of clinical research proposals before they are undertaken. However, for the clinical investigator this represents a large administrative burden. Promotion of well-designed, well-planned, and well-resourced clinical research projects, calls for a harmonised, efficient, professional and accessible national source of

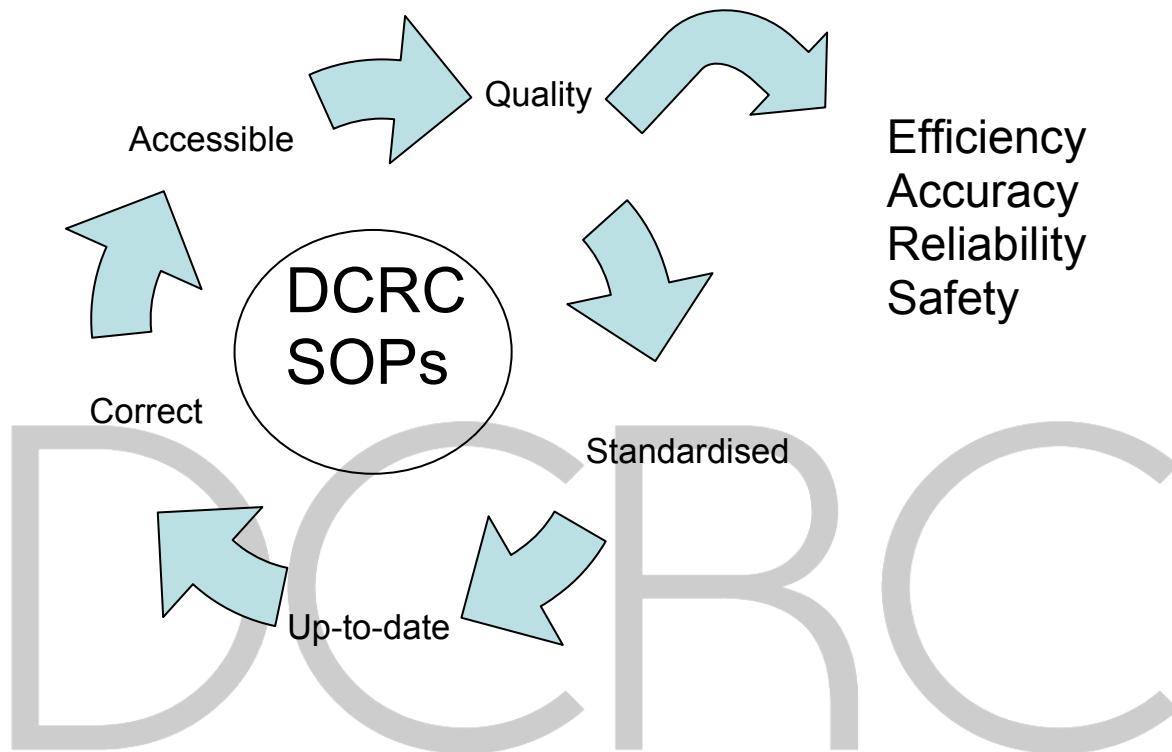


support for clinical investigators. Lack of national clinical research infrastructures has been identified as a principle bottleneck for conducting research in European countries.<sup>8</sup>

The DCRC infrastructure shall be based on competence centres able to provide support through a consistent set of services for clinical trialists and sponsors of trials and will harmonise the way for national clinical trials to be performed (e.g., by using common quality assurance documents such as standard operating procedures (SOPs)). Support to interaction with regulatory affairs is one of these services, which are a time consuming process and an essential part of conducting good quality, regulatory coherent, and transparent clinical research. This encompasses regulatory advice and approval, good manufacturing of biotherapy products (GMP); quality assurance; trial monitoring (GCP); and adverse event reporting.

DCRC

**Figure 2: DCRC SOPs**



A Danish clinical research infrastructure will allow a more harmonised, efficient and accurate conduct of both local, regional, and national Danish clinical trials as well as allow participation and benefiting from multinational trials in Europe, taking advantage of the EU population and competencies. The DCRC will also facilitate to make Denmark a country in strong demand to collaborate with.

#### **2.2.4. The opportunities presented by ECRIN**

The European Clinical Research Infrastructures Network (ECRIN, [www.ecrin.org](http://www.ecrin.org)) is, until 2011, funded by the 7th Framework Programme of the European Commission and is active in supporting sponsors and investigators in its first pilot pan-European clinical trials. Trials can benefit from ECRIN through access to patients, expertise, and services in the 13 ECRIN countries. It cannot be over exaggerated how invaluable such access is to clinical research investigators and sponsors who otherwise face administrative, logistical, political, financial, and regulatory barriers alone.

Denmark was the fourth Member State to join ECRIN and has been a key contributing partner in setting up this ambitious European infrastructure. It is now for Denmark to reap the benefits. Denmark has been able to participate actively in ECRIN due to a small team of dedicated professionals. Individuals have contributed their expertise and knowledge of the Danish regulatory requirements to the working groups of ECRIN from 2004 until today. These individuals, as well as a national European Correspondent (funded by the ECRIN project), and the Danish National Coordinator, make up Danish Clinical Research Infrastructures Network (DCRIN).

Participation in ECRIN means that Denmark can initiate multinational projects, and also participate in projects initiated by other countries. The first clinical trial to be accepted from the ECRIN Scientific Board was a Danish trial, the 6S trial. This trial has now recruited 30 participants. Of the 12 additional clinical research projects currently positively evaluated by the ECRIN Scientific Board, 5 include Denmark as a participating country. Denmark must secure continued participation in ECRIN in order to ensure participation in these and in future clinical research projects.

Such participation can be secured with 2 structures in place:

- a coordinated, functioning, national network of clinical research centres, clinical trial units, centres of competences, hospitals, and GCP units in Denmark; this is what the DCRC can provide.
- a dedicated connection point to ECRIN, a Danish European Correspondent and a Danish National Coordinator; this is what DCRIN can provide.

Participating in ECRIN provides Denmark the capacity to easily initiate in multinational clinical research projects, strengthening competitiveness and allowing the conduct of large-scale clinical trials, genetic studies, or studies on rare diseases and personalised treatments. It also allows easy collaboration in clinical trials initiated in other countries. This capacity to initiate, or to collaborate in multinational trials is critical to access high impact factor medical journals.

Now ECRIN is in its most active phase; ECRIN-supported clinical research projects are underway and ECRIN will expand to include other European countries. Four new countries are in the process of joining, and five other countries have expressed a wish to join. Denmark needs to secure its position within ECRIN and commit itself as a partner.

#### **2.2.5. The establishment and experience of DCRIN**

The Danish Clinical Research Infrastructures Network (DCRIN) has been a full national partner of ECRIN since 2004. DCRIN is the knowledge sharing unit, the 'knowledge link', between Danish clinical research and European clinical research (ECRIN). The focus is on multinational collaboration and conduct of and quality development of multinational clinical research from which experience can develop and benefit the Danish patients and citizens.

The work of DCRIN has resulted in the first, and as of today, the only clinical trial accepted by ECRIN's independent and international Scientific Board to be a Danish sponsored trial.

DCRIN is without any monetary founding, all initiatives are pro bono, and this is a threat to the collective of expertise as it is fragmented and dependent on availability. This makes us confident that that Danish clinical research needs a substantiated infrastructure through establishing the DCRC – a single national clinical research consortium. The time is ripe due to:

- lack of sufficient funding for clinical research;
- the advanced stage of ECRIN, enabling Denmark to gain from this international collaboration; and
- the evident synergistic effects that will be obtained through increased Danish clinical research collaboration and knowledge sharing.

The DCRC can significantly increase the speed and quality of local, regional, and national Danish clinical research as well as turn the DCRIN into a partner in strong demand for multinational clinical trials for the benefit of citizens and patients in Denmark as well as abroad.

The loose structure of DCRIN allows its participants to participate no more than time and monetary potential allow. Presently DCRIN consists of a number of Danish clinical research experts and affiliated centres and clinical trial units, i.e.:

- Ethics: Mette Rasmussen, Vibeke Graff, Maj Vigh (the Danish National Committee on Biomedical Research Ethics), Ebbe Eldrup (Regional Ethics Committee of the Capital Region).
- Competent authorities: Steffen Tirstup (Institute for Rational Pharmacotherapy, Danish Medicines Agency).

- Adverse event reporting: Charlotte Calov (GCP unit at Odense University Hospital), Ove Andersen (The Research Unit, Hvidovre Hospital, Copenhagen University Hospital,) Jens Sandahl Christiansen (Department of Endocrinology, Aarhus University Hospital), Lina Seam Støy (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital (coordinating DCRIN centre)).
- Data management: Nader Salas (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital (coordinating DCRIN centre)), Jens Lauritsen (Orthopedic Department, Odense University, Hospital and Institute of Public Health, Dept. of biostatistics, Southern Denmark University, Odense).
- Education: Annette Jørgensen (GCP unit at Aarhus University Hospital), Maria Skoog (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital (coordinating DCRIN centre)).
- Finance: Jane Lindschou Hansen (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital (coordinating DCRIN centre)).
- Monitoring: Karin Friis Bach (GCP Unit of Copenhagen University Hospital), Brigitte Schlemmer (GCP Unit of Copenhagen University Hospital).
- Danish European Correspondent: Kate Whitfield (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital (coordinating DCRIN centre)).
- Danish National Coordinator: Christian Gluud (Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital (coordinating DCRIN centre)).

DCRIN is an expanding structure and will involve more national experts and clinical research centres, clinical trial units, and centres of competences as more Danish expertise is sought in the multinational collaboration within ECRIN. This expansion is facilitated by, and dependent on, the substantiation of a national infrastructure, the DCRC.

### **2.2.6. The poor quality of most clinical research**

There is an urgent need for improvement of the quality of clinical research - in both Denmark and the rest of the world:

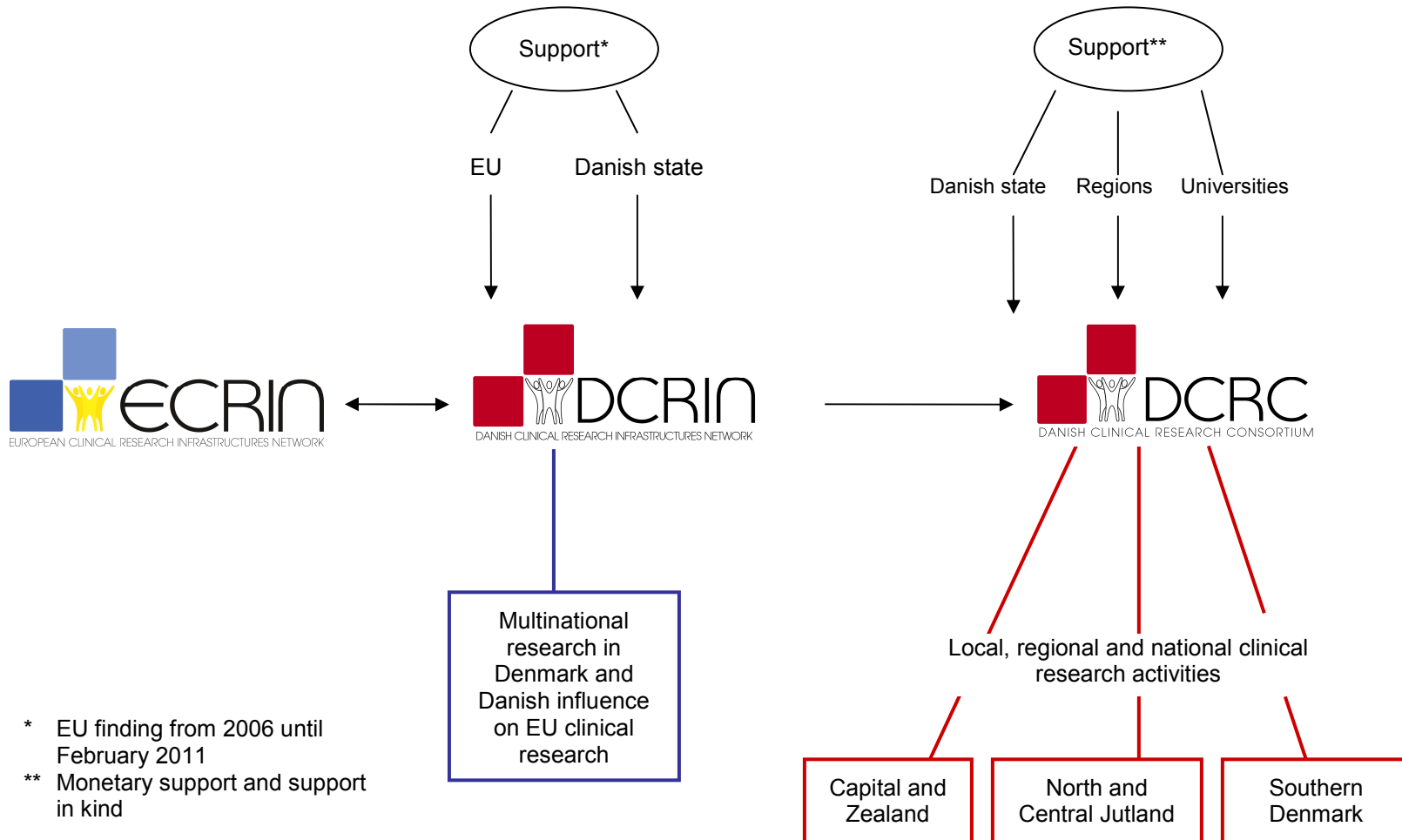
- Most clinical research is conducted with methodologies that are insufficient or unclear and thereby increasing the risks for systematic errors ('bias').
- Most clinical research is conducted with too small participant groups increasing the risks for random errors ('play of chance').
- Most clinical research is conducted with 'design errors' (the wrong design to answer the research question).

These error mechanisms threaten the validity and reliability of clinical research results. Without internal validity it becomes irrelevant to consider the external validity of the results that is the generalising to the wider patient population. This leaves most current clinical research results wide open to critique.<sup>9-20</sup>

To improve the quality of clinical research we need to minimise the risk of the three types of error listed above. We need to adopt risk-based monitoring strategies that encompass all types of clinical trial throughout all the stages of the trial. Danish clinical research must absolutely meet the standards of the World Health Organisation and the World Medical Association's Declaration of Helsinki,<sup>21</sup> which states that clinical investigators must register the trial protocol before recruiting the first trial participants and must report the findings of their research regardless of whether the results were positive, negative, or neutral.

These vital quality improvements can be best achieved through a systematic approach. The DCRC will realise these improvements in quality across Denmark.

**Figure 3: ECRIN, DCRIN and DCRC**



## 2.3 Description of the DCRC

The DCRC will be a virtual Danish clinical research infrastructure building upon experiences obtained at the three University Hospitals in Denmark, the GCP units affiliated with the University Hospitals as well as other clinical research centres and centres of competences.

The DCRC will have a website to display the set of services; collaborators and contacts; organisational structure; missions; status reports of progress in the DCRC, all to maximise the utility, transparency, and effectiveness of the DCRC.

The DCRC will provide harmonised, 'one-stop shop' services to Danish investigators and sponsors in local, regional, and national clinical trials on all types of interventions as well as multinational clinical trials through:

- support in trial design and collection of current evidence (e.g., systematic reviewing including meta-analyses and trial sequential analyses);
- support in recruitment and investigation of healthy participants and patients across regions in Denmark;
- support to the interaction with ethics committees;
- support to the interaction with competent authorities and other regulatory authorities like the Danish Data Protection Agency;
- support to drug dispensing;
- support to circulation and storage of blood and tissue samples;
- support in data management;
- support in adverse event reporting;
- support in sample size estimation, interim analyses, and statistical analyses;

The DCRC shall do so following common national standard operating procedures (SOPs).

The set of services provided by the DCRC are particularly relevant for research on rare diseases, for academic clinical researchers, and for clinical trials initiated by biotechnology biotechnology small to medium sized enterprises (SMEs), who often lack the capacity to conduct clinical trials.

The use of the DCRC is not obligatory, and it is the investigator or the sponsor who decides whether or not to utilise the consultancy and services that the DCRC offers.



## **2.4 Access to the DCRC services**

Users of the DCRC will be investigators and sponsors in both the academic sector and the industry sector. The DCRC will be an easily accessible infrastructure, with an informative website and several contact points in the working parties for the set of services.

The consultancy and services offered by the DCRC can be free of charge for the majority of the smaller clinical projects that are initiated in Denmark each year (e.g., requiring less than 50 hours of services). This can encompass: protocol development, sample size estimation, basic statistical analyses, cost assessment, regulatory affairs, quality assurance, trial conduct, and data management. Based on the cost assessment, the investigators and sponsors are then requested to raise the necessary money (through sponsorship from public and private funds and from the industry) for investment in the individual clinical research projects.

## **2.5 The mission and objectives of the DCRC**

The mission of the DCRC is to:

- Provide not-for-profit, independent, and comprehensive clinical research consultancy and services across Denmark - from phase I to phase IV encompassing drug trials and trials involving other types of interventions (preventive measures, diagnostic methods,<sup>22</sup> surgery, physiotherapy, etc.).
- Prioritise high-quality and transparent clinical research, focusing on participant safety and health-society benefits.
- Promote a harmonised and improved Danish clinical research environment, in order to improve the health of patients and citizens.

The objectives of the DCRC are to promote the following:

- The DCRC shall conduct all trials after the best recommendations and guidelines from international bodies, like the Declaration of Helsinki,<sup>21</sup> the Cochrane Collaboration<sup>23</sup> and the CONSORT Group,<sup>24</sup> and according to Danish laws and regulations. Only clinical trials with a high relevance to Danish citizens and patients shall be conducted in Denmark.

- The DCRC will develop and maintain a set of common standard operating procedures (SOPs) for conductance of clinical research within the DCRC. The SOPs will reflect Danish national law, guidelines from regulatory authorities, good clinical practice guidelines, and the ethical principles described in the Declaration of Helsinki.<sup>21</sup> The SOPs are a service that sponsors and investigators are encouraged to use to the extent they are relevant to their clinical trial.
- The DCRC shall train students, Ph.D. students, and post-docs or post-doctorals in clinical research, e.g., by arranging and hosting annual workshops and 'on demand'. This will spread the 'know-how' and the standard operating procedures (SOPs) across Denmark and contribute to the break down of translational blocks from basic research into clinical practice.
- The DCRC will only invest and collaborate in research projects leading to improved methods for diagnosis, prevention, and treatment.
- An investment in the DCRC is likely to result in a number of well-conducted Danish clinical trials, which otherwise would not be feasible, resulting from the collected experiences on the activities in the DCRC. Furthermore, once the DCRC is established and operational, the investment offers cost-effective solutions poising Denmark for the future of clinical research.
- The DCRC will measure the improvement in quality and successful conducts of Danish clinical trials by: assessing the number of Danish clinical trials registered on the [www.clinicaltrials.gov](http://www.clinicaltrials.gov), number of publications of Danish clinical trials according to journal impact factor, and according to the quality standards defined by Cochrane Hepato-Biliary Group:<sup>25</sup> sequence generation; allocation concealment; blinding; incomplete outcome data; selective outcome reporting; baseline imbalance; early stopping bias; and vested interest bias.
- The DCRC research activities will all have direct positive consequences for Danish patients and relatives to patients. Furthermore, by improving the clinical research infrastructure in Denmark, the Danish drug and device industry will directly benefit. This will increase Denmark's competitiveness on the international markets, for the benefit of all citizens.

## 2.6 The implementation of the DCRC

During the four years 2010 until 2014, the DCRC infrastructure will develop within three phases: 1) preparation; 2) construction; and 3) operation. The preparatory phase of the

infrastructure will transform the network, sharing tools and practice, into an operating Danish virtual institution with financial sustainability, providing high-quality services, and prepare the construction of data centres and statistical analyses centres.

The preparatory phase will be progressive, as the infrastructure will be able to provide increasingly integrated consultancy and support to clinical trials during this period, resulting in a gradual transition from the preparatory to the operation phase. As a result, the preparation and construct will cover:

- Selection and securing of a *legal status* allowing contracts with sponsors, efficient financial management within the network, extension to new partners, and adaptation of the *governance* structure allowing efficient decision-making regarding the access of users to the infrastructure, and the strategic co-operation with ECRIN.
- Agreement on a *financial plan* leading to a long-term sustainability. This will require surveys on construction and operation costs and revenues of clinical research infrastructures. Funding of the DCRC should be based on the support from this call, from partners, investment of industry partners, self-financing, EU funding to the operation of integrated infrastructures, and on the support for individual clinical research projects.
- Survey on needs and existing resources in terms of *good manufacturing practice (GMP) facilities* (biopharmaceuticals, biotherapy) performed jointly with the EATRIS (European Advanced Translational Research Infrastructure in Medicine) project through ECRIN, then design and planning, in co-ordination with EATRIS, of the construction of such GMP facilities.
- An *education programme* to train the personnel within the DCRC the requirements of and to conduct clinical trials, with the support of ECRIN train-the-trainers summer schools and of the ECRIN e-learning tools.
- The *extension* to other national clinical research partners (CTUs, CRCs, centres of competences and patient organisations) will be sought, and the set-up of an extensive, robust DCRC will be stimulated.
- A *capacity building* programme will help strengthening the capacity of national co-ordination to perform sponsor's tasks in national and EU-wide trials.
- A *quality assurance* system will play a critical role in the project. Standard operating procedures (SOPs) and guidelines for local, regional, and national as well as multinational clinical trials will be constantly updated through the activity of the corresponding working groups (ethics, regulation, adverse event reporting, monitoring), some of these activities being shared with ECRIN in other European countries as well

as the BBMRI (Biobanking and Biomolecular Resources Research Infrastructure) and the EATRIS (European Advanced Translational Research Infrastructure in Medicine) projects. In addition, the quality assurance system will be upgraded, as national centres will be demanded to fulfil quality assurance requirements to ensure the high quality of services.

- Various tools will promote *internal communication* within the network, and *external communication* with users of the infrastructure, with patients, and with citizens. The DCRC will have an active website reporting on activities. A major event will be the annual ECRIN meeting where we will organise the celebration of the International Clinical Trials' Day ([www.ecrin.org](http://www.ecrin.org)).
- Specifications on the requirements for the DCRC *data centres* will be prepared, then implemented through a first call for accreditation of a prototype data centre. The lack of a unified data management system (or systems) that is compliant to the GCP requirements hampers the quality assurance of clinical trials. Data management systems shall be put in operation that will allow tracking of all data actions, secure validity of data, and ease trial monitoring. Most trial monitoring can be conducted centrally in case no major problems are detected.
- Support to *pilot projects* corresponding to various types of clinical studies will be necessary to assess the validity of the services, such as sample size estimations, protocol quality assurance, systematic reviewing with meta-analyses of the potential experimental and control interventions, as well as statistical analyses.
- Also, support to *pilot projects* corresponding to various types of clinical studies will be necessary to assess the validity of the overall organisation and of the quality assurance system, and to refine the cost evaluation.

At the end of 2012 the DCRC is in its construction phase, and from 2013 the DCRC is expected to be operative.

## **2.7 European Clinical Research Infrastructures Network (ECRIN) and Danish Clinical Research Infrastructures Network (DCRIN)**

The infrastructure of the DCRC will through the 'knowledge link' DCRIN become closely involved in research and gain experiences from the research community in Europe (ECRIN, [www.ecrin.org](http://www.ecrin.org)). ECRIN was established as European infrastructure to benefit patients and citizens by:

- facilitating multinational clinical research across Europe with a view to harmonising EU clinical research;
- securing that clinical research conducted through ECRIN is of high quality, independent, and fully transparent.

ECRIN is presently represented by national networks in Austria, Finland, France, Germany, Hungary, Ireland, Italy, Spain, Sweden, Switzerland, the United Kingdom, and Denmark, with the participation of the European Organisation for Research and Treatment of Cancer (EORTC) data centre, and the contribution as associated participants of the European Forum for Good Clinical Practice (EFGCP) and of the German Telematikplattform (TMF). This integrated clinical research infrastructure, unique in Europe, will provide support to any type of multinational clinical research, and in any medical field.

The EU Framework Programme (FP) 6-funded **ECRIN-I** during 2004-2006 (ECRIN-RKP) helped identify bottlenecks to multinational co-operation, highlighting the poor capacity of public institutions to act as a sponsor in national and multinational studies.<sup>26,27</sup>

The FP6-funded **ECRIN-II** during 2006-2008 (ECRIN-TWG) has focused on trans-national working groups in charge of defining procedures and guidelines for multinational trials in Europe. These activities ended in 2008 with the production of a large number of quality assurance documents describing all details of conducting clinical trials in Europe. The DCRC will be able to benefit directly from these quality assurance documents regarding the multinational clinical trials the DCRC becomes involved in. The quality assurance documents have all been developed by international experts on the respective issues (interaction with ethics committees; interaction with competent authorities; drug dispensing; circulation and storage of blood and tissue samples; data management; adverse event reporting; interim analyses and statistical analyses; recruitment and investigation of healthy participants and patients; clinical trial monitoring).

The FP7-funded **ECRIN-III** takes place during 2008-2011 (ECRIN-PPI). This preparatory phase for the construction and operation of an infrastructure for EU-wide clinical trials and biotherapy, based on the integration of competence centres coupled to data centres and biotherapy facilities, is taking place. With the local contribution of ECRIN correspondents embedded in each national network, the ECRIN will provide integrated, 'one-stop shop' services to investigators and sponsors in multinational studies. In addition, consulting will be provided to investigators and sponsors during protocol development (including regulations and ethical considerations, centre selection, cost evaluation, funding opportunities, insurance). Close collaboration will be established with the other EFSRI-

BMS FP7 (European Strategy Forum on Research Infrastructures – Biological and Medical Sciences) infrastructure projects, particularly the BBMRI and EATRIS projects in order to develop synergies and avoid duplication.

It is through linking with these activities that the DCRC can participate in multinational clinical trials. Furthermore, the DCRC can implement the experiences it obtains through the collaboration within ECRIN for the benefit of local, regional, and national Danish clinical trials.

### **2.7.1 Added value of partnership with ECRIN**

Participating in ECRIN gives added value for Denmark through:

- Facilitating the initiation of, and the participation in multinational clinical research projects. This capacity to initiate, or to collaborate in multinational trials is critical to access high impact factor medical journals.
- Access to multinational funding of clinical research projects, particularly through Innovative Medicines Initiative (IMI) and FP7 applications where cooperative clinical research now receives substantial support.
- Structuring and strengthening the capacity of DCRC as the Danish clinical research infrastructure in line with the EU standards, tools, making use of procedures developed by ECRIN, and to increase harmonisation.
- Increasing the attractiveness of Denmark for multinational industry-sponsored as well as investigator-initiated projects, and strengthening national competitiveness in clinical science.
- Training of the clinical researchers in Denmark, developing and providing access for all the national clinical research professionals to education programmes in multinational clinical research. Denmark will be able to participate in the IMI training platform, (EMTrain, coordinated by ECRIN), as well as in the portfolio of structuring projects ECRIN is involving in.
- Initiating and participating in high quality multinational clinical research projects in all fields initiated by other countries.

The DCRC will greatly benefit from the experiences of ECRIN. The individuals, as well as the ECRIN European Correspondent and the Danish National Coordinator have gained a lot of experience in working within and building up a clinical research infrastructure that transcends geographical boundaries. This wealth of good ideas for infrastructure

management and expansion as well as developing quality assurance systems will poise the DCRC to function effectively from the outset. It is essential for Denmark to remain a partner of ECRIN. Connection of Denmark to ECRIN is possible through DCRIN.

### 2.7.2 ECRIN's mission

ECRIN's mission consists of facilitating multinational clinical research in the European Union, taking advantage of its population and of its high health-care standards, and improving quality and transparency for the benefit of patients, citizens, and health-care systems. This multinational and distributed infrastructure makes the European Union an integrated area for clinical research, unlocking latent scientific potential, spreading best practices and highest quality standards, thus fostering the attractiveness of Europe for clinical research and increasing the competitiveness of European biomedical research for academic institutions, SMEs, and health industry. To achieve this goal:

- The European Clinical Research Infrastructures Network (ECRIN; [www.ecrin.org](http://www.ecrin.org)) is a European research infrastructure that benefits the health of patients and citizens across the world.
- ECRIN supports, services, coordinates, and manages high-quality, independent, and fully transparent multinational clinical research. ECRIN strives for harmonisation of European clinical research.
- Through ECRIN's facilitation of clinical research we contribute to the 'European Research Area', the 'society of knowledge', and the European competitiveness.

### **3. Plan for organisational structure of the DCRC**

#### **3.1 Partners of the DCRC**

- Institute of Clinical Medicine, Faculty of Health Sciences, Aarhus University.
- Institute of Clinical Research, University of Southern Denmark.
- Department of Human Nutrition, Faculty of Life Sciences, University of Copenhagen.
- Department of Surgery and Internal Medicine, Faculty of Health Sciences, University of Copenhagen.
- Faculty of Pharmaceutical Sciences, University of Copenhagen.
- BioPeople, Danish innovationnetwork for biotech, medtech and pharma.
- Copenhagen Trial Unit, Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital.

The centres involved in the DCRC already have built up large experience in clinical research and the DCRC will extend to participation of other Danish clinical researchers and research groups. Also the involvement and collaboration with participant organisations will actively be sought.

#### **3.2 Leadership of the DCRC**

The DCRC infrastructure shall be directed by a Steering Group, in which all involved institutions and research groups are entitled to have one seat. The Steering Group shall:

- meet twice a year face to face;
- have bi-monthly telephone conferences, in which the progress of the work is monitored;
- be directed during the five-year implementation phase by three co-chairs, Jens Sandahl Christiansen from Aarhus, Kim Brixen from Odense and Christian Gluud from Copenhagen. Thereafter, the three chairs shall be elected among members of the Steering Group.

In order to secure a smooth running during the implementation phase as well as to secure the sustainability of the DCRC after 2013 an administrative direction will be established with senior representatives from the three executive committees of the DCRC, the three Danish Regions, and the three universities.



In order to integrate local activities, three Executive Committees will be established in the regions of Copenhagen, Aarhus, and Odense.

### **3.3 Legal status of the DCRC**

The legal status of the DCRC will be determined after consultation with lawyers from the Danish regions, University Hospitals, and Universities. ECRIN will apply for the status European Research Infrastructures Consortium (ERIC) in the year 2010.

Selection of a legal status shall allow for contracts with sponsors, efficient financial management within the network, and extension to new partners. Further, adaptation of the governance structure shall allow efficient decision-making regarding the access of users to the infrastructure, the financial plan for the construction and operation phase, and the strategic co-operation with ECRIN.

### **3.4 The DCRC working parties**

The steering group of the DCRC shall establish nine working parties, each headed by a chairperson, dealing with each of the services the DCRC shall provide:

- trial design and collection of current evidence (e.g. systematic reviewing including meta-analyses and trial sequential analyses);
- interaction with ethics committees;
- interaction with competent authorities;
- drug dispensing;
- circulation and storage of blood and tissue samples;
- data management;
- adverse event reporting;
- sample size estimation, interim analyses, and statistical analyses;
- site selection and recruitment of healthy participants and patients;

Each of these working parties will consist of 3-9 persons with experience and expertise in the topic and will assure development and maintenance of national common standard

operating procedures (SOPs) for the conduct of clinical trial activities. These SOPs will be in English to strengthen the transparency and increase the availability of the Danish clinical research method.

### **3.6 The physical placement of the DCRC**

The DCRC will not need extra buildings, but the additional staff will be placed in the premises of the partners of the DCRC.

### **3.7 Financial plan**

#### **3.7.1 Financial plan for DCRC**

It is requested that the Ministry of Science Technology and Innovation, the Universities and the University Hospitals (Danish Regions) will provide funding for the DCRC. The total expenses/budget are expected to be about DKK 11 million annually during the 5 year implementation period, where DKK 10 million shall be provided as funding, and DKK 4 million shall be financed by the DCRC partners themselves.

The investment in the DCRC provided is going to be distributed with 45% for Copenhagen, 35% for Aarhus, and 20% for Odense. This is based on a rough assessment of the present day clinical research activities in the three regions as well as the national distribution of research projects approved by the regional Ethics Committees in 2007 and 2008.

The DCRC investment will be divided in 20% for education, office equipment, computer hardware, computer software, education and training and 80% for salaries. Accordingly, the research groups in Copenhagen, Odense and Aarhus expect to be able to employ:

- Copenhagen:
  - 2 experienced trialists
  - 1,5 statistician
  - 3 data managers
  - 1 secretary
- Aarhus:

- 1 experienced trialist
- 1,5 statistician
- 2 data managers
- 1 secretary
- Odense:
  - 1 experienced trialist
  - 0,5 statistician
  - 1 data managers
  - 0,5 secretary

According to these projections, the total manpower for clinical research is going to be expanded by 18.5 people providing a yearly work.

Apart from the 'core funding' described above, individual budgets shall be developed for each of the clinical trials that are going to be conducted within the DCRC. The necessary 'project funding' is then to be raised through industrial and academic sponsors as well as through public and private funds in Denmark and abroad.

The trial units and the GCP units of the DCRC infrastructure have a current estimated annual budget of about DKK 50 million. This budget is rather stable each year and it is estimated that the future budget for non-DCRC activities will remain on DKK 50 million. It is proposed that the DCRC partners shall provide DKK 1 million each year. This money shall cover the regular activities among the partners that relate to DCRC. This amount represents a 10% co-financing of the total amount of DKK 50 million that will be sought as funding.

Detailed budget for the four year implementation and construction phase of the DCRC and continued partnership of DCRIN:

### Detailed yearly budget

- DKK 2,000,000.- shall be spend on hardware, software, information technology infrastructure, education and training, and office equipment.
- DKK 8,000,000.- shall be spent on employing the following persons
  - 6 x data mangers of 450,000,- a year .....2,700,000.-
  - 2½ x secretaries of 320,000,- a year .....800,000.-
  - 4 x trialists, preferably physicians with a good knowledge of Denmark of 600,000,- a year .....2,400,000.-

- 3½ x statisticians of 600,000,- a year .....2,100,000.-
- DKK 1,000,000.- shall be spent on regular activities among the DCRC partners that relate to DCRC activities.
  - 3 x Ph.D.s
  - VIP and TAP time and activities

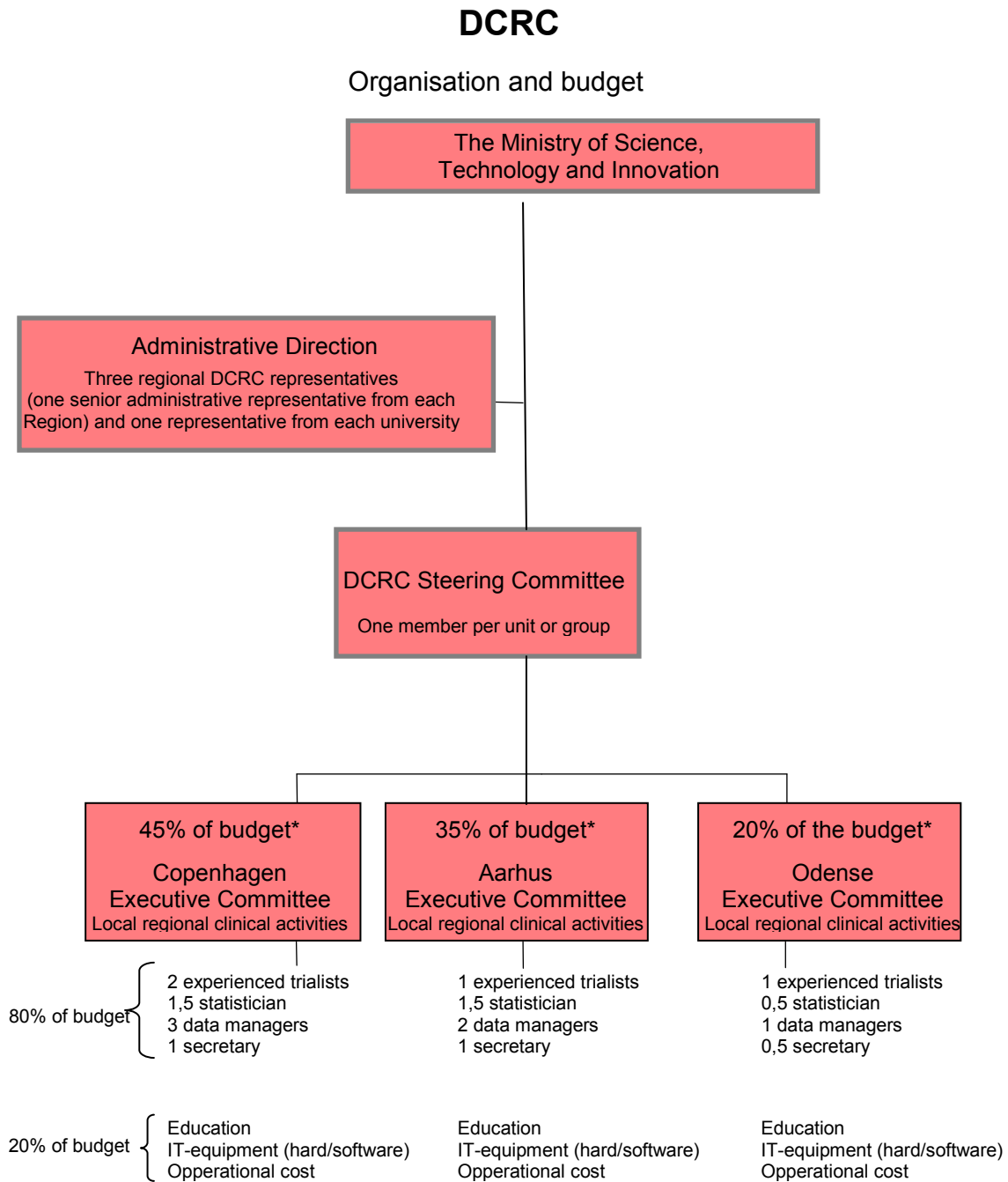
### 3.7.2 Financial plan for DCRIN

To secure the partnering with ECRIN, i.e. to cover the expenses and to ensure the financial sustainability of the DCRIN, a contribution is requested from the Ministry of Science, Technology and Innovation.

Detailed budget for continued partnership of DCRIN in ECRIN:

- DKK 1,500,000.- shall be spent on the partnering with ECRIN. This contribution to ECRIN is composed of a fixed contribution of € 100.000 (approximately DKK 750.000) per country and per year and a variable contribution, stratified according to the GDP, meaning Denmark is requested to contribute an additional € 100.000 (approximately DKK 750.000) per year. This will cover a Danish fulltime employee as well as contributions to the ECRIN management office.

**Figure 4: Organisational diagram**



\* of the DKK 10 million provided by funding annually

## **4. Coherence with Danish research policies**

### **4.1 Coherence with research policies of the Danish University Hospitals**

The proposal to establish the DCRC is in full accord with the research policy of the Capital Region of Denmark (Region Hovedstaden).<sup>28</sup> The vision of the Capital Region is to carry out world-class health research in prioritised areas for the benefit of each citizen, the health-care services, and the society in general. This shall occur by supporting a strong research culture, thereby providing the basis for development, innovation and inventions in the Region's enterprises and among general practitioners (GPs) and specialists, interacting with educational institutions, knowledge environments, municipalities and the private sector – nationally as well as internationally, while at the same time ensuring that researchers and health-care professionals have a nurturing, motivating work environment.

The foundation for good health research is already present. However, a number of challenges call for improvement. This policy determines the overarching areas of focus for health research in the years ahead for the Region's enterprises as well as GPs and specialists. The research policy should help to ensure:

- that clinical research is given top priority and that elite, quality and relevance are paramount issues, supported by the development of tools for research assessment and procedures for prioritising areas of focus and technical research;
- that it becomes more attractive for all health-care professions and staff groups to pursue a career in research for instance by establishing more flexible research positions, more flexible clinical-training processes, and a better framework for career options across disciplines and sectors;
- that better research environments are generated by ensuring that management groups of the Region's enterprises support research, provide good research facilities, and establish research management in the individual units of the Region's enterprises and in the GP and specialist sector;
- that high-quality service and support functions are provided through the establishment of a central Research and Innovation Support Unit and through a dynamic framework for technology transfer;
- greater synergy among areas of research and, primarily, patient treatment – but also in relation to the private sector, educational institutions, knowledge environments,

municipalities and society in general. This will be ensured through incentives such as performance-related contracts, earmarked funds, improved administrative procedures and a dynamic framework for disseminating knowledge and collaborative projects;

- that interaction with Copenhagen University Hospital and the private sector is maintained and developed.

The University Hospitals of Odense and the University Hospitals of Aarhus have similar research objectives, and the University Hospitals of Aarhus further states that research should be internationally renowned and that the research should be of high activity in order to improve the treatment of patients.

## **4.2 Coherence with research policies of the Danish Universities**

The Ministry of Science, Technology, and Innovation is expressing that Danish research shall be innovative and of quality comparable to the best performed research in the world.<sup>29</sup> The proposal to establish the DCRC is in full accord with the research policy of the health scientific faculties of the three Danish universities.

### **Copenhagen University**

The strategy of the Copenhagen University<sup>30</sup> is aimed at facing the future, with realisation of the high goals of ambitions with focus on specific target areas. This shall occur by producing health research that is independent and of the highest quality; a central key is to acquire new knowledge and innovation. Moreover, it is the strength of the faculty the many small units bridging and contributing to the overall knowledge and the necessity of greater collaboration, especially in long-term projects with ambitious goals, is endorsed. The strength of the DCRC will be the collected latent knowledge scattered in the many small units building up the DCRC, and the DCRC will acquire the best knowledge from the European research area by its strong association with the ECRIN. The Copenhagen University faculty is also focused on the synergistic effects of research in the preclinical and clinical field “from bench to bedside”, which is a multi-step process that DCRC will facilitate with its linking of clinical trial sites.

### **University of Southern Denmark**

The vision of University of Southern Denmark<sup>31</sup> is to contribute to the improved human welfare, with a visual and key influence on health-care development and on public health. This shall occur by distributing research result to the public and professionals in health services and by educate and do research at the highest international level, in areas of relevance for public health and effect of health-care treatments. The DCRC will actively improve and make an impact on the on health-care development and on public health. The DCRC will also promote transparency in health-care research by distributing clinical research.

Also, the University of Southern Denmark has established a research infrastructure for Southern Denmark.<sup>32</sup> This infrastructure is very much in line with the mission and vision of DCRC, who, however, wants to establish a more comprehensive and national infrastructure.

The University is expressing a wish for collaborations where they can participate in the improvement and as a supporter of the DCRC this will be the case, as DCRC will not only benefit Denmark but will also take advantage of the international collaborations in ECRIN.

### **Aarhus University**

The vision of Aarhus University<sup>33</sup> is to be a key player in the development of health-scientific research at the highest international level, the faculty shall create new knowledge that will benefit people and contribute to the development in the community. The faculty point at the importance to secure the communication and knowledge exchange within the whole health-care area. The DCRC will be a strong structure in the area of health-care research in Denmark, and will bring and implement and synergistically influence the international standards through its close association with ECRIN.



## 5. Curriculum vitae for partners in the DCRC

- Arne Astrup, Professor, Dr. Med. Sci., Department of Human Nutrition, Copenhagen University;
- Allan Vaag, Professor, dr.med., overlæge, Steno Diabetes Center, Copenhagen University Hospital;
- Christian Gluud, Head of Department, Dr. Med. Sci., Ass. Professor, Copenhagen Trial Unit (CTU), Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital;
- Daniel Steinbrüchel, Professor, Dr. Med. Sci., Department of Thoracic Surgery, Rigshospitalet, Copenhagen University Hospital;
- Gedske Daugaard, Chief Consultant, Dr. Med. Sci., Department of Oncology, Rigshospitalet, Copenhagen University Hospital;
- Hans Jørn Kolmos, dr.med., Professor, forskningsleder, Klinisk Mikrobiologi, University of Southern Denmark;
- Henrik Enghusen Poulsen, Klinisk professor, overlæge, Kliniske Institutter, Rigshospitalet, Klinisk Farmakologisk Afdeling, Copenhagen University Hospital;
- Jane Lindschou Hansen, Clinical Research Assistant, MSc, Copenhagen Trial Unit (CTU), Centre for Clinical Intervention Research, Rigshospitalet, Copenhagen University Hospital;
- Jens Christian Djurhuus, professor, dr.med. Klinisk Institut, University Hospital of Aarhus;
- Jens Kastrup, Klinisk forskningslektor, overlæge, dr.med, Kliniske Institutter, Rigshospitalet, Hjertemedicinsk Klinik, Copenhagen University Hospital;
- Jens Lauritsen, overlæge, Ortopædkirurgisk Afdeling, University Hospital of Southern Denmark;
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