

Proposals for measures to create better conditions for clinical trials

– for better welfare and a stronger life
science sector

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Summary

This inquiry is one of a series of inquiries and initiatives that have been directly or indirectly commissioned to address conditions for clinical studies and clinical trials in Sweden. We describe how these have progressed over the past ten years and present concrete proposals for improving conditions to the benefit of the patient as well as the profession's ability to "say yes" to conducting clinical trials, thus benefiting the Swedish life science sector's competitiveness.

The inquiry is based on materials produced by others, our own external analysis and an inventory of obstacles and opportunities, as well as extensive dialogues with actors in the Swedish life science sector.

The clinical trial forms part of a complex ecosystem in which the pace of change is high and the opportunities can be considered inexhaustible. The inquiry does not purport to be exhaustive, and in our proposals we have struck the necessary balance between far-reaching reforms and concrete action plans that can be implemented immediately. Our opinion is that Sweden needs to act now, which has coined the inquiry's priorities. The obstacles that clinical trials are facing today require putting new solutions in place swiftly and sustainably.

1. Remit and execution

The purpose of a clinical trial is to develop tomorrow's options for preventing ill health, curing disease or offering relief. The conditions we lay down for clinical trials today play a crucial role in enabling the development of healthcare and early access to new treatments.

To enable submitting proposals that take account of the inhabitant, patient and society perspective and contribute new knowledge, our analysis has proceeded on the basis of the term *clinical study*, after which proposals and measures have specifically targeted the clinical trial, particularly the company-initiated drug trial.

The inquiry's work has consisted of three main elements: external analysis, dialogue meetings and a mission-driven design process. In the external analysis, we have taken account of past and ongoing official government inquiries, commissions for government agencies and a series of published materials relevant to clinical research, clinical studies and clinical trials.

The progression in the number of clinical studies and clinical trials worldwide for 2008–2021 is primarily based on data from the ClinicalTrials.gov database, and for Sweden for 2013–2022 on data from the Swedish Medical Products Agency and the Swedish Ethical Review Authority.

To gain perspective on actor-specific issues we have, based on the inquiry's remit and targets, held dialogue meetings with representatives of the healthcare sector, academia, industry, government agencies and patient organisations.

To further the image of Sweden in an international perspective, we have held interviews with relevant representatives from Australia, Norway and Denmark. The inquiry has developed a *'Roadmap for Clinical Trials'* through a mission-driven design process established by Vinnova in its work on changes at the systemic level. In order to structure the work of the inquiry and create a common reference to enable specifying obstacles, opportunities and proposed solutions, we have drawn up a simplified *process description of the clinical trial*.

2. Sweden has not been able to reverse the negative trend for clinical drug trials

During the period 2013–2022, clinical trials had the same progression as described in SOU 2013:87; i.e. a downward trend for the total number of approved clinical drug trials in Sweden. In 2021, an increase is seen in the number of approved applications, which is probably a “pandemic effect”; that is, heightened research activity related to the covid-19 pandemic, which we consider to be of a

temporary nature. The statistics for 2022 show a return to 2019 levels. The decline in the total number of approved clinical trial applications for the period 2013–2022 is 22 per cent. The distribution between commercial and non-commercial sponsors is relatively evenly distributed over time, with 70 per cent of trials with commercial sponsors and 30 per cent of trials with non-commercial sponsors.

In the inquiry’s dialogue meetings, the participants return to the experience that clinical studies and clinical trials in the healthcare system are downprioritised¹ and that it is difficult to obtain time and resources for these activities in parallel with core healthcare operations.

Figure 2.1 Total number of approved clinical drug trials, 2013–2022

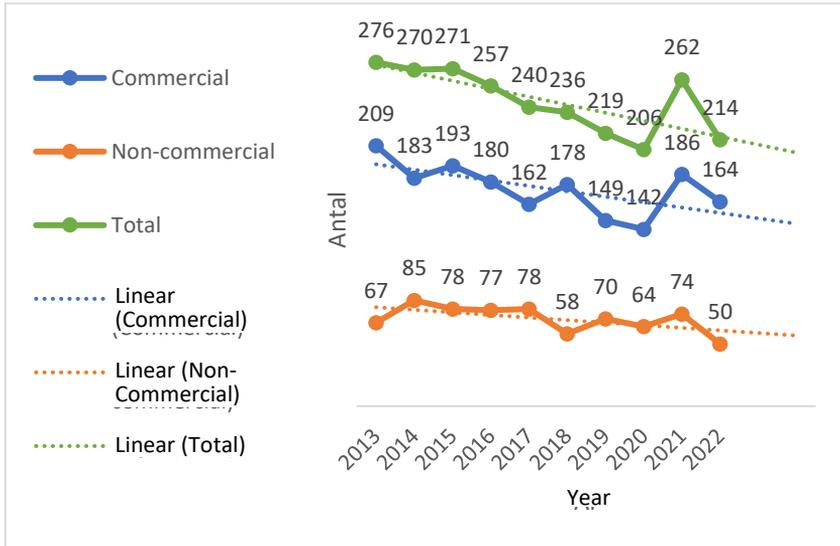


Source: The Swedish Medical Products Agency

When we break down the material and look at the progression in the number of commercial (i.e. company-initiated) clinical trials, the decrease over the same period is 22 per cent, and for 2022 the number is on a par with the 2017 level. In 2022, the non-commercial, or investigator-initiated, trials show a historically low number for the period, with only 50 approved drug trials in 2022, representing a decline of 25 per cent over the period.

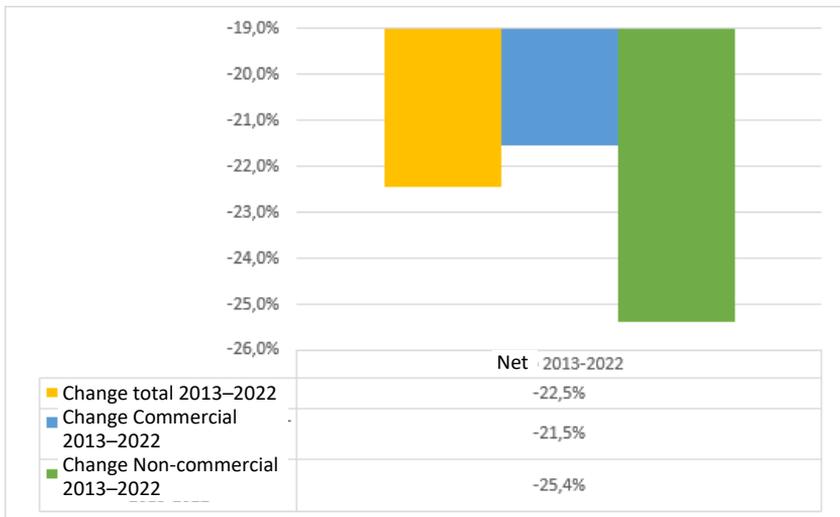
¹ Reference inquiry’s dialogue meetings.

Figure 2.2 Total number of approved clinical drug trials, 2013–2022
 Broken down by commercial and non-commercial sponsor



Source: The Swedish Medical Products Agency

Figure 2.3 Change (%) in the number of approved clinical trial applications in Sweden broken down by type of sponsor, 2013–2022



Source: The Swedish Medical Products Agency

In the material broken down by type of sponsor, there is pronounced covariation in the trend curves over time; that is, when

one type increases, the other appears to fall, and vice versa. The progression over time as a percentage also varies depending on the time period we choose to look at. If we exclude the 2020–2021 pandemic years, where we see a significant increase in research activity related to covid-19, we obtain different numbers. If we go back in time and include data from the analysis commissioned by SOU 2013:87, we obtain other absolute numbers. Irrespective of which cross-section of data, type of sponsor or between which years we choose to report, Sweden has not been able to reverse the continuing downward trend in the number of drug trials.

The number of clinical trial applications can be placed at parity with the number of ethical review applications for medical research on humans. When we perform that analysis, it can be seen that the clinical trial represents 5 per cent on average for the period. It is worth noting that the number of ethical review applications for medical research on humans shows a positive trend, as these have increased by an amount equalling 29 per cent (including different types of studies, i.e. observational and interventional studies). It is not possible to break down the ethical review applications by entity responsible for the research, i.e. commercial or non-commercial. The Swedish Ethical Review Authority does not currently provide this information. The proportion of clinical trials out of the total number of ethical review applications in Sweden is low in absolute numbers, and lower than the corresponding number for Denmark and Norway, where the proportion is ~15–25 per cent. In our opinion, this percentage figure may be worth monitoring over time in Sweden and in relation to other countries.

For medical technology trials, there are unfortunately no statistics on the progression, which both the inquiry and industry organisation Swedish Medtech find regrettable. Extensive regulatory changes at the European level in the application and authorisation procedure have affected the number of applications received for medical technology trials and the information available should therefore be interpreted with caution. The inquiry determines that it is important to take measures to enable monitoring the progression of medical technology trials also. In interviews conducted by Swedish Medtech, member companies point to a shift in medical technology trials from Europe to the US and link this to the new European regulation on CE marking in Europe.

2.1 Volumes of phase I trials are stable in Sweden

In an in-depth analysis of the progression in clinical trials (phases I–IV) in Sweden, based on statistics from the Swedish Medical Products Agency, a stable trend curve is seen with ~30 approved phase I trials/year. The commercial sponsor represents around 70 per cent of all approved phase I trials in the past ten years. Our opinion is that Sweden has stable planning and implementation capacity for early-phase trials, particularly with reference to phase I. The inquiry invited representatives of the six phase I units in Sweden that regularly undergo supervision by the Swedish Medical Products Agency, as well as representatives from the Swedish Ethical Review Authority, Biobank Sweden and the Swedish Medical Products Agency, into a dialogue aimed at identifying measures that could further improve Sweden's early-phase competitiveness. The representatives highlighted a number of priority areas for development, including time, merit value and incentives for physicians to serve as clinical trial investigators in a company-initiated early-phase trial, the often advanced biomaterials management and the desire for increased implementation capacity in the healthcare system. Also, the participants pointed to the potential in facilitating the referral of patients from a different county or country to clinical trials, for whom the cost burden for routine healthcare is often unclear. Finally, proposals were presented for advanced national cooperation between the phase I units, which could strengthen Sweden's position within early phase internationally.

2.2 Lead times and delivery capabilities

Companies in the life science sector apply far more detailed measures for clinical trial performance than those available to us at the national level; that is, the number of clinical trial applications, and approved applications. Today, there is no nationally recognised practice and directly comparable key numbers, which has made it difficult for the inquiry to evaluate and provide a fair depiction of Sweden's performance, individually and compared with other countries. We asked industry representatives to provide the inquiry with data for an analysis of performance at the national level. This

has proven impossible with the resources we have had at our disposal and instead we invited the industry organisations for pharmaceutical and CRO companies to a dialogue meeting. It is clear that lead times (especially start-up times) and patient recruitment (in relation to set targets) are absolute key performance indicators and that, in the past few years, Sweden appears to have gone from being “the fastest country” to exhibiting instead rising lead times and declining patient recruitment in relation to targets.

In the UK, a report is presented annually that ranks countries globally on the basis of competitiveness indicators and key numbers for the life science sector. Based on the latest report from 2022² that presents median times, for a subset of commercial trials with new drugs including all trial phases, the lead time from application for clinical trial to the first patient receiving an initial dose was 140 days up to 260 days during the period 2018–2020³. The equivalent length of time for Sweden, in our material from our dialogues, is 155 days, which suggests that, in terms of start-up lead times, Sweden is on par with a number of other European countries. In terms of the number of recruited patients in relation to set targets (delivery capability), the same dialogue meetings reveal highly disparate information, which suggests that Sweden has deteriorated in some cases and in others is on a par with or above the global average. The flow of requests for studies to Sweden remains stable according to the dialogues with pharmaceutical companies, CRO companies and a number of clinical trial units and other healthcare representatives. However, it is concerning that the number of requests that lead to contractual cooperation – i.e. an activated trial site (corresponding to a clinic or operational area) – is as low as 20 per cent in some cases. Here, there are probably tremendous variations for different therapeutic areas and in trial protocol complexity, etc. and Sweden is better equipped for certain indications and therapeutic areas than others. All in all, lead times and delivery capabilities are two of many important key performance indicators that are essential to follow at the national level and with a common nomenclature. We note that

² Life science competitiveness indicators 2022, published 21 July 2022 (gov.uk).

³ The countries compared are Canada, France, Italy, the United Kingdom, the Netherlands, Germany, Switzerland, Spain, Australia, and the United States.

countries like Denmark have developed methods and systems for following these key performance indicators at the national level.

3. Sweden in an international comparison

In the inquiry's international overview, we describe the development of company- and publicly funded clinical studies and clinical trials over the period 2008–2021, based on data from the ClinicalTrials.gov database⁴. We highlight the progression globally and for a sample of nine different countries. From there, we narrow the overview down to four countries that we find comparable to Sweden and of particular interest to the inquiry based on the actual progression of clinical trials, organisation and funding of healthcare or type of measures implemented to reverse the same type of trend that we are currently witnessing in Sweden.

The global volume of clinical studies – i.e. the broader term than a clinical trial – increases during the period 2008–2021. The heightened research activity described by various materials as being due to the covid-19 pandemic is also found in this body of data. For 2021, it is reported that 4,238 studies (12 per cent) are covid-19-related studies and the corresponding figure for 2020 is 2,802 studies (8 per cent) – a substantial volume of studies linked to an extraordinary event.

In this material, the company-funded clinical studies globally make up 24–47 per cent of the total number of clinical studies. These decline by 6 per cent during the period 2008–2019, i.e. excluding the covid-19 effect. A larger decline, equalling a drop of 21 per cent, is seen in 2008–2013. During the same period, the global number of non-company-initiated clinical studies also rises – an increase that should be interpreted with caution as it might be partly due to heightened reporting. The total number of clinical trials (phase I–IV) globally is unchanged, while company-initiated clinical trials globally fall by 21 per cent.

When we narrow down the material further and look at company-funded drug trials globally by category, we see that phase I trials increase by ~70% and phase II trials recover after a decline during 2008–2013, to return in 2019 to the 2008 levels. Non-trials (i.e.

⁴All data has been retrieved from ClinicalTrials.gov in October and November 2022.

interventional studies that are non-drug trials) are increasing and phase III and phase IV trials are unchanged or declining. The companies fund ~50 per cent of clinical drug trials globally and the remainder are publicly funded.

It is reasonable to assume from this data that Sweden is competing for a globally dwindling volume of company-initiated drug trials. The progression of phase I–IV trials and non-trials shows that phase I–II are increasing and phase III–IV are decreasing, which could reflect the prioritisations of companies. At the same time, we note that companies fund a considerable volume of clinical studies, including non-trials, which are not within the direct scope of this inquiry.

In terms of the progression of company-initiated drug trials measured as number per 100,000 inhabitants, we note that for 2021 countries with a relatively small population basis, such as Denmark and Belgium, report 3–5 clinical trials per 100,000 inhabitants, while countries like Sweden, Norway and Finland rank much lower with 1–2 clinical trials per 100,000 inhabitants. Countries with a much larger population basis, such as Germany and the UK, report <1 clinical trials per 100,000 inhabitants. Thus, population basis is not decisive in attracting company-initiated clinical trials to a country. By trial phase, the progression in these countries differs, and Denmark stands out in retaining its total volumes and increasing the number of phase I and II trials. Norway reduces its volumes with the exception of phase I trials where, like in Sweden, it appears to retain its volumes. The UK continues to show a decline across all phases.

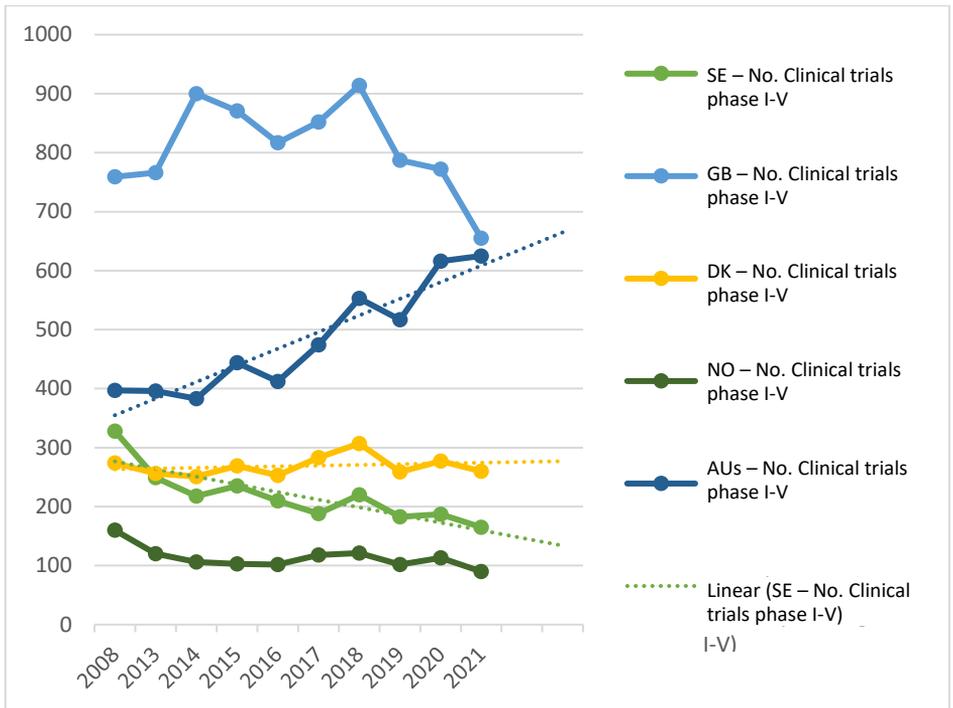
As early as ten years ago, Denmark and the United Kingdom put measures in place aimed at improving the conditions for clinical trials, and the results differ today in terms of actual progression over time. Australia and Norway were not included in the report⁵ to which we refer in our memorandum, but both countries, like Denmark and the UK, have made targeted efforts to reverse a trend similar to that we are witnessing in Sweden.

The progression in the number of clinical trials in Australia, Denmark, Norway and the UK for 2008–2021 differs from that in

⁵ Clinical trials – policy initiatives and trends 2014:01, Swedish Agency for Growth Policy Analysis.

Sweden and in terms of the total number of phase I–IV clinical trials irrespective of type of sponsor (commercial and non-commercial). In Sweden, the trend we described earlier is still declining, while Denmark maintains its levels and the UK has fluctuated, albeit showing a decline since 2017. Norway also shows a decline in this material, while the statistics for Australia show a clear upswing.

Figure 3.4 Total number of clinical trials (phase I–IV) irrespective of type of sponsor, in Australia, Denmark, Norway, the UK and Sweden



Source: ClinicalTrials.gov (autumn 2022).

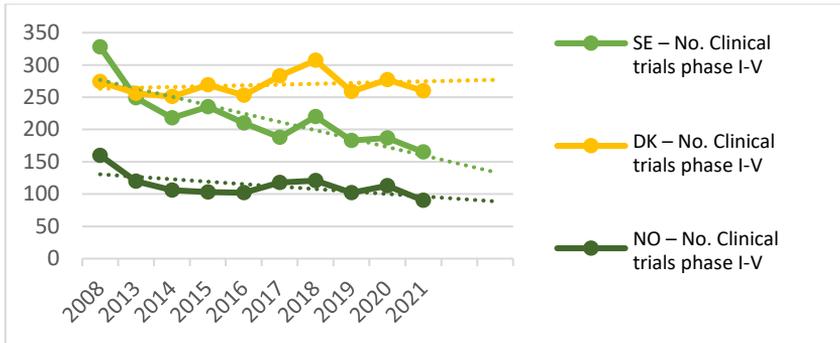
We have placed the actual progression of company- and non-company-funded clinical studies in the last fifteen years in relation to the organisation and funding of the healthcare system, and the specific measures and initiatives that have been aimed at improving the conditions for company-funded clinical trials in the various countries. We find that the organisation and funding of the healthcare system does not appear to be decisive for implementing measures to improve conditions and attract and conduct company-initiated clinical trials. We find, however, that overarching central-

government responsibility for specialised inpatient care, like in Denmark and Norway, has been an advantage in terms of ability to implement measures, generate effects, monitor efficiency and report concrete results in a relatively short space of time. Australia has in turn achieved good results with a healthcare organisation that better resembles that in Sweden.

The ability of the countries and life science sector to find forms of collaboration between the central government, region and industry with respect to clinical trials is a common success factor. This includes the ability to cooperate in drawing up common objectives, action plans and the continuous monitoring and evaluation of implemented initiatives. All four countries have invested in implementation capacity in the healthcare system in various ways, including through therapy- and diagnosis-centric networks of clinics and clinical research staff as well as research support staff/units. Common to all countries is that they have prioritised keeping to their lead times for starting clinical trials and aiming for high delivery capabilities in terms of including the agreed number of patients. Australia, in turn, has introduced financial subsidies and made targeted efforts for certain types of early-stage clinical trials, which has shown through in the statistics and international competitiveness. In Australia, implemented initiatives enjoy high-level support in the national political arena and the regional healthcare system. The picture in Norway largely resembles that in Sweden, with the exception that the decline in the number of clinical trials is even more pronounced. The areas for initiatives in Norway's national action plan largely address the obstacles and opportunities that we have identified for Sweden. In its measures, Norway has studied the Danish model TrialNation and established the Norwegian equivalent NorTrial in 2022.

The common success factors can be summarised into a stated ambition, national overarching responsibility and concrete action plans, the sector's ability to cooperate, investments in implementation capacity in healthcare and a clear focus on delivery security and development of synergies with academic research.

Figure 3.5 Total number of clinical trials phase I–IV irrespective of sponsor type, in Sweden, Denmark and Norway, 2008–2021



Source: ClinicalTrials.gov (autumn 2022).

In an international comparison from 2019 of company-initiated clinical trials in Europe, North America and Asia, Denmark ranks in a “top 15 analysis” in 13th place. The Danish partnership TrialNation was formed in 2018 through combining previous initiatives undertaken more than ten years ago in Denmark. The five Danish healthcare regions are all members and represented on the board. Denmark has a well-established cooperation culture between private- and public-sector actors and it is experiencing – and has experienced – partly the same challenges that we are witnessing in Sweden today, for example in healthcare. The cooperation within TrialNation is described as having emerged, been flexible and matured over time, based on a common endeavour to be able to “say yes” to company-initiated clinical trials.

4. Reasons for the developments in Sweden

The obstacles and opportunities identified by the three parts of the inquiry have been compiled and categorised into six different categories:

- Infrastructure and expertise
- Law and regulations
- National and international scope
- Processes and support systems

- Cooperation and management
- Governance and funding

In this inquiry, we point out 125 unique obstacles and 104 opportunities, each of which, of course, does not affect the clinical trial to an equal extent. We find that understanding details is important to see how obstacles and opportunities interact, but that we must maintain the systemic perspective at the same time. The mission-oriented process has brought to light the consequences of an uncoordinated system, and the vast majority of the obstacles and opportunities identified in the inquiry are found, as a whole, in how we interact; that is, processes and support systems, infrastructure and funding and, to a lesser extent, in our laws and regulations. When linking obstacles and opportunities to the stages of the clinical trial process, it is primarily not our ability to plan, conduct or complete a trial that is challenging; rather, there is consensus among the ecosystem actors on what we need to change, such as addressing the allocation of responsibilities, access to infrastructure and expertise, and the role of the healthcare system in terms of participating in company-initiated clinical trials. It is concerning however that, in many respects, the picture of the obstacles is consistent with aspects that have emerged in previous reports and inquiries, although there are also new, contemporary insights and knowledge to consider when contemplating opportunities and solutions.

The factors that we consider have had the greatest impact on the progression of clinical trials in Sweden, and in particular company-initiated drug trials can, without ranking them in any order, be summarised into the following:

- Growing global competition for company-initiated clinical trials.
- A lack of Swedish competitiveness linked to declining delivery capabilities.
- Lack of implementation capacity for clinical trials in healthcare.
- Lack of regeneration of research and research-supporting expertise.

- Administratively overloaded processes and lack of appropriate support systems.
- Lack of national coordination, a common objective, concrete action plans and appropriate cooperation forums.
- Sustained restrictive factors and restrictive specific national requirements in law and regulations.

There are still restrictive factors in law and regulations that we do not find, individually or at the systemic level, to be crucial to reversing the trend. However, by nature they affect the possibilities of the individual to be considered for a clinical trial; that is, they considerably amplify inequalities between individuals. During the course of the inquiry, we have held dialogues with other ongoing inquiries with a bearing on our remit, and above all with regard to the effect that the exchange and use of health data could have on conditions for clinical trials. The complexity of the system surrounding the clinical trial does not make matters easier, and there are tendencies in our dialogues and in our external analysis to point to someone else's responsibility for bringing about change, rather than the actors working together and taking responsibility for steering the big picture and jointly evaluating new solutions.

4.1 National and regional support systems

The inquiry has assessed the aptness of Clinical Studies Sweden, the clinical trial unit concept and Swedish biobank infrastructure, expressed in terms of *high*, *limited* or *low* as regards serving as an aid and method for creating better conditions for clinical trials, particularly company-initiated clinical trials.

4.2 Clinical Studies Sweden

Clinical Studies Sweden's national unit at the Swedish Research Council, the six regional nodes and implemented development initiatives have, in the past six-year period of 2017–2022, been funded in the amount of SEK ~300 million. Based on the inquiry's dialogues, this appears to have contributed to harmonisation and

improved quality within academic research in Sweden, but has not had equivalent implications for clinical trials, particularly company-initiated drug trials. The government inquiry that presented proposals for national coordination of clinical studies SOU 2013:87 was followed by broad commissions in appropriation directions for the Swedish Research Council and in the agreements signed with the regions of cooperation. The commissions or agreements made no distinction between clinical trials and clinical studies in a broader sense, and did not describe how the initiatives should allocate their resources or which measurable results and effects the system – i.e. Clinical Studies Sweden – was expected to deliver. We find that the absence of explicit national goals and action plans, governance and prioritisation, combined with a lack of follow-up and evaluation – i.e. how the commission for Clinical Studies Sweden was originally designed – has led to a lack of impact on the conditions for and number of clinical trials, particularly company-initiated drug trials in Sweden.

Over the past six years, the national unit has been funded to a total of 19 per cent of the overall budget – approximately SEK 56 million. Until 2020, these resources included funds for the now discontinued Clinical Studies Committee as well as a committee coordinator at the Swedish Research Council's governance and coordination unit. The Swedish Research Council states in a response to the inquiry that although the Swedish Research Council has established a clinical studies unit, it does not only pursue work to support and develop the conditions for clinical studies in Sweden. The unit also works with other matters and commissions within the bounds of the Swedish Research Council's annual operations plan. The six regional nodes that were established follow Sweden's six regions of cooperation⁶ and receive SEK 5 million annually, or 10 per cent of the total annual budget. The nodes enter into an agreement with the Swedish Research Council, which stipulates what the parties undertake within the scope of the cooperation. However, these agreements are, like the unit at the Swedish Research Council, broad and general and the grants are not linked to performance. Here again, the agreements do not specifically refer to clinical trials or the company-initiated clinical trial. We note that the work of the

⁶ The Health and Medical Services Ordinance (2017:80), Chapter 3 Regions of cooperation for health and medical services.

nodes has been affected by the government grant having been distributed equally between the regions of cooperation and not according to number of inhabitants, which results in considerable disparity in the contribution per inhabitant between the regions of cooperation. For 2017–2022, the contribution per inhabitant has varied between SEK 12 and 32 per inhabitant, and the inquiry notes that the regional grants paid to the nodes do not compensate for the differences. A total of SEK 67.1 million has been allocated to development initiatives over the past six years. The inquiry finds that that development initiatives, with the exception of the national process for requests for studies, have had a limited effect for the clinical trial. We note that some of the development initiatives and the preliminary studies conducted have in some respect applied to – but not specifically targeted – the clinical trial. The inquiry finds that the commission for the Swedish Research Council concerning an advisory function for better use of health data overlaps with the work in progress within two official government inquiries on health data and the work associated with European Health Data Space (EHDS)⁷.

4.3 Clinical trial units

Clinical trial units are healthcare infrastructures with premises, resources and expertise for planning, conducting and completing clinical studies and clinical trials. As a support system, they are highly apt with a pronounced and positive impact on the conditions for clinical trials, particularly company-initiated drug trials. The clinical trial units are essentially entirely externally funded, meaning that they do not receive any funding from the healthcare regions; rather, their operations consist of commissioned services – i.e. contracted commitments with companies or academia. The degree of coverage regionally and for different specialist areas varies tremendously within the university hospitals as well.

⁷ Proposal for a regulation – The European Health Data Space, COM (2022) 197/2.

4.4 Biobank Sweden and regional biobank centres

Biobank Sweden and regional biobank centres are necessary and highly apt in relation to clinical trials, especially company-initiated drug trials. We find that there is no mandate and funding for dealing with biobank samples for research purposes, which includes the clinical trial. The existing two-stage procedure for decisions on the release of tissue samples, with a national reasonableness assessment of biobank samples and a further local assessment by a pathologist, impedes the process of planning, conducting and completing a clinical trial.

5. Clinical trials and precision medicine

The development of precision medicine in several fields, including cancer, has come a long way, and experience and expertise in precision medicine clinical trials are growing at the same pace. In our opinion the possibilities of effective introduction of precision medicine improve when the healthcare system is involved in planning, conducting and completing clinical trials with a precision medicine approach. This enables the healthcare system, in practical application at an early stage, to design and test their processes and infrastructure and to build know-how throughout the entire flow from diagnosis, treatment and through follow-up. Part of the learning process lies in the approach; that is, new elements, new technology and often new points of contact both within and outside of own operations. In a report, the Swedish Agency for Health and Care Services Analysis illuminates Denmark, Norway and the UK as countries that are considered to have come a long way with national infrastructure for precision medicine⁸. We note in our country comparison that these are the same countries that have come far with their action plans for improving conditions for clinical trials in general. These countries have also organised their specialised healthcare in a similar way, with a higher degree of national governance and monitoring. Clinical trials in precision medicine are complex and carry specific requirements. We find however that a crucial first step in the ability to implement precision medicine in

⁸ Ibid p. 17.

healthcare is to establish and secure basal implementation capacity for clinical trials.

6. Proposals

The inquiry's proposals and measures are directed specifically at the clinical trial, particularly the company-initiated drug trial.

We believe it is possible to steer the progression for clinical trials in Sweden in a positive direction by means of the following:

6.1 Establish SweTrial – a national partnership and national therapy network with a base of trial units for strengthened implementation capacity in healthcare

We propose that industry representatives in the life science sector and regional representatives of the six healthcare regions of cooperation enter into a new partnership – *SweTrial* – by invitation of the Ministry of Health and Social Affairs. As part of this, an appropriate number of national thematic networks (within therapy, diagnosis or equivalent) are established and coordinated, and at national level a regional coordination secretariat is installed at a host university hospital. SweTrial is proposed to develop *a national action plan for clinical trials*, which is anchored in the national life science strategy, with related annual action plans including a stated benefits perspective to promote the interests of patients, healthcare and the life science sector as well as international relations. We propose that the central government take an active role in funding the national secretariat by means of annual appropriations, and assume responsibility for coordinating national networks. It is proposed that the central government, through the agencies Vinnova and the National Board of Health and Welfare, contribute to the strategic development, follow-up and evaluation of the partnership. At the same time, the inquiry proposes that central government funding be earmarked for reinforcing the *implementation capacity* of the healthcare system for clinical trials, to bolster already established trial units and to stimulate the establishment of new ones. Clinical trial units are proposed to be made part of the necessary *national infrastructure for clinical research in healthcare*.

6.2 Develop existing structures by modifying the remit for Clinical Studies Sweden and create synergies and interoperability effects with clinical studies and broader clinical research

Clinical Studies Sweden has helped to harmonise and improve quality in academic research in Sweden, but has not served as a specialised support system for clinical trials or company-initiated drug trials in a similar way. The inquiry proposes that Clinical Studies Sweden be reorganised and that the remit and objective of the regional nodes be clarified and directed specifically at academic research and clinical studies, that the remit for the Clinical studies unit at Swedish Research Council be discontinued, and that the remit for the Swedish Research Council concerning statistics and information within the field also be discontinued. We propose that Clinical Studies Sweden, through the establishment of a special working group as part of the Committee for clinical therapy research at the Swedish Research Council, be organised with national governance that promotes coordination, prioritisation and follow-up of the remit. Clinical Studies Sweden and SweTrial are proposed to establish a common *national reference group* to enable acting jointly in issues that are a national or international concern with respect to clinical studies and clinical trials. As a result of the modified remit and organisation of Clinical Studies Sweden, funds are reallocated in favour of establishing and running SweTrial.

6.3 Invest in skills enhancement and further training for clinical research staff and research-supporting professions in healthcare

In order to increase implementation capacity for clinical trials in healthcare, Sweden needs to create career paths for other professional categories also which, together with the licensed healthcare professions, can contribute to the clinical trial administratively and clinically. Already established education providers within life science will, with relatively limited effort, be able to swiftly train up substantial volumes of expertise within a nationally quality-assured programme for clinical research staff and research-supporting healthcare professions. We propose that the

Swedish Medical Products Agency be commissioned with leading the work on developing and managing *a nationally harmonised training plan* that includes theory and practical experience for different roles involved in clinical trials together with participants such as the Ethical Review Authority, Biobank Sweden, the healthcare system and industry. It is crucial that this work be performed in close consultation with the experienced clinical investigators and trial units that operate in Sweden today, and with industry, whose experience and expertise can ensure renewal in the form of the next generation of clinical investigators.

Further training should be directed at existing licensed professions (doctors, dentists and nurses) and skills which, with due consideration for law and regulations and through a shift in activity, could contribute to work elements associated with clinical studies/clinical trials in healthcare. Well-defined remits, clear skills development paths and opportunities for further training help to clarify incentives for the individual employee, and enable rewarding clinical trial-related performance in the clinical merit system within healthcare.

6.4 Provide central-government funding to regional biobank centres (RBC) and for Biobank Sweden's remit

The Biobank Act aims to ensure sound care and protection of the individual's personal integrity. A recurring view in our inquiry is that the two-stage process for managing biomaterials/tissue samples poses an obstacle to the ability to assess applications (approvals) and manage sample releases (withdrawals) effectively at the national and local level. The researching organisations' need for swift access to biobank samples for research purposes is not effectively met, and there are currently no formal remits, requirements or funding for the regional biobank centres in the healthcare regions and Biobank Sweden for participating in the new approvals procedure under the EU Clinical Trials Regulation. The biobank actors in Sweden do this voluntarily, recognising that it is vital to clinical trials. The time and resources invested by the regional biobanks and Biobank Sweden are entirely self-funded. The regions' biobanks and the regional biobank centres are absolute core infrastructures, and their responsible organisations and funding prioritise the duty of healthcare today. In

order to meet the need for infrastructure and support for clinical trials associated with issuing opinions, considering and managing biobank applications, we propose that the central government co-fund infrastructure and resources for research purposes in the amount of SEK 15 million annually, and that the grant be disbursed and monitored through the Health and Social Care Inspectorate to the regional biobank centres (RBC) and Biobank Sweden.

6.5 Prioritise measures to collect national statistics on clinical trials for evaluation, follow-up and continuous learning

Despite a number of different initiatives concerning information and statistics for clinical studies and trials, there is still no national searchable entry point for Sweden that enables inhabitants and healthcare providers to search for information on planned and ongoing clinical studies and trials. A national system is key for equal recruitment of patients and to enable conducting follow-up, measuring performance and marketing Sweden's capabilities for clinical trials as a country. A proposal on how information on planned and ongoing clinical trials can be made available for more equal inclusion of patients has been prepared and presented at the end of August 2022 by the Ethical Review Authority⁹. We propose extending the Ethical Review Authority's remit to include lead times and delivery capabilities for clinical trials in Sweden, and to create a national point of entry to bring together existing regional and local initiatives. This system can be used to evaluate performance within SweTrial and enable continuous learning.

6.6 Investigate how Sweden can effectively remove regulatory obstacles and avoid specific national requirements that affect Sweden's competitiveness for clinical trials

A number of Swedish regulations that fall within the Ministry of Health and Social Affairs' field of responsibility continue to present obstacles to clinical trials in Sweden. Examples of these obstacles are repeatedly found in various preparatory works and in our inquiry. In

⁹ Possibilities of maintaining and presenting statistics on clinical studies in Sweden
Report 2022:1, Swedish Ethical Review Authority

the ongoing efforts to align Swedish legislation with European regulations, particular consideration is needed to avoid introducing specific national requirements that affect patients' ability to participate in clinical research and clinical trials. In this inquiry, we summarise the laws and ordinances that each pose a direct or indirect obstacle to clinical trials today. We propose that the Government allow these to undergo further inquiry with a view to drawing up legislative proposals to eliminate the obstacles.

7. Consequences

The inquiry's proposals have different consequences for the actors in the clinical trial ecosystem and for the Government in the form of central-government funding. Our overall assessment is that the benefit and transfer of value to society outweigh the risks and consequences presented by the proposals.

The proposals strengthen the patient perspective in terms of clinical trials while at the same time paying due consideration to personal integrity. Without clinical trials, there is a heightened risk and likelihood of patients not being granted the opportunity to inform themselves of and decide on care and treatment as part of a clinical trial. The risk of resources for the clinical trial competing with regular routine healthcare will persist if infrastructure for the clinical trial is not developed. Our proposals entail that the country's management bodies for healthcare services need to coordinate themselves within their region of cooperation, which is necessary and in keeping with established rules of procedure. Our proposals do not have any implications for municipal self-government or employer responsibility.

The proposal for a new national partnership between representatives of industry and the management bodies of healthcare services in the regions of cooperation is founded on a voluntary approach. For the actors that choose to participate, there will be financial consequences in the form of committing time.

Academia-initiated (non-commercial) clinical trials compete for the same time and resources in healthcare as company-initiated clinical trials. The risk of academic clinical research being pushed aside by company-funded clinical trials is considered to be low. Both

academia and industry have the same need for expertise, resources and infrastructure to plan, conduct and complete a clinical trial. We believe that academic clinical research will benefit from the inquiry's proposals, and the proposal for investment in implementation capacity, as well as a partnership between industry and the healthcare system. The inquiry's proposals are aimed at the company-initiated clinical trial, and are based on life science companies acting in line with a common national objective and jointly prioritising initiatives that benefit the life science sector as a whole. The cooperation model is intended to be founded on a voluntary approach and the industry associations' ethical rules as a complement to regulations and applicable codes that regulate cooperation between the parties.

The change to the remit and funding of Clinical Studies Sweden has organisational implications within the Swedish Research Council, which can be made gradually. The recommended discontinuation of the national health data advisory remit is not considered to introduce risks that cannot be addressed in the two ongoing government inquiries that concern health data specifically.

The inquiry's proposals do not have any regulatory consequences, and the partners within SweTrial can, for example, regulate the legal aspects of their cooperation in a consortium agreement.

The inquiry suggests that the proposals be funded by means of a redistribution within the existing budgetary framework, with a contribution of funds in the order of SEK 95.4–104.5 million as a total annual cost, of which SEK 21 million – that is, SEK 7 million annually for three years – are one-off costs. In addition, the economic consequences of a separate inquiry or a ministry inquiry need to be calculated as part of the regular budgetary process at the Ministry of Health and Social Affairs and the Prime Minister's Office.

8. Concluding remarks

The decisions now being made – or not made – on the future of clinical trials in Sweden will affect patients' ability to participate in clinical trials, the ability of the healthcare system to “say yes” to requests for clinical trials, and the competitiveness of the Swedish life science sector.

The inquiry's proposals and measures specifically target the clinical trial and particularly the company-initiated drug trial. The proposals provide scope for synergies and interoperability effects with clinical studies and broader clinical research and should, individually and as a whole, be seen as building blocks for achieving long-term competitive and sustainable ecosystems for clinical trials in Sweden. The inquiry proposes concrete actions in five areas, including *objective, partnership and collaboration, funding and infrastructure, training and marketing, and follow-up and learning*.

Representatives of the actors in the clinical trial ecosystem have, in the inquiry's dialogue meetings and work on the roadmap, voiced in unison their commitment and readiness to improve the conditions for clinical trials. Together with the necessary policy decisions, this can help to achieve the overall mission for clinical trials to be an established tool that will help us create the healthcare of the future together by 2030.

The inquiry would like to thank all the actors, organisations and individuals who have contributed with dedication to the work of the inquiry. We extend our special thanks to Emma Sernstad and Elham Hedayati at Karolinska University Hospital, who have assisted the inquiry with statistical data, USIFY for their cooperation in the mission-driven design work and the Swedish Institute for Health Economics (IHE) Lund for in-depth dialogues.