Research Council of Norway – Research Infrastructure
Call for proposals with deadline 10 October 2018

Title
Continuation and strengthening of the Norwegian Clinical Research Infrastructure Network (NorCRIN) – "NorCRIN 2"

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Host institution	St. Olavs hospital HF
Project manager	Director of Research, Innovation and Education, Gunnar Morken

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1. Relevance to the call for proposals

Better health and healthcare are main objectives of Norwegian research policy. High quality clinical research is a prerequisite for the development of new knowledge and improved clinical practice, thus clinical research is a priority area. However, clinical studies are strictly regulated and must meet international harmonised guidelines for good clinical practice (GCP). Medical and health science research relies on support from advanced research infrastructures manned with qualified personnel with interdisciplinary skills. Norwegian Clinical Research Infrastructure Network (NorCRIN), started in 2012, is a distributed service-based infrastructure for facilitating and increasing high quality and collaboration in national and international clinical studies. The NorCRIN consortium includes all six university hospitals in Norway, which in 2017 were responsible for 70 % of the clinical research projects registered in Norway[1]. From start of NorCRIN and through the Research Council of Norway (RCN) supported NorCRIN 1 project in 2015, the network partners have facilitated and standardized the clinical research process by providing easily accessible, nationally accepted guidelines and Standard Operational Procedures (SOPs). For a small country like Norway, networking is the only way to reach and maintain an international quality levels in this field.

The application for NorCRIN phase 2 (NorCRIN 2) addresses additional specific needs in clinical research, corresponding to the goal of the call: to give the Norwegian research community access to relevant state-of-the-art infrastructures that promotes clinical research of high quality. NorCRIN 2 aims to further advance and broaden its capacity in each partner and the consortium as a network to provide high quality research support, advice and information, to involve the public and increase national and international cooperation . The Government has drawn up a long-term plan for research and higher education up to 2024, and among the six priority areas are more efficient welfare, health and care services (Meld.St.7, 2014-2015). Within this area the National Research and Innovation Strategy HelseOmsorg21 (2014) and Action plan for follow-up (2016) prioritizes several strategic efforts; improved clinical interventions, high quality internationalization, the health care industry as an industrial policy priority, health data as national comparative advantage, increased user involvement, and strategic and evidence-informed governance and management. In other words, a national aim is to increase the number of clinical studies and to implement relevant results into clinical practice (HelseOmsorg21).

NorCRIN, through the 5-year funding period from the RCN in 2015 (NorCRIN 1) has been further developed into an important national infrastructure supporting clinical research. The recommendations of the National Research Infrastructure Strategy - Research Tools (2018) are to provide long-term funding. The Norwegian government's Long-term Plan for Research and Higher Education (2015-2024) emphasizes the need for Norway to participate in European cooperation on research infrastructures, to attract international top researchers to Norway and to ensure access for Norwegian professionals to the best research infrastructures in Europe. NorCRIN 1's ground-breaking development of common procedures and guidelines, and the mapping of available resources and possible risk factors have allowed partners to build robust environments in efficient and quality-assured manners. NorCRIN 1 has focused on national

[1] Numbers for 2017 from Current Research Information System in Norway (Cristin) and projects imported from the Regional Committees for medical and health research ethics application portal (SPREK) https://app.cristin.no/projects/search.jsf

standardization and alignment of practical issues, through work packages (WPs). These are national standard operating procedures (SOP) for pharmaceutical and non-pharmaceutical interventions, monitoring, data management, cooperation with industry and mapping of early phase research facilities. NorCRIN 1 has contributed to enhanced quality of clinical studies, has simplified and facilitated collaboration on clinical research within Norway, and toward international collaboration as a national node in the European Clinical Research Infrastructure Network (ECRIN ERIC (European Research Infrastructure Consortium)).

However, new national and international challenges have emerged, and an expanded and renewed work plan has become essential. NorCRIN 2 will contribute to standardization and harmonization of clinical studies according to RCN's strategies and the FAIR principle - findable, accessible, interoperable and reusable. The NorCRIN board, the Ministry of Health and Care Services (HOD), RCN, the industry and researchers all expect that NorCRIN is a visible and relevant infrastructure that actively contributes to increase the number of clinical studies in Norway. To support national goals, NorCRIN 2 hereby applies for a total amount of **53.089 MNOK** for continuation and strengthening of its operations through 8 WPs.

2. Status of current research and infrastructures

Norway has several advantages for clinical studies, including a homogenous hospital system, national registries enabling the collection of event rates and strong commitment for clinical research among citizens, resulting in low dropout rates in long-term follow up in clinical studies. Another advantage is that large clinical studies can recruit from a stable population base. Based upon available resources and priorities, the university hospitals are establishing and continuously developing Clinical Research Centres (CRC) and Clinical Trial Units (CTU) to promote, support and conduct clinical research. NorCRIN 1 has facilitated and standardized the process by providing easily accessible, nationally accepted guidelines and harmonized SOPs. Development of CRCs and CTUs with high-quality skills in GCP, Good Laboratory Practice (GLP), monitoring, data management, biobanking, novel trial designs, as well as expertise in research ethics and regulatory aspects, are important to make Norway an attractive partner for international multicentre studies. Access to Good Manufacturing Practice (GMP) study drug supply is also important to foster clinical research in Norway. NorCRIN website (norcrin.no) hosts a public service available for all partners from the Norwegian university hospitals, as well as sharing information freely open to all users interested in clinical trials. NorCRIN has since 2013 contributed to quality assessment of clinical studies in Norway and supported several successful clinical multicentre studies as for example the Ipi4 study, the RituxME study and the Nor-Switch study[2].

NorCRIN 2 will contribute significantly to establish new crucial issues for facilitation and improvement of clinical research in Norway. Regarding research support, collaboration in advanced statistics and new methodologies will provide leading-edge knowledge to all partners. Moreover, new patient and public involvement strategies will maintain the high public accept for clinical trials in Norway. Finally, it is important for NorCRIN 2 to develop valuable and well-functioning models for collaboration with industry and relevant national and international research infrastructures. NorPedMed (Medicines for Children Research Network Norway) is a nationwide paediatric clinical drug trials network and affiliated to NorCRIN with a NorPedMed-representative in the NorCRIN board. Several national initiatives like Biobank Norway, Norwegian centre for Minimally invasive Image guided Therapy and medical technologies (NorMIT), and the Norwegian Primary Care Research Network (PraksisNett) are potential collaborators. Also, the ongoing and large Norwegian population studies (The Nord-Trøndelag Health Study, HUNT; the Tromsø study; the Hordaland study, HUSK) are powerful platforms for clinical research with high societal impact when combined with national registers, such as the Cancer Registry, the Norwegian Prescription Data Base (NorPD) and the Medical Birth Registry. Digitalization in the health care services will give new possibilities for research and require adjustments of study designs and statistical methods.

The ESFRI Landmark ECRIN ERIC is a European network with the objective to improve the health of patients and citizens across the world through clinical research. ECRIN ERIC is engaged in multiple activities. The network supports, coordinates, and manages high-quality, independent, and fully transparent multinational clinical research. It draws on synergy of the capacities and capabilities of clinical research.

[2] Jorgensen, K.K., et al., *Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial.* Lancet, 2017. **389**(10086): p. 2304-2316.

Norway is one of nine members of the ECRIN ERIC, which allows Norway to participate in strategic discussions about facilitation and quality assessment of clinical research in Europe. Furthermore, NorCRIN is an observer in the Clinical Research Initiative for Global Health (CRIGH), which aims to support structure for international collaboration on clinical research for benefit of patients, healthcare professionals and health systems, and for optimizing collaboration and communication between stakeholders (academia, industry, patients, caregivers etc.). NorCRIN has already established contact with the Norwegian node of European Advanced Translation Research Infrastructure in Medicine (EATRIS ERIC), which contributes significantly to innovation and standard settings with faster introduction of innovative technologies and new or repurposed drugs to benefit Norwegian patients. Further, the plan in NorCRIN 2 is to explore closer relations to the Norwegian nodes of other relevant ESFRI Landmark infrastructures like Biobanking and Biomolecular Resources Research Infrastructure (BBMRI ERIC), European Life sciences Infrastructure for Biological Information (ELIXIR) supporting life science research and its translation to medicine, environment, and the bio-industries and society, and EuroBioImaging providing open access to innovative biological and medical imaging technologies for European researchers. Using international infrastructures to increase the innovative potential of Norwegian research as well as shifting the balance from discovery towards end-products in collaboration with industry will result in enhanced commercial and industrial competence.

3. Description of the Research Infrastructure

NorCRIN, started in 2012, as a distributed infrastructure based on research facilities already available at the partner institutions, the six Norwegian university hospitals (Figure 3.1). The project management and secretariat are localized at St. Olavs hospital, Trondheim University Hospital. In 2015 the project NorCRIN 1 received 50 MNOK from RCN for the period October 2015 to September 2020, while the total project period runs until 30 September 2025.

Figure 3.1:
Location of the partners in NorCRIN

NorCRIN's vision is "more research, better quality and less management". In NorCRIN 1 the partners have collaborated to develop, harmonize and deliver high-quality services to the users. Information to the users has been electronically accessible by the website (norcrin.no). This proposal concerns an upgrade of the existing infrastructure. Through NorCRIN 2, the provision of scientific key services will expand within the successfully established organizational framework. Tasks and responsibilities implemented in NorCRIN 2 will reflect the changing challenges facing the researchers and the industry. NorCRIN 2 will fulfil national goals by establishing new work packages, as shown in Table 3.1.

Table 3.1: A brief overview over the basic organization and work packages for both NorCRIN 1 and 2

	WP	2015-2020	2020-2025	2025-2030	Title
NorCRIN1	3				Monitoring
	4				Cooperation with the industry
	5				eCRFs
	6				SOPs for non-pharmacological trials
	7	2017→			First in human units
NorCRIN1 + NorCRIN2	**1**				Management and coordination of NorCRIN
	2				Standard Operating Procedures for clinical trials
	8	2018→			Data management
	9	2019→			Statistics and advanced methods in clinical trials
NorCRIN2	**10**				Organizational units for the conduct of clinical trials
	11				Strategies for facilitating collaborative clinical trials/ Streamlining and facilitating academia- industry collaboration
	12				Pragmatic clinical trials, including registry based randomized clinical trials (RRCT)
	13				Patient and public involvement (PPI) in clinical trials

Finance from NRC | Self-finance

The backbone of NorCRIN 1 has been the development and maintenance of comprehensive procedures (SOPs) for the implementation of drug trials (NorCRIN 1 WP2). This important work is essential to be continued in NorCRIN 2. Procedures developed through all new work packages will be updated and maintained in WP2. This work package ensures that all procedures are updated at any time, cf. national and international laws and regulations. NorCRIN 2 will focus on further development and strengthening of the services according to strategic efforts prioritized in Action plan for follow-up of HelseOmsorg21. The following strategic areas are identified; data management (WP8), statistic and advanced methods in clinical trials (WP9), harmonization of CTUs (WP10), further strengthening of the cooperation with industry (WP11), web-based registry solutions and novel strategies to utilize registry platforms for interventional clinical studies (WP12), development of tools for patient and public involvement in clinical trials (WP13). Moreover, collaboration with relevant international infrastructures (see chapter 2) such as ECRIN ERIC, CRIGH, EATRIS ERIC and BBMRI ERIC, allows Norway to participate in strategic discussions about facilitation and quality assurance of clinical research in Europe (WP1). On the national level NorCRIN 2 will expand the collaboration with relevant health related infrastructures (see chapter 2) as part of WP1.

Norway has since 2016 been a member of ESFRI Landmark, ECRIN ERIC, a major tool to increase the number of independent, multinational trials as key instruments for optimisation of healthcare solutions and promotion of evidence-based medical practice in Europe and globally. NorCRIN as the national ECRIN node, offers a network of units supporting clinical research through the provision of local services (ethical and regulatory submissions, adverse event reporting, monitoring), complying with the ECRIN quality policy. Thus, NorCRIN is contributing to quality assurance of clinical studies, is simplifying and facilitating collaboration on clinical research within Norway and toward international collaborators through ECRIN ERIC.

4. Impacts of the Research Infrastructure

The NorCRIN infrastructure has strengthened the quality and quantity of support to clinical researchers throughout Norway, and clearly benefited the clinical study activity. In 2017 the NorCRIN partner institutions were involved in 89 academic projects with international funding, 106 academic projects with external national funding, and 48 academic projects with funding support from the host institution. In addition, NorCRIN partners were involved in 174 studies partly (23) or fully (151) funded by industry partners. The increased demand of monitoring service shows that the number of academic drug and medical device trials has increased. It should be noted the monitoring group in NorCRIN has received very good reviews by study management groups, i.e. in the Nor-Switch study.

Standardized operating procedures (SOPs) have been developed and implemented throughout the network, facilitating national multicentre trials. Particularity, SOPs has not only been generated for pharmaceutical studies, but also for studies involving medical- technical devices, as well as for other interventional studies such as for instance physical exercise interventions. The Regional Health Trusts and NRC requests applicants to large national programs like KLINBEFORSK and BEHANDLING to use the services of national research support infrastructures, and explicitly mention NorCRIN to secure, improve and standardize study quality. National procedures for pharmaceutical trials, data management and statistics within NorCRIN are key contributors to the standardization of study conduct. Sharing best practice through regular interactions within WPs improves quality and encourages implementation of new knowledge.

The NorCRIN board has identified additional services that have to be developed and harmonized to meet future needs, and to reach the national goals; more clinical trials in Norway and access to clinical studies for more patients. Thus, NorCRIN 2 will expand and strengthen all services through the local partners. Strict requirements are imposed for clinical trials following good clinical practice. Major challenges related to state-of-the-art aspects of clinical and translational medical research that still need to be addressed are;

1. personalised/precision medicine requires new trial designs
2. existing data in registries and biobanks should be reused and shared
3. the added value of new methods for diagnosis, therapy and prevention must be validated through clinical trials
4. the requirement to facilitate collaboration between the healthcare services and pharmaceutical and medical technology industry (both small national companies as well as large international companies)
5. the need for models for user involvement
6. the use of innovative clinical study designs such as pragmatic clinical trials to explore already established infrastructure for larger patient recruitment at a low cost

According to these challenges, NorCRIN 2 includes 8 WPs (Table 3.1 and chapter 10). NorCRIN 2 aims to strengthen partners through following WPs; strengthening the research support units at each partner (WP8, 9 and 10), development and harmonization of the procedures for conducting clinical trials (WP2) and development of guidelines (SOPs) for patient and public involvement (WP13). To enable capturing of data in modern multicentre trials, there is a need for web-based registry solutions that satisfy the demands of clinical studies as well as novel strategies to utilize registry platforms for interventional clinical studies (WP12). In addition, NorCRIN 2 will increase the competitiveness of Norwegian clinical research projects on the international funding arena (WP1), and Norway's position as an attractive partner also for the industry (WP11). Norwegian researchers and clinicians will therefore be in the forefront when new knowledge emerges, and patients will have access to the latest treatments and technologies.

Through the Norwegian membership in ECRIN ERIC, NorCRIN has contributed both to the selection of Norwegian study sites in international academic studies and given researchers access to ECRIN's clinical research support. Norwegian research groups have also made benefit from using ECRIN ERIC to expand their studies throughout Europe, and thereby given Norwegian patients the possibility to participate in international multicentre studies and access to new treatment. Hence, ECRIN provides excellent opportunities for increased clinical trial activity in Norway and for increased international collaboration. It should also be noted that HECRIN, the Hungarian ECRIN ERIC node, came to NorCRIN discuss and learn how to run an ECRIN node. NorCRIN has currently status as observer in the CRIGH (www.crigh.org) organization. CRIGH aims to support international collaboration in clinical research to maximise access to patients, enable resource sharing and increase the applicability of research findings by developing global standards on clinical research. Further CRIGH promote the take-up of innovative methodology and technologies to develop global core competencies, training harmonisation and establishing a collaborative framework to address health issues worldwide.

5. Importance of the research infrastructure for various user groups

Potential users of NorCRIN are researchers, research assistants and administrators, pharmaceutical industry, SMEs (within medical technology/biotech), patient organizations and others (Table 5.1). Continuous efforts are being made to improve the accessibility for all users, and for researchers and the industry in special.

Table 5.1: Overview of current and proposed involvement of various user groups in NorCRIN

User group	NorCRIN 1 2016-2020 (2025)	NorCRIN 2 2020-2025 (2030)
Researchers in clinical studies at university hospitals	User conference 2017, user survey 2018	WP13 + biannual user conferences
Researchers in clinical studies at non-university hospitals		WP13 + biannual user conferences
Patient organizations	Representative in advisory board of NorCRIN	Representative in advisory board of NorCRIN, user panel + WP13
Research support (monitors, data managers, statisticians, research nurses, research advisers)	WP 2,3,6,8,9	WP 2,8,9,10,12,13
Research managers	User conference 2017/ NorCRIN board	Biannual user conferences/ NorCRIN board
Relevant national infrastructures	Project manager	WP1
Relevant international infrastructures	Project manager	WP1
TTO	User conference 2017/ Dialogue meeting WP4 2018	User panel + biannual user conferences
Industry	Dialogue meeting WP4 2017+ 2018/ User conference 2017	User panel + biannual user conferences + participate in meetings and workshops in WP11
The Government /HOD	User conference	User panel + biannual user conferences

NorCRIN has gained experience from several academic national and international studies, and industry studies (Table 5.2). As an example, NorCRIN contributed with counselling, monitoring and other services in

the HOD-initiated multi-centre study, Nor-Switch that was later published in the prestigious journal The Lancet[3].

Table 5.2: Present degree of utilization of the infrastructure

	2016	2017	Comment
Number of academic users (n)	382	623	Underestimation, as based upon the number of projects that have received assistance from NorCRIN.
Number of industry users (n)		348	Underestimation, as based upon the number of projects that have received assistance from NorCRIN.
Projects with international funding (n)		89	No data available from 2016
Projects with national funding (n)		154	No data available from 2016
Projects with industry funding (n)		348	No data available from 2016
New industry-initiated studies (n)	161	174	
Number of accessions of website	33 525	42 622	

We expect a steady increase in utilization of the NorCRIN infrastructure in the years to come (Table 5.3). As the RCN has several initiatives to increase EU funding to Norwegian researchers, we estimate a 15% increase in projects with international funding using NorCRIN. Beyond the service provided to national interests, the collaboration with ECRIN and CRIGH enables the Norwegian researchers to expand their participation in international clinical studies. NorCRIN 2 intends to improve collaboration with industry, aiming at a 15 % increase in industry-funded projects. We also expect the number of academic users to increase steadily by 10 % yearly. Particularly, we expect more national initiatives for clinical research supported by the regional health authorities through KLINBEFORSK and supported by NorCRIN.

Table 5.3: Estimated degree of utilization of the infrastructure

	2020	2021	2022	2023	2024	**Aim**, annual increase %
Number of academic users (n)	829	912	1003	1103	1214	10
Number of industry users (n)	529	609	700	805	926	15
Projects with international funding (n)	135	156	179	206	237	15
Projects with national funding (n)	205	225	248	273	300	10
Projects with industry funding (n)	529	609	700	805	926	15
New industry-initiated studies (n)	265	304	350	403	463	15

In September 2017 NorCRIN arranged a user conference which gave important valuable input. In addition, a user survey was conducted in September 2018. The survey showed that researchers visiting norcrin.no are essentially searching for SOPs and general contact information. Those who had received assistance from NorCRIN were satisfied with services, such as the SOPs (WP2), monitoring, data management (WP8), statistics (WP9), support on solutions for the collection and storage of data (WP12) and extensive GCP-support provided by CTUs (WP10). The industry representatives want more dialogue/communication and speed-dating/arenas between academia and industry (WP11), support with budget and contracts in the hospital (WP4 NorCRIN 1) and help with identifying excellent research partners within selected therapy areas (WP11).

6. Plan for access and knowledge management

In general, all tools and information developed and generated through NorCRIN have been and will be published on the NorCRIN website (norcrin.no). The NorCRIN website was visited more than 42 000 times in 2017, and the traffic on the website has gradually increased. All partner institutions have implemented the procedures developed by NorCRIN in their hospital's quality system and encouraged the researchers to actively use the NorCRIN web pages. A communication plan describes attendance at relevant local, regional and international meetings.

Also, in NorCRIN 2, easy access to the infrastructure will be secured by the clear and transparent information published on NorCRIN website. This includes NorCRIN services, access policy, data management policy and the terms and conditions.

[3] Jorgensen, K.K., et al., *Switching from originator infliximab to biosimilar CT-P13 compared with maintained treatment with originator infliximab (NOR-SWITCH): a 52-week, randomised, double-blind, non-inferiority trial.* Lancet, 2017. **389**(10086): p. 2304-2316.

Expertise developed by activities in NorCRIN 2 WPs will be made available to users through courses and provided by the committed local contact persons and other qualified personnel in the local clinical research support units.

In addition, the communication and collaboration with the National secretariat for Health Technology Assessment and relevant infrastructures will be further emphasized. NorCRIN 2 will develop new models for interaction with the industry to strengthen Norway's position as a prioritized arena for clinical trials and to bring new treatment methods to the patients.

To promote and improve NorCRIN 2, information will also be given in regular biannual user meetings and user surveys will be arranged to receive feedback for future development.

7. Data management

NorCRIN's objective is not to generate research data for own use, but to provide research infrastructure for clinical trials. The data management WP8 aims to develop competence and provide infrastructure for safe and high-quality data management in clinical trials in accordance with national and international regulations.

8. Partners

The NorCRIN consortium consists of the six university hospitals in Norway (Table 8.1) and is regulated by the NorCRIN consortium agreement that was first signed in 2014 and revised in 2016. The consortium's ability to implement and host the infrastructure in all partner institutions and St. Olav Hospital's ability to lead the project and host the secretariat, have proven to be successful by the well-functioning collaboration and documented goal achievement both before and during the NorCRIN 1 period.

It should be noted that NorCRIN partners have since 2012 continuously strengthened their local research infrastructure units/CTUs. Research support units/CTUs are working according to procedures developed by NorCRIN.

Table 8.1: Overview of the representative person at each partner hospital.

Institutions (Norwegian short names)	Representative persons
Oslo University hospital, (OUS)	Kristin Bjordal, Head of Research support services OUS / Prof UiO
Bergen Health Trust, Haukeland University Hospital (HUS)	Bjørn Tore Gjertsen, Director of Research HUS / Prof UiB
St. Olavs hospital, Trondheim University Hospital (St. Olav)	Gunnar Morken, Director of Research, Innovation and Education St. Olavs / Prof NTNU
Akershus University hospital (Ahus)	Helge Røsjø, Director of Research and Innovation Ahus
Stavanger University hospital, Stavanger (SUS)	Inger Hjørdis Bleskestad, Research director SUS
University hospital of North Norway (UNN)	Einar Bugge, Director, Centre for Quality Improvement and Development, UNN

Health related research production in Norway has increased steadily by one percent annually since 2014 and reached 4115 scientific publications in 2017, cf. National system for measuring research activity. The NorCRIN partners are involved in the majority of the research publications. Table 8.2 describes the partners' different scientific and technological competence and expertise.

Table 8.2: Description of the partners capacity (2017 numbers)

	OUS	HUS	Stolav	Ahus	SUS	UNN
Health Region	South-East	West	Central Norway	South-East	West	North
No. of employees	23400	12400	10500	9000	7850	6300
Patient basis	1 200 000	1 000 000	725 600	555 000	370 000	500 000
Budget in billion NOK	22.4	11.5	10	8.7	6.8	7.2
% for research costs	8.5	4.5	2.25	2.75	1.9	3.1
Industry agreements (new/ongoing)	68/245	37/170	15/52	20/53	22/58	4/32
No. of publications/ PhD[4]	2014/123,25	753/40	531/44.25	361/16	260/10	324/19
Organizational units for clinical research (FTEs)	CTU: 27.8 CRW: 3.2 CRW*: 15.05 CRW**: 4.8	CTU: 13 CRW**: 3,8 CRW***:	CTU: 6.4 CRW***: 3.5	CTU: 10 CRW: 7	CRW: 3	CTU: 13 CRW: 27

[4] Regjeringen. Helse- og omsorgsdepartementet, *Nasjonalt system for måling av forskningsaktivitet*. 2018.

		7,7				
WP Leader	WP8, 9, 10, 11	WP2	WP1	WP12		WP13
% of international authorship of the publications[3]	56.9	57.9	49.7	48.3	63.1	48.8

CTU: Research support, including project coordination, monitoring, data management and statistics; CRW: Clinical Research Ward - Adults, no specific therapeutic area; CRW*: Clinical Research Ward - Early phase cancer unit; CRW**: Clinical Research Ward - Children, no specific therapeutic area; CRW***: Clinical Research Ward - Adults, no specific therapeutic area & Early phase cancer unit; FTEs: Full-time equivalents.

The consortium for NorCRIN 2 is the same as for NorCRIN 1. Through the signed Letter of Confirmation, the partners confirm their responsibilities for operation and upgrade of NorCRIN 2 by making available qualified relevant personnel and resources for the fulfilment of the project, both in the establishment and operational phases.

9. Project management

The basis for both NorCRIN 1 and 2 is the NorCRIN infrastructure, established by the Regional Health Authorities in 2012, anchored at St. Olavs Hospital, and the director of research at St. Olav´s Hospital will act as the applicant for NorCRIN. If funded, the identified WP leaders will start preparatory work in order to be able to activate the WPs in October 2020 (Table 10.1).

The governance model is based on the Consortium agreement, the NorCRIN Board, The Executive Group, the organization of working groups, and the homepage-based communication channel. The Project Manager together with the Operational manager who is responsible for the operation of the secretariat at St. Olav, reports to the Central Norway Regional Health Authority (RCN) (Figure 9.1).

The NorCRIN Board is the decision-making body in the project. Each partner has two vote representatives. On the advice from the RCN (negotiation meeting 2015), today's NorCRIN Board consists of people from the strategic leadership of the partners, as described in Table 9.2. This structure will be continued in NorCRIN 2. A representative for patient organizations is also on the Board and some observers from relevant collaborators are also present. The Board is led by the Chairman. The work in the Board is consensus-driven, but all decisions require a 2/3 majority. The Board monitors the implementation of the project and ensures that the objectives and deliverables outlined in the project mandate are performed within the stipulated timeframes. The Board meetings rotate between the partners and consist of two parts. In Part I, the project meeting, leaders of WPs will be invited to each physical meeting to report their activities and thus make first - hand information available to the Board. The Part II is a regular Board meeting including acting board members, observers, invited guests, the Project manager and representatives from the secretariat. The Board meets twice a year with options for necessary telephone/SKYPE-based consultations.

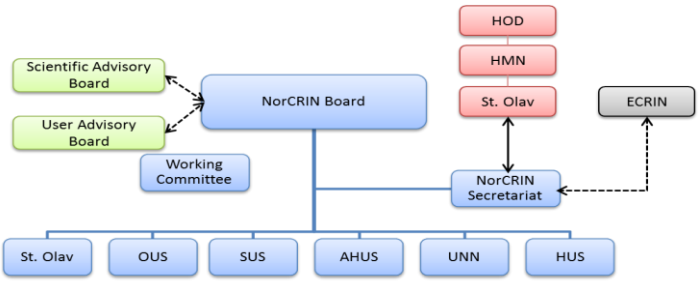

Figure 9.1: Organization of the NorCRIN core team (blue), advisory board (green and communication lines to Norwegian authorities (red) and international infrastructures (grey).

A **Working Committee** (WC) has been established to streamline the executive processes in the network. The WC adopts matter prepared by the Secretariat for the biannual Board meetings and telephone conferences. WC consists of Chairman and Deputy Chairman (elected among partners), Project Manager and Operational manager. The WC meets four times a year.

The Regional Health Authorities' strategy group for research has appointed the **Advisory Board** with members representing each region, to ensure a broad national representation. The Advisory Board meets once a year and shall act as an observer for the Health Authorities of the project and ensure the necessary anchoring of NorCRIN in Regional Health Authorities.

The **User Advisory Board** is composed of stakeholders and users of NorCRIN services. These are patient organization, pharmaceutical industry, SMEs (within medical technology/biotech) or other relevant representatives. It shall provide strategic input for the development of NorCRIN and its operation and is important for the work in WP13.

The **NorCRIN Secretariat** consists of the project manager, who will be a person with extensive scientific and administrative knowledge on the organization and conducting of clinical trials. She or he will understand the political framework of the research infrastructure and will demonstrate a personal suitability

for the task. The project manager should preferably be employed at the project owner institution. The operational manager is responsible for the daily progress, implementation, facilitation and coordination of the WPs, follow-up on WP leaders. The operational manager and project manager work closely together to reach NorCRIN's goals. The ECRIN correspondent is a liaison between ECRIN and NorCRIN and will be the primary contact point between clinical researchers, centres and networks in Europe and Norway. The national scientific member represents Norway in the ECRIN network committee. The controller has the overall responsibility of the project economy. The controller reports to the NorCRIN Board and is the main contact point between controllers at each partner together with the operational manager.

Each partner has a **local NorCRIN contact** to secure effective overall and local communication and cooperation.

After the project period, the Consortium agreement safeguards the consortium partners' rights and obligations. Through the signed Consortium agreement, all partners are legally bound by the agreement in minimum 5 years after end grants of NorCRIN 2. Most WP activities will be adapted into ordinary work in the research support units in each of the institutions. However, some of the established networks will be continued on a national level, financially supported by the partners or covered by user payments.

Each of the WP leaders are highly qualified personnel (Table 9.1), working with similar tasks in their daily position.

Table 9.1: A brief overview of competence of the operational manager (coordinator) and work package leaders

WP	Leader	Competence	Skills/ expertise
1, Operational manager	Sigrun K. Sæther	Cand. Scient Biology (1992) Teacher competence (1992) Project management (2000) Medicine for non-medicine (2012)	St. Olav as NorCRIN Coordinator since 2012; Part of the operational team in NorCRIN (Table 9.3). >15 year in pharmacy industry as CRA. Several years as project leader, quality and risk manager for private companies.
2	Anne Mathilde H. Kvamme	M.Sc.Pharm (1994) Project Management (2002)	Team leader clinical studies/research support from 2016 Specialist advisor clinical studies/biobank 2015-2016 20 years in pharma industry as project manager clinical trials and Head of Clinical Operations (7 yrs)
8	Cecilie Moe	BSA Health management and health economics (2014) M.Phil. public health science (2018)	>20 years' experience as a clinical data manager in clinical research organisations and in hospitals At OUS, responsible for developing the section and Head of Data Management Section since September 2017. NorCRIN: Work package leader WP8 Data management since 2018 and deputy leader of WP5 eCRF since 2016.
9	Inge C. Olsen	PhD Statistics (2006)	12 years of experience in Clinical Trials statistics, both in the pharmaceutical industry and academic 47 publications in international peer-reviewed journals
10	Jon B. Borgaard	M.Sc. (Biophysics), MM	Extensive experience from drug development as a line and project manager in Clinical R&D, in large and smaller Norwegian and international companies. Department manager for the OUS CTU since 1 Sep 2017.
11	Peder Utne	Law degree (1996) Master degree, Management (2005)	20 years' experience in Research Administration, both Hospital and Academia. Special skills and expertise related to collaboration research, IP and ethical issues, including organisation and management skills.
12	Magnus N. Lyngbakken	Administration and management (2002), Cand. Med. (2011), Ph.D. (2017)	Senior researcher in the Cardiothoracic Research Group and until recently Head of Clinical Trial Unit, Division of Medicine, Akershus University Hospital
13	Tove Aminda Hanssen	Registered Nurse (1987) Cand. Polit. (1995) PhD (2009)	Experienced researcher in clinical trials, e.g. the NorStent national megatrial, and research management units since 2002 (HUS and UNN). Head of the Clinical trial unit at UNN and member of the NorCRIN board.

Key members of research support staff are actively participating in all working packages in the RCN project. Through LoC (Letter of confirmation) and the Consortium agreement the partners have committed themselves to continue the collaboration and to participate further in the operational phase of NorCRIN 2.

Table 9.2: A brief overview of competence of the operational team in NorCRIN

Name	Function in NorCRIN	Competence	Skills / expertise
Gunnar Morken	St. Olavs Hospital	MD, PhD Psychiatrist	Extensive experience in clinical research and management of research projects and research departments
Kristin Bjordal	Chairman and Board member OUS	MD, PhD Oncologist	Extensive experience in clinical research and management of research infrastructure

Camilla Tøndel	Deputy Chairman and Board member ,Haukeland Hospital	MD, PhD Paediatrician	Broad experience from clinical trials and networking for increase of drug trials
Sigrun K. Sæther	Operational manager St. Olavs Hospital	Cand. Scient Biology (1992)	St. Olav as NorCRIN Coordinator since 2012; Part of the operational team in NorCRIN 1

10. Work plan, time-schedule and deliverables

NorCRIN is based on the existing research support infrastructures at the six partner institutions, providing facilitation, support and services to clinical research from academic and industrial sponsors. NorCRIN 1 strengthened local and regional coordination at all partner institutions, and standard operation procedures on multiple tasks have had national acceptance. NorCRIN 2 has an increased attention on national and international cooperation (WP1), harmonize and strengthened research support in all aspects including industry partners (WP8, 9, 10, 11 and 12) and user involvement (WP13); related to patients, patient organizations and their next of kin, and on other users as described in chapter 5. To meet the political strategic goals for the upcoming period the network has identified critical factors and defined new strategic areas described in 8 WPs in the following sections and tables (Table 10.1-10.10).

As showed in Table 10.1, operational activities in the WPs of NorCRIN 1 will be continued; some of them interconnected with the new activities in NorCRIN 2. Each of the described WPs can start and work independently. The Secretariat and the Board will assure that overlapping interests between the WPs are clarified. Each of the WP leaders has the obligation of managing the WP budget and to report twice a year to the NorCRIN Operational manager.

If funded, all WP leaders will prepare a detailed progress plan, which will be approved by the board members. A detailed progress plan will be prepared for each year to come and followed up in scheduled board meetings. This way of working has proven to be effective in NorCRIN 1 and will continue in NorCRIN 2.

Table 10.1 Overview over operational activities (WP) plan and source of finance

	WP	2015-2020	2020-2025	2025-2030	Title	Leader NorCRIN1	Leader NorCRIN2
NorCRIN1 + NorCRIN2	1				Management and coordination of NorCRIN	St. Olavs	St. Olavs
	2				Standard Operating Procedures	OUS	HUS
	8	2018 →			Data management	OUS	OUS
	9	2019 →			Statistics and advanced methods in clinical research	OUS	OUS
NorCRIN2	10				Organizational units for the conduct of clinical studies		OUS
	11				Collaboration between researchers and industry		OUS
	12				Pragmatic clinical trials, including registry based randomized clinical trials (RRCT)		Ahus
	13				Patient and public involvement (PPI) in clinical trials		UNN

Finance from NRC | Self-finance

WP1- Management and coordination of NorCRIN 2

Establishing and streamlining the network started in 2012 and has been facilitated by the partners signing of a consortium agreement. Management and coordination of the secretariat and WPs are an important ongoing process and NorCRIN will continue with development and strengthening of the network in the years to come (for details see chapter 9). The secretariat will continue with overseeing the work in all WPs, in addition to performing defined secretariat tasks as described in the Consortium agreement. The Norwegian Research Council has financed several infrastructures within the area of medicine and health, which all are relevant for clinical research projects. NorCRIN (WP1) plans to facilitate and strengthen the collaboration and communication with these infrastructures and other relevant national and international research infrastructures. The aim is to secure optimal utilization of the knowledge gained in ongoing initiatives, and to promote synergy between the different initiatives. Through coordination by the secretariat, NorCRIN participates in ECRIN work packages, and partners participate in several clinical studies through ECRIN. Our representation in assemblies and steering groups, and participation in WPs in both ECRIN and CRIGH will improve Norway's position internationally.

The budget for WP1 covers the following costs elements; contact persons at all partners, maintenance of the website, coordination and travel expenses associated with international academic community, and extra travel expenses in work packages (after application).

Table 10.2: Work package description of WP1

Work package number	WP1	**Lead partner and contact person**	St. Olav - Sigrun K. Sæther
Work package title	Management and coordination of NorCRIN 2		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:

1. To strengthen and simplify the collaboration within clinical research in Norway by
- Set up and maintain a sustainable national infrastructure for single- and multicentre clinical research, and for Norwegian participation in international clinical studies.
- Suggest and implement measures that improve, streamline and harmonize the foundation for good clinical research including support for study design, the application process, conduction and GCP reporting.
- Identify and implement opportunities related to the membership in ECRIN-ERIC, and work to safeguard Norway's position in European clinical research.
- Evaluate the areas in which members of the network should implement joint action.
- Coordinate the collaboration with relevant ministries, universities, directorate, RCN, and other relevant national and international actors to support the above tasks.

2. Interaction and cooperation with relevant national and international research infrastructures - In times where we see a high and growing number of national and international initiatives, identifying the key networks and coordinate the efforts put into these, might avoid duplicate work and optimize the outcome of such collaborations.

Description of work (tasks, lead partner and role of participants):

The Project Manager and the Operational manager are responsible for the operation activities of the Secretariat. St. Olav´ (by the Secretariat) reports to the NorCRIN board and RCN. The coordination of activities in the infrastructure is of vital importance and will be strengthened in NorCRIN 2 with a 40 % position for the project manager, 100% NorCRIN Operational manager, 100 % European Correspondent, 20 % to chairman, 10 % position to a controller at the secretariat, 10 % to coordinate international work-tasks and a 50 % position for local coordination at each partner.

Lead partner:
- Secure sufficient resources to the secretariat and handle assigned tasks
- Follow up on WP leaders and deliveries in work packages
- Collect information about all relevant infrastructures
- Establish informal and formal representation in relevant infrastructures
- Make sure the knowledge gained in different research networks are made available to the Norwegian healthcare system.
- Ensure Norway is represented, and have influence, in the relevant networks/collaborations, giving Norwegian research organizations access to international arenas.

Local participants:
- Main communication channel between local NorCRIN node and Secretariat
- Main communication channel between local NorCRIN node and European Correspondent
- Provide support and advice to clinical research projects in accordance with NorCRIN SOPs and guidelines
- Contribute to the work of raising the quality of study staff
- Ensure that procedures and guidance that is anchored to the board are implemented in own hospital and health region
- Propose relevant infrastructures to be included
- Active participation in the collaboration based on local expertise and interests

Deliverables (brief description and month of delivery measured from the project start):

1. Secretarial functions including financial and professional reporting twice a year to NorCRIN Board and RCN

WPs and streamline network;
- follow-up deliverables in all WPs
- arrange combined project and board meetings twice a year (February and September) and working committee meetings - before and after board meetings
- follow up on decisions taken by NorCRIN Board

Policies for publication and the dissemination of research results
- Prepare Annual reports
- Implementation and annually evaluation of communication plan

Participate in regular ECRIN ERIC meetings including summer school (once a year)

2. Obtain and maintain an overview of the most relevant research networks/infrastructures, their scope, goals and outputs.

Ensure Norwegian participation or close collaboration with such infrastructures, to allow Norwegian hospitals and research units to take part in international collaborations and ensure knowledge gained in such networks become available to the Norwegian healthcare system. Will be part of the communication strategy (communication plan) and presented at autumn board meeting

3. NorCRIN will develop well-functioning models for collaboration with relevant research infrastructures. These models will be implemented in each partner institution. Followed-up in board meeting, twice a year.

Estimated cost of the work package and funding from the Research Council: 37,974 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	5 694	5 863	6 040	6 219	6 408	30 224
Other operating expences	1 550	1 550	1 550	1 550	1 550	7 750
Total from participating Institutions	7 244	7 413	7 590	7 769	7 958	37 974

WP2 - Standard operating procedures (SOP) for clinical trials

NorCRIN 1 has published national procedures (SOPs), attachments (templates, checklists, logs), overview documents (laws and regulations and definitions of central terms) and guidelines for clinical trials i) of medical devices and ii) of other interventions iii). These documents are revised according to changes in e.g. the regulatory environment. A major revision of the SOPs for drug trials according to upcoming the Clinical Trial Regulation is in process.

In NorCRIN 2, the SOP group will ensure harmonization of national procedures for all clinical intervention studies (drug, medical devices and other types of interventions), and existing SOPs will be regularly reviewed to mirror national and international clinical research requirements including regulatory changes. The group will work closely with other WPs to ensure an updated and harmonized procedure collection.

Table 10.3: Work package description of WP2

Work package number	WP2	**Lead partner and contact person**	HUS - Anne Mathilde Henden Kvamme
Work package title	Standard operating procedures (SOP) for clinical trials		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:
- Ensure that the SOPs are at all time in line with applicable legislations
- Broaden the scope of the SOPs to include SOPs developed as part of the other WPs such as WP8, WP9, WP10, WP11, WP12 and WP13
- Strive to keep the SOPs user friendly both in terms of their content, and how they are presented on norcrin.no, in close collaboration with WP1

Description of work (tasks, lead partner and role of participants):

Lead partner and deputy leader:
- Collect feedback and suggestions for improvement of the SOPs and templates
- Keep up-to-date with changes in the regulatory environment affecting the SOPs
- Write or ensure needed SOPs/templates are written and aligned the already existing documents
- Coordinate the release of the documents on norcrin.no in a user-friendly way with WP1
- Keep the local participants informed about planned revisions, new releases, regulatory or other changes that might affect the content of the GCP courses
- Report twice a year to the NorCRIN operational manager and to the board (as described in chapter 9)

Local participants from NorCRIN partners:
- Suggestions and quality review for improvement of the SOPs/templates, to SOP/template writing, and to present SOPs in a user-friendly way
- Review SOPs within given timeframe as applicable for SOP release/update
- Participate in scheduled telephone/skype/web meetings
- Ensure the SOPs are incorporated in the hospital's quality system and promote the new SOPs/templates internally in the hospital and towards the other hospitals in their health region

Deliverables (brief description and month of delivery measured from the project start):
- Revised SOPs at least every third year
- Revised SOPs due to regulatory or other major changes affecting the conduct of interventional clinical studies when applicable

Estimated cost of the work package and funding from the Research Council: 1,617 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	290	298	307	316	326	1 537
Other operating expences	40	40				80
Total from participating Institutions	330	338	307	316	326	1 617

WP8 –Data management

Data management is a key element to ensure data collected in clinical studies have the required quality.

The focus in NorCRIN 2 will be standardization of procedures and templates and training of data managers at research support units in all health regions. The Data management unit at OUS has over the years developed into a competent team with a broad project portfolio and will be the driving force in this WP. OUS is expecting to be certified by the ECRIN Data Centre Certification in 2018 and this will serve as a guideline for the work of the WP. The WP will cooperate with the national monitoring group which was a WP under NorCRIN 1, and national meetings will be attended by both groups. The involvement of statisticians (WP9) would also be a clear advantage. Several cross-regional studies will benefit from collaboration between data management, statisticians and monitoring units.

Table 10.4: Work package description of WP8

Work package number	WP8	**Lead partner and contact person**	OUS – Cecilie Moe
Work package title	Data management		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:
The main objective is to develop data management units at all partners' local research support units with competent data management staff, as well as the required quality systems adapted to the local data capture systems. A second objective is the focus on data management as an important part of the interdisciplinary team work facilitating the conduct of clinical studies.

Description of work (tasks, lead partner and role of participants):
Lead partner and deputy leader
- Contribute to the development of local data management units
- Specify requirements for the competence and education of data managers
- Provide training in development of required standards, templates and SOPs
- Create the network of clinical data managers and set up meeting arenas such as workshops and gatherings
- Develop courses in data management for clinical trials
- Promote interdisciplinary cooperation with the national monitoring group and group of statisticians
- Report twice a year to the NorCRIN operational manager and to the board (as described in chapter 9)

Local participants
- Lead the development of data management units at their premises
- Develop and implement international standards, templates and SOPs at their local data management units
- Contribute with suggestions for improvement of the SOPs/templates
- Contribute to SOP/template writing adapted to the local data management unit and data capture system
- Ensure the SOPs are incorporated in the local hospital's quality system and the local data management unit
- Contribute to workshops and gathering
- Contribute with suggestions for the development and improvement of courses
- Contribute to the interdisciplinary cooperation with the national monitoring group and group of statisticians.

Deliverables (brief description and month of delivery measured from the project start):
SOPs and templates for local data management units
Standardisation of data to facilitate data sharing
Meetings/workshops
Course for data management, also for other professional groups and researchers

Estimated cost of the work package and funding from the Research Council: 1,225 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	193	199	205	211	217	1 025
Other operating expences	40	40	40	40	40	200
Total from participating Institutions	233	239	245	251	257	1 225

WP9 – Statistics and advanced methods in clinical research

Statistics is an important area for clinical studies. The discipline is under development, and statisticians with competence and understanding of the proper use of statistics in randomized clinical studies are required to plan and analyse data in a manner that is utilizing the data in a valid, reliable and efficient way.

Table 10.5: Work package description of WP9

Work package number	WP9	**Lead partner and contact person**	OUS – Inge C. Olsen
Work package title	Statistics and advanced methods in clinical research		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:
To ensure good research quality in planning, implementation and reporting of clinical studies, cf. ICH E9 Statistical Principles for Clinical Trials. To create a network of Norwegian statisticians involved in clinical trials and to use this network to increase the quality of research by better design and implementation of statistics.

Description of work (tasks, lead partner and role of participants):
Lead partner and deputy leader:
- Create and lead the network of clinical trials statisticians
- Develop the required templates and SOPs
- Specify requirements on competence and education

- Identify statisticians working with clinical trials in all health regions
- Set up or support meeting arenas such as workshops, gatherings and seminars
- Initiate, coordinate and support courses in statistical methodology for clinical trials
- Participate in relevant national/international working groups or organizations
- Link statisticians to national and international working groups or organizations
- Report twice a year to the NorCRIN operational manager and to the board (as described in chapter 9)

Local participants:

- Contribute with their local expertise to the knowledge transfer within the network (courses or workshops)
- Provide real life examples to illustrate statistical challenges
- Implement consecutively new statistical guidelines and SOPs in their own institution/region

Deliverables (brief description and month of delivery measured from the project start):

- Support framework for statisticians
- SOPs and templates
- Meetings/workshops

Estimated cost of the work package and funding from the Research Council: 1,225 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	193	199	205	211	217	1 025
Other operating expences	40	40	40	40	40	200
Total from participating Institutions	233	239	245	251	257	1 225

WP10 - Organizational units for the conduct of clinical studies

The management and conduct of clinical studies require expertise and skills. The availability of a network of Clinical Trial Wards/Centres (CRW/Cs), Clinical Trial Units (CTUs) and may be other types of units, should ensure consistent quality and offer the necessary infrastructure and service to researchers. The level of maturity related to the organization of core services to conduct clinical trials varies between partners. Thus, in Norway we need to develop a stronger network of such units, developing the capacity in Norwegian hospitals to take part in national and multinational clinical (e.g. ECRIN) studies.

Table 10.6: Work package description of WP10

Work package number	WP10	**Lead partner and contact person**	OUS – Jon B. Borgaard
Work package title	Organizational units for the conduct of clinical studies		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:
The operational goal is to create a stronger national organizational infrastructure to support clinical trials. The overall objective is to increase the number and quality of national and multinational clinical studies, and to encourage more research collaboration nationally and internationally.

Description of work (tasks, lead partner and role of participants):

Lead partner and deputy leader:

- Collect experience from establishing and running CRW/Cs, CTUs and other relevant organisational units, in Norwegian hospitals and corresponding units and infrastructures in other Nordic countries and Europe.
- Define what types of units are relevant in the Norwegian hospitals, and the minimum requirements associated with each type of unit.
- Lead partner and deputy leader will lead and manage the activity of the work in the WP.
- Report twice a year to the NorCRIN operational manager and to the board (as described in chapter 9)

Local participants:

- All partners, independent of their status regarding developing similar units, will be actively involved in all aspects of the work.
- Implement consecutively new guidelines and SOPs in their own institution/region

Deliverables (brief description and month of delivery measured from the project start):

- A description of the types of units and the tasks/responsibilities/structure/expertise of each unit (e.g. CRW/Cs, CTUs and lead CTUs) providing standardised services on a national level (e.g.; study treatment of patients in a ward/bed-side setting, monitoring, data management, project management, pharmacovigilance, regulatory services, etc.)
- A set of requirements/standards to be met for each type of unit providing standardised services within national and multinational studies.
- Advice and support hospitals wanting to establish new or develop existing structures to meet national requirements.
- A certification mechanism for units wanting to conduct clinical trials.
- A description of any barriers to the introduction of a standardised set of requirements for clinical trial support units in the Norwegian setting.

Estimated cost of the work package and funding from the Research Council: 1,225 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	193	199	205	211	217	1 025
Other operating expences	40	40	40	40	40	200
Total from participating Institutions	233	239	245	251	257	1 225

WP11- Framework for facilitating collaborative clinical trials/ Streamlining and facilitating academia-industry collaboration

It is proposed that NorCRIN, in cooperation with the Norwegian Medicines Industry Association, Medtech Norway and other Biotech Cluster Organizations, examine the prerequisites and model for an organizational solution or suitable structure to facilitate and streamline collaboration between academia and industry. Furthermore, and in line with this focus we believe that NorCRIN 2 and WP11 could be of strategic and operational importance in connection with the implementation of the announced "Innovasjonsmelding" from the Norwegian Government which will have a special emphasis on the health sector and how to create a health industry through strategic partnership and collaboration.

The budget for WP11 covers a 20 % position to all partners.

Table 10.7: Work package description of WP11

Work package number	WP11	**Lead partner and contact person**	OUS-Peder Utne
Work package title	Framework for collaborative clinical trials/ Streamlining and facilitating academia- industry collaboration		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:
NorCRIN will gather clinical researcher and other stakeholders such as TTO`s, biomedical, Medtech cluster organizations, to examine and develop models and framework for collaboration between researchers and industrial partners. The aim should be to create a legal and ethical environment for collaboration and to professionalize the collaboration process from beginning to the end. The assignment will also include how to model an efficient network to support researchers, research organisations and industry in formalizing collaborating projects.

Description of work (tasks, lead partner and role of participants):
Lead partner and deputy leader:
- Take initiative to develop a specific working plan for WP11 with milestones and deliverables, including a plan for involvement of stakeholders in relevant activities
- Coordinate the work with the goal to identify needs and bottlenecks in different phases of industrial collaborations; from feasibility to how to secure legal and ethical aspects regarding ownership and reuse of data
- Collect and examine existing national and international SOPs and templates for industrial collaboration
- Coordinate and facilitate workgroups among the partners and other stakeholders (incl. TTO`s and cluster organisations in the field of biomedicine and medtech) to construct a code of conduct by developing a set of procedures and templates
- Developing Guideline for best practice with the aim to support both the research institutions and the industry when engaging in research collaboration
- Initiate a pilot to test the SOP in the WP for Innovation and industrial relations expected to be embedded in the Centre for Clinical Research in regenerative medicine
- Establish and coordinate network for dissemination and support among the partners and other stakeholders on how to operationalize the SOP among the Consortium partners and other relevant stakeholders
- Report twice a year to the NorCRIN operational manager and to the board (as described in chapter 9)

Local participation from NorCRIN partners
- Responsible for gathering input and identify relevant cases from own organisation to fully understand different aspects of industrial collaboration and the environment for such collaborations both structurally and the ethical and legal framework
- Participate in workgroups initiated by Lead partner
- Contribute to develop guidelines and testing of SOPs in local environment to collect value input for own researchers and industrial partner on how to create a professional and sound framework for collaboration
- Responsible for dissemination and implementation of SOP in own region and institution

Deliverables (brief description and month of delivery measured from the project start):
- Identify the needs among researcher, industry and cluster organisations on how to create a mutual understanding on how to build a competitive and professional framework for collaboration.
- Develop a first set of SOP based on the identification process.
- Implementation of SOP as part of a pilot
- Review, adjust and develop new SOPs as part of the results from the Pilot
- Finalize the SOP and dissemination on the NorCRIN web-platform
- Establishment of supporting group among the partners and relevant stakeholders
- Contribute in the implementation of the announced "Innovasjonsmelding" and other national initiatives focusing on innovation in the field of biomedicine and medtech.

Estimated cost of the work package and funding from the Research Council: 7,174 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	1 351	1 393	1 434	1 477	1 519	7 174
Other operating expences						-
Total from participating Institutions	1 351	1 393	1 434	1 477	1 519	7 174

WP12 – Pragmatic clinical trials, including registry based randomized clinical trials

Pragmatic clinical trials are characterized by 3 attributes: (1) focus on informing decision-makers (e.g. patients, politicians, administrators) on optimal clinical medicine practice, as opposed to elucidating a biological or social process; (2) intent to enrol a population representative to the decision in practice and for whom the decision is relevant; and (3) either an intent to streamline procedures and data collection in the trial or to measure a broad range of outcomes. Accordingly, pragmatic clinical trials use designs from RCTs in general hospital wards to test already implemented strategies head-to-head with intent to inform decision-makers concerning what is the best strategy for real-life patients. Moreover, by utilizing resources already paid for by the hospitals (physicians and nurses in daily clinical practice), pragmatic clinical trials can include a larger number of patients at a short time duration and at a lower cost than studies utilizing traditional RCT designs with an external study organization (e.g. study nurses, study physicians). One specific subtype of pragmatic clinical trial is registry-RCT, which utilizes the platform of a clinical quality registry to recruit and randomize patient in prospective interventional studies. To conduct such trials in Norway there is a need to bring together infrastructures related to interventional trials, registries and clinical researchers, and WP12 will aim to lead this process in Norway. Important issues related to data protection, ethics and trial monitoring will also need to be resolved.

Table 10.8: Work package description of WP12

Work package number	WP12	**Lead partner and contact person**	Ahus – Magnus N. Lyngbakken
Work package title	Pragmatic clinical trials including registry based randomized trials (RRCT)		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:
To establish what is needed to be able to run pragmatic clinical trials in Norwegian patients within the legal framework based on data generated from routine clinical practice or registries.

Description of work (tasks, lead partner and role of participants):
Lead partner and deputy leader:
- To bring together infrastructures related to interventional trials, registries, and clinical researchers with the aim of starting pragmatic clinical trials
- Identify the possibilities and hurdles existing today, in order to be able to run RRCTs or pragmatic studies
- Collect and provide the clinical research community with updated information on national and international initiatives to solve these challenges
- Identify the possibilities and hurdles existing today, in order to be able to perform pragmatic clinical trials, including issues related to data protection and ethics
- Develop and provide to partners national SOPs that will enable start and execution of pragmatic clinical trials, including registry-RCTs
- Report twice a year to the NorCRIN operational manager and to the board (as described in chapter 9)

Local participants:
- Provide information about local technical systems and challenges
- Provide relevant examples for pilot-testing of new systems
- Implement national systems in own region/institution

Deliverables (brief description and month of delivery measured from the project start):
- A clear understanding of any barriers existing today, and a proposal on how such barriers can be overcome
- Guidelines on how to technically conduct this kind of research
- The support by NorCRIN 2 of initiation of one or more interregional pragmatic clinical trials.

Estimated cost of the work package and funding from the Research Council: 1,425 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	193	199	205	211	217	1 025
Other operating expences	80	80	80	80	80	400
Total from participating Institutions	273	279	285	291	297	1 425

WP13 – Patient and public involvement (PPI) in clinical trials

The Norwegian Health & Care strategy and action plan point out that patient and public involvement (PPI) is essential to improve relevance and quality in clinical health research. Both national and international guidance emphasize that PPI in health research should be considered at all levels in the research process from deciding on areas to be researched, input to the design and planning of research, carrying out the research, to dissemination and implementation of research results.

Table 10.9: Work package description of WP13

Work package number	WP13	**Lead partner and contact person**	UNN – Tove Aminda Hanssen
Work package title	Patient and public involvement (PPI) in clinical trials		
Partners	Representatives from all NorCRIN partners (local participants)		
Start month	01/2020	**End month**	12/2024

Objectives:
The aim is to provide an overview of models, assess learning needs and develop tools to involve users including patients and public in clinical trials. Further to collaborate with relevant Norwegian partners to successfully involve users, patients and stakeholders in all relevant aspects of the research process to promote quality and relevance in clinical trials; hence reduce research waste.

Description of work (tasks, lead partner and role of participants):
Lead partner and deputy leader:
- Describe systems and practice for PPI in Norwegian clinical trials
- Initiate collaboration with relevant Norwegian partners on PPI (Norw Cancer Soc, EUPATI, Research Council Norway, others)
- Assess infrastructure needs for successful PPI in clinical trials
- Assess researcher and patient learning needs for successful PPI in clinical trials
- Develop and evaluate e-learning material/course on PPI in research for researchers and patients
- Report twice a year to the NorCRIN operational manager and to the board (as described in chapter 9)

Local participants:
- Provide information on local practices for PPI in clinical trials
- Take part in data collection regarding patients, users, researchers and other stakeholders learning needs
- Contribute and participate in work groups for guidance and educational meetings
- Implement consecutively new guidelines and SOPs in their own institution/region

Deliverables (brief description and month of delivery measured from the project start):
1. Documentation of systems/models and practice for PPI in Norwegian clinical trials
2. Description of infrastructure needs for PPI in clinical trials
3. Description of learning needs in users and researchers related to PPI in clinical trials
4. Educational guidance is harmonized in SOPs for researchers and patients/users
5. E-learning material on PPI for researchers and patients is developed and evaluated in collaboration with relevant partners
6. Information and e-learning material about PPI in clinical trials is available on NorCRIN web site for Norwegian researchers
7. Workshops and meetings to contribute to national development on PPI in Norway

Estimated cost of the work package and funding from the Research Council: 1,225 MNOK

Budget i 1000 NOK	2020	2021	2022	2023	2024	Total
Payroll and indir expenses	193	199	205	211	217	1 025
Other operating expences	40	40	40	40	40	200
Total from participating Institutions	233	239	245	251	257	1 225

The major deliveries in NorCRIN 2 are listed in Table 10.10.

Table 10.10: List of deliverables

Number	Deliverable name	Work package number	Lead partner (Contact person)	Delivery date (in months from project start)
1	Management and coordination of NorCRIN2	WP1	Sigrun K. Sæther	31. December 2024
2	Standard Operating Procedures SOPs) for clinical trials	WP2	Anne Mathilde H. Kvamme	31. December 2024
3	Data management	WP8	Cecilie Moe	31. December 2024
4	Statistics and advanced methods in clinical trials	WP9	Inge C. Olsen	31. December 2024
5	Organizational units for the conduct of clinical studies	WP10	Jon B. Borgaard	31. December 2024
6	Strategies for facilitating collaborative clinical trials/ Streamlining and facilitating academia- industry collaboration	WP11	Peder Utne	31. December 2024
7	Pragmatic clinical trials, including registry based randomized clinical trials (RRCT)	WP12	Magnus N. Lyngbakken	31. December 2024
8	Patient and public involvement (PPI) in clinical trials	WP13	Tove Aminda Hanssen	31. December 2024

The major milestones in NorCRIN 2 are listed in Table 10.11.

Table 10.11: List of milestones

Number	Milestone name	Related work package(s)	Due date (in months from project start)	Means of verification
1	Partner report twice a year	All WPs	June/December	Project manager, operational manager and member of Board meeting
2	Board meeting twice a year	All WPs	February/September	Members of Board meeting
3	Status meeting with RCN	All WPs	Before 1. Oct each year	Project manager, operational manager and controller
4	Annual report to RCN. Responsibility: Operational manager	All WPs	January each year	Project manager and Charmain

11. Risk analysis and mitigation measures

The major risks in NorCRIN 2 are listed in Table 11.1.

Table 11.1: Risk analysis and mitigation measures

Description of risk	Likelihood	Consequence	WPs involved	Proposed risk mitigation measures
Risks related to the organisation and structure				
The partners are hospitals of different size and resources. • Doing different kind of studies • With personnel being more or less specialized • Costs for travelling can be problematic for UNN	low moderate	moderate moderate	All WPs WP1, 2, 10, 12	Ensure that all partner's needs are covered by agreements in the board Extra travel expenses are included in the budget
Changes in major roles such as project leader, chairman	moderate	severe	All WPs	Followed up in board meeting
NorCRIN 2 has a larger scope that NorCRIN 1 involving more people from the partners and requiring more coordination	Low	moderate	WP 1	Ensure commitment from the secretariat and partners to rapid response to questions
The partners must allocate the needed resources with the right competence	Moderate	moderate	All WPs, especially WP 8, 9 and 12	Committed trough LoC, follow up in project- and board meeting
NorCRIN 2 need to collaborate with other infrastructures and institutions/ enterprises. Coordination and communication can be challenging.	Moderate	severe	WP 1, 11, 13 and (8)	Ensure the expectations of the different external parties/collaborators are realistic and clearly communicated
The purpose with NorCRIN 2 is to support clinical research and the researchers. To achieve this the researcher must view NorCRIN as relevant and accessible for them	Low	severe	All WPs	Communication and feedback from the researchers should be sought in general and for the relevant WPs
NorCRIN 2 as NorCRIN 1 is not a legal entity and has no formal authority towards its partners	Low	moderate	WP1, 2, 10, 12, 13	Commitment to NorCRIN decisions. A well-functioning executive committee
Collaboration and sharing of information, also sensitive data has to adhere to GDPR. The practice regarding this differs among the partners. This makes it difficult to establish national e-solutions.	high	severe	WP1	Departments in partner institutions working with data protection must cooperate in WP12
Economic consequences with a reduced budget (chapter 12)	moderate	moderate	All WPs	Customize the work
Risk related to technology Norcrin.no not being available	moderate	low	All WPs	The contract specifies 24-7 support

Likelihood are described in term of Low / Likely / Highly likely
Consequence are described in term Minimal / Moderate / Severe

Mitigation plan for risks that are "likely to occur" and risk with a "low probability and high consequence" will be produced. The identified risks and actions (in Table 11.1 marked in red) will be follow-up in scheduled project meetings, board meetings and meetings in the work committee as listed in Table 10.11 List of milestones. Deviations from the progress plan will be followed up annually with RCN. In addition, risk and mitigation will be described in the RCN Annual Report.

12. Cost- and funding plan

Cost centres include existing infrastructures (NorCRIN 1), and the infrastructure applied for (NorCRIN 2) is shown in Table 12.1.

The Establishment phase is estimated to 426.7 MNOK and operational phase is estimated to 426.3 MNOK, the total amount of 853.0 MNOK. Differences among partners in the way own budget is presented are due to variation in organization of research support.

Table 12.1: Overview resources invested in NorCRIN by the partners Cost centres and applied infrastructure

Overviev Cost center - (in 1000 NOK)	2020	2021	2022	2023	2024	Sum Etab. Fase	2025	2026	2027	2028	2029	Sum Driftsfase	Total
University Hospital of Northern Norway	18 394	18 943	19 508	20 090	20 679	97 614	20 260	20 866	21 490	22 133	22 794	107 543	205 157
St. Olavs hospital, Trondheim University hospital	12 080	12 379	12 689	13 006	13 335	63 489	8 317	8 550	8 789	9 035	9 288	43 978	107 467
Haukeland University Hospital, Bergen	12 909	13 790	14 332	14 916	15 502	71 449	15 945	16 402	16 871	17 354	17 851	84 424	155 873
Stavanger Universtity Hospital	5 843	5 965	6 142	6 323	6 508	30 781	5 920	6 097	6 279	6 466	6 659	31 422	62 202
Oslo University Hospital	28 035	28 867	29 724	30 184	30 253	147 062	27 507	28 325	29 168	30 036	30 930	145 967	293 029
Akershus University Hospital	3 065	3 154	3 246	3 381	3 438	16 286	2 453	2 527	2 602	2 680	2 761	13 023	29 309
Total from participating Institutions and NRC	80 325	83 098	85 642	87 900	89 715	426 680	80 403	82 766	85 199	87 705	90 284	426 357	853 036

The Establishment phase: The Establishment costs are related to the work-months for development of the infrastructure, and to cover personnel and other costs for establishing the infrastructure (description of WPs, chapter 10). Table 12.2 specifies the costs related to the establishment phase and the operational phase.

Table 12.2: Overview cost elements invested in NorCRIN by the partners Cost centres and applied infrastructure

Overviev cost element (in 1000 NOK)	2020	2021	2022	2023	2024	Sum Etab. Fase	2025	2026	2027	2028	2029	Sum Driftsfase	Total
Payroll and indir expenses	74 133	76 870	79 367	81 539	83 273	395 181	75 526	77 792	80 125	82 529	85 005	400 977	796 158
Other operating expences	6 192	6 228	6 275	6 361	6 442	31 498	4 877	4 974	5 074	5 175	5 279	25 380	56 878
Total from participating Institutions	80 325	83 098	85 642	87 900	89 715	426 680	80 403	82 766	85 199	87 705	90 284	426 357	853 036

Table 12.3 shows how the NRC funds are spread across the WPs. Budget details for each work packages are presented above under "Work plan, time-schedule and deliverables" chapter 10.

Table 12.3: RCN financial distribution toward each work package

WP	Work package (in 1000 NOK)	2020	2021	2022	2023	2024	Total
1	Management and coordination of NorCRIN	7 244	7 413	7 590	7 769	7 958	37 974
2	Standard Operating Procedures for clinical trials	330	338	307	316	326	1 617
8	Data management	233	239	245	251	257	1 225
9	Statistics and advanced methods in clinical trials	233	239	245	251	257	1 225
10	Organizational units for the conduct of clinical trials	233	239	245	251	257	1 225
11	Strategies for facilitating collaborative clinical trials/ Streamlining and facilitating academia- industry collaboration	1 351	1 393	1 434	1 477	1 519	7 174
12	Registry based randomized clinical trials (RRTC)	273	279	285	291	297	1 425
13	Patient and public involvement (PPI) in clinical research	233	239	245	251	257	1 225
	Total	10 130	10 379	10 596	10 857	11 128	53 089

Funding sources for the establishment/implementation of the infrastructure including own funding from the host institution, partners and RCN are shown in Table 12.4.

Table 12.4: NorCRIN infrastructure budget

Overviev financial element (in 1000 NOK)	2020	2021	2022	2023	2024	Sum Etab. Fase	2025	2026	2027	2028	2029	Sum Driftsfase	Total
Own financing	61 365	62 289	63 354	63 329	63 731	314 068	65 380	67 443	69 581	71 785	74 057	348 245	662 313
Other public funding	2 620	3 220	3 652	4 540	4 900	18 932	4 900	4 998	5 098	5 200	5 304	25 500	44 432
Other private funding	5 370	6 171	6 856	7 694	8 356	34 446	8 523	8 693	8 856	9 022	9 191	44 286	78 732
International funding	840	1 040	1 184	1 480	1 600	6 144	1 600	1 632	1 665	1 698	1 732	8 326	14 470
Research Council Grant	10 130	10 379	10 596	10 857	11 128	53 089						-	53 089
Total from participating Institutions	80 325	83 098	85 642	87 900	89 715	426 680	80 403	82 766	85 199	87 705	90 284	426 357	853 036

Operation of the infrastructure: Running and operation of the infrastructure (including the project period) for a period of 10 years are shown in Table 12.2. Costs related to personnel, ECRIN-ERIC and CRIGH fee are covered by the budget in WP1. Funding sources for the running costs of the infrastructure after the funding from the Research Council will be own funding from the host institution(s) and the other partners and funding from the user groups, as shown in Table 12.4.

Annual income: User payments are defined by each partner in most cases and during common agreement in other cases. Table 12.5 shows the estimate for the annual income from projects that pay to use the infrastructure.

Table 12.5: Estimate of user payments

Overviev financial element (in 1000 NOK)	2020	2021	2022	2023	2024	Sum Etab. Fase	2025	2026	2027	2028	2029	Sum Driftsfase	Total
University Hospital of Northern Norway	200	204	208	212	216	1 041	221	225	230	234	239	1 149	2 190
St. Olavs hospital, Trondheim University ho	330	337	343	350	357	1 717	364	372	379	387	394	1 896	3 613
Haukeland University Hospital, Bergen	3 000	3 570	4 080	4 590	5 100	20 340	5 202	5 306	5 412	5 520	5 631	27 071	47 411
Stavanger Universtity Hospital	500	510	520	531	541	2 602	552	563	563	563	563	2 804	5 406
Oslo University Hospital	4 300	5 300	6 020	7 500	8 100	31 220	8 132	8 295	8 461	8 630	8 802	42 319	73 539
Akershus University Hospital	500	510	520	531	541	2 602	552	563	574	586	597	2 872	5 474
Total from participating Institutions	8 830	10 431	11 692	13 714	14 856	59 522	15 023	15 323	15 619	15 920	16 227	78 112	137 634

The activities in the project are non-economic activity, as defined in the EFTA Surveillance Authority's (ESA) Guidelines for State Aid for Research, Development and Innovation, paragraph 19 and with reference to the dialog meeting for project 245876. The activities consist of tasks that are necessary in any research organization, and partly by exchanges of expertise between hospitals and industry. NorCRIN will not offer sales to industry or have economic profits. Costs of the activities carried out in cooperation with industry account for about 2% of the total budget in NorCRIN. The health enterprises have established an accounting separation between economic and non-economic activity, so that no cross-subsidization occurs.

NorCRIN 2 applies funding of **53.089 MNOK**. The applied budget is a minimum budget to ensure that the infrastructure will still have significant potential for utilisation even if the Research Council does not provide additional funding. Consequences and mitigation are discussed in chapter 11. A reduction of the local contact nodes from a 50 % position to a 40 % position may be acceptable. The minimum infrastructure budget will be 50.527 MNOK.

13. Environmental and ethical perspectives

Strengthening of the NorCRIN infrastructure and establishment of high-quality coordinated CTUs in each health region will have positive natural environmental impact, as it may modernize communication strategies and streamline local support in each region to clinical research. As an example, the access to similar SOPs, coordinated monitors and similar procedures at each CTU will decrease the need for travel related to monitoring activities in multi-centre studies. In NorCRIN 2, we aim to improve communication channels using modern facilities for video conferences at each CTU, all to reduce needs for personnel travelling. Additionally, NorCRIN 2 will promote the use of electronical trial master files for multi-centre clinical studies, which will dramatically reduce the use of paper and less CO_2 emission. Re-use of data and facilitating synergy between various relevant infrastructures will also reduce the environmental carbon foot-print of clinical research.

Global ethical and regulatory guidelines and national regulations are established to secure the safety and integrity of human subject in clinical research. The gold standard for performing clinical studies relies on "Good Clinical Research Practice" (GCP). GCP ensure that clinical research participants are not exposed to undue risk, and that data generated from the research is both internally and externally valid. This was expanded beyond pharmaceutical interventions in NorCRIN 1. In NorCRIN 2 we will continue the work of promoting the importance of GCP courses. We intend to reach a larger audience by promoting local GCP courses, but also electronical courses. As associated to CRIGH we will benefit from knowledge from their ongoing comparisons and harmonization of research ethics system in non-commercial clinical trials.