Research Assessment

Groningen University Institute for Drug Exploration (GUIDE)

University Medical Center Groningen

2015-2021

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Summary SEP assessment of the Groningen University Institute for Drug Exploration (GUIDE)

The PRC finds GUIDE research to be of excellent quality, and especially commends the societal mission to contribute to individualized drug treatment and the vibrant interdisciplinary environment. The position of GUIDE research groups is a key strength leading to productive integration of basic and clinical research, and diagnostics and therapy innovation. This should be an important strategic pillar for the future, and the PRC advises to further strengthen it by developing "creative hubs" to work with other institutes and schools. Most programs are aligned with the UMCG-focus on healthy aging, although some could more strategically address this overarching issue. The environment is productive and collaborative making the Institute agile and adaptable to urgent health care developments (as evidenced by its response to COVID-19), and enabling researchers to make major contributions.

Research quality

- Efforts to strengthen and centralize immunology research are encouraged, while the interplay, structural interaction and cross-fertilization between research programmes should be organized at the Institute level and engage all staff. at all levels.
- GUIDE should further support junior researchers by identifying all available career paths; support and career guidance should be in line with the Institute's research strategy.
- Providing additional funding and compliance support for investigators is advised.

Societal relevance

- Ensure a clear vision, goals and expectations on societal impact through shared reflection.

Viability

- GUIDE is advised to consider long-term support of the Institute's critical assets of biobanks and patient data, and of centralized, state-of-the-art technical facilities.
- The reduction of funding from industry and other external sources is a point of concern - GUIDE should identify areas of staff expertise which meet industry needs.
- The importance of succession planning is emphasized, given that a relatively large fraction of senior researchers and many of these PI's will be retiring in the near future.

CONTENTS

Assessment of the Groningen University Institute for Drug Exploration (GUIDE)

1. Introduction to the Institute

The Groningen University Institute for Drug Exploration (GUIDE) was founded in 1993 and its researchers are embedded within the University Medical Center Groningen (UMCG) and the Faculty of Science and Engineering (FSE) of the University of Groningen. From the start, GUIDE has focused on education and research covering the entire drug R&D lifecycle, and in recent years has integrated overarching topics in its activities, such as Healthy Ageing and Personalized/Precision Medicine. GUIDE consists of 12 research programmes, each of which is coordinated by two or three programme leaders:

3GI: Groningen Institute for Gastro Intestinal Genetics and Immunology;
CAPE: Critical care, Anesthesiology, Perioperative and Emergency medicine;
CLDM: Center for Liver, Digestive and Metabolic diseases;
CVC: CardioVascular Center;
GIOT: Groningen Institute for Organ Transplantation;
GKC: Groningen Kidney Center;
MHD: Microbes in Health and Disease;
TRIGR: Translational Immunology Groningen
BDDD: Biopharmaceuticals, Discovery, Design and Delivery;
MCB: Medicinal Chemistry & Bioanalysis;
GRIAC: Groningen Research Institute for Asthma and COPD;
PEGET: Real world studies in Pharmaco-Epidemiology, -Genetics, -Economics, &-Therapy

The GUIDE programmes BDDD and MCB consist mainly of researchers employed by the Groiningen Research Institute of Pharmacy (GRIP) of the Faculty of Science and Engineering, whereas the programmes GRIAC and PEGET consist of researchers from both GRIP and UMCG. Like many UMCG researchers, GRIP investigators also collaborate with other GUIDE programmes and they may even be affiliated to other programmes or institutes.

GUIDE is managed by a Director (Prof. J.G.W. (Jos) Kosterink), Deputy Director GUIDE and Scientific Director GRIP (Prof: H.W. (Erik) Frijlink), and three MT members responsible for research (Dr. Udo Mulder), education (Prof. Sven van Ijzendoorn) and societal impact (Prof. Barbro Melgert). At the moment, GUIDE had 252 full members, consisting of researchers from numerous research groups within the UMCG and the Groningen Research Institute of Pharmacy (GRIP). Participation in GUIDE is mainly bottom-up. Researchers and clinicians are appointed in departments organized around their medical specialisms. On top of that, they choose a research institute that they feel best covers their research interests. The Director of GUIDE reports to the UMCG Dean of Research, whereas the Scientific Director of GRIP reports to the Dean of FSE.

2. Aims and strategy

During the evaluation period, GUIDE's mission and vision have been to prevent and cure disease by getting the best (drug) treatment for each individual patient. GUIDE's aim is to create an interdisciplinary research and educational environment that encourages communication and cross-fertilization between medical, pharmaceutical, and other researchers and professionals, both inside and outside the Institute, leading to output with high societal relevance.

According to GUIDE, the best treatment for each patient is *personalized* treatment. Its research covers all aspects of the drug-intervention lifecycle from its inception to its use in daily clinical practice and aims to deliver an improved therapy model for anybody that needs it.

This overarching mission and vision are supported by concrete strategic goals, with a focus on:
1. Target finding (pathophysiology/disease mechanisms)
2. Methods and technologies used in the drug research and development trajectory
3. Post-marketing surveillance and practice-oriented research

In the period under review, GUIDE invested in various aspects of the Institute to capitalize on its strengths and opportunities, first of all by focusing on personalized and precision medicine and expanding the multidisciplinary environment (fundamental, pharmaceutical, preclinical, and clinical) covering all aspects of drug discovery and development. It also focussed on aligning research, activities and objectives with the new foci of the UMCG and securing strong reciprocal relations with the UMCG Patient Care Centers.

To effectively address weaknesses and threats, and following recommendations of the previous PRC, the Institute focused on improving its governance and organizational structure at the board, programme and department level. In 2018, GUIDE implemented a new governance structure by appointing a Management Team (MT) covering the 3 portfolios of research, education and societal activities. A thorough evaluation of the GUIDE programmes resulted in the dissolution of two programmes (VAL and LM), and redistributing the PI's to strengthen other programmes. One new programme was included (PEGET) to the GUIDE portfolio, which focuses on *real world assessments* and innovative data methodologies to study outcomes of pharmaceutical interventions and their implementation in daily practice. PEGET houses researchers from the UMCG, as well as from GRIP (FSE).

For the future, GUIDE aims to change the current "one size fits all" treatment approach to "a fit for each size". To underline its intensified focus on personalized medicine, GUIDE has rephrased its mission for the following period: "The Groningen University Institute for Drug Exploration (GUIDE) strives to fill the unmet need in cure and prevention by getting the best drug treatment for each individual patient." To realize its goals, and create optimal conditions for multidisciplinary collaboration and exchange in personalized drug research, the Institute will prioritize new inter-programme platforms, support collaborative grant applications, stimulate active participation in larger, multi-user infrastructural UMCG initiatives and further develop strategies for increasing its societal relevance and impact.

3. Qualitative Evaluation

The well-prepared, comprehensive critical reflection and the open nature of the interviews allowed the committee to gain in-depth insight into the quality of research, the societal impact and viability of GUIDE. The committee was very much impressed with the constructive, inspiring and insightful conversations it had with all of the representatives of GUIDE.

Research quality

In its evaluation of GUIDE, the committee encountered an open and stimulating research environment. According to the committee, the overall mission to contribute to finding the best drug treatment for each individual patient is highly relevant and demonstrates the Institute's desire to truly achieve societal impact. It applauds the strong commitment of the leadership of GUIDE and its talented staff in creating a vibrant interdisciplinary research and training environment. Despite the

complexity and substantial size of the Institute as a whole, the joint aspiration to improve drug therapy and the strong focus on personalized medicine is clearly felt by the committee. The position of the research programmes of GRIP within GUIDE is enviable, allowing for a productive integration of basic and clinical research as well as innovations in diagnostics and therapies. The GUIDE research portfolio is aligned with the research strategy of the UMCG which addresses three themes: mechanisms of disease, innovative diagnostics and therapies and (secondary) prevention. Most programmes show an alignment with the UMCG-focus on healthy aging. However, many deal with novel treatments of diseases, which simply occur more frequently at higher age. Only some programmes address overarching issues of aging research. This, however, does not diminish the excellent quality of most of the programmes.

Governance

The committee is positive about the restructuring of the governance of GUIDE and thinks that the addition of a Management Team with responsibility for research, education and societal activities is a positive intervention that clearly strengthens the implementation of its overall mission and goals. This has indeed allowed for a more structured and integrated approach of the research programmes, and is recognized as such by the Programme Leaders of the different programmes. The structure also puts the Institute in a good position to pursue societal impact in a more coordinated manner, for example by supporting the programmes in defining their own criteria for societal impact. The restructuring of the portfolio through the redistribution of PI's of two smaller programmes over other existing programmes is appreciated by the committee. Given the wide scope and size of the Institute, this increased focus will contribute to a stronger and more cohesive research environment.

Research environment

The committee is impressed with the breadth and scope of the GUIDE research portfolio which covers the wide spectrum of research on (personalised) drug development and treatment, with each programme having a particular approach and focus: some programmes are more horizontally oriented with an orientation towards cross-cutting methodologies, broad-based approaches and technology, such as CAPE, MHD, BDDD, MCB, 3GI and PEGET, whereas others are more vertically structured and concentrated around the treatment of certain diseases and symptoms, such as CLDM, CVC, GIOT, GKC, TRIGR and GRIAC.

The documents and conversations with representatives of the Institute testify to strongly developed multidisciplinary and translational research lines, an ongoing investment in collaboration and cross-fertilisation between clinical and non-clinical sciences, and productive connections and collaborations with partners and stake-holders within and outside the Institute/UMCG. GUIDE is indeed very successful in supporting its research programmes to initiate and participate in internationally competitive investigations such as the involvement in prestigious European funding programmes. What also became clear is that the institution actively invests in finding funding for strategic activities. The committee considers the biobanks and patient data deployed by the Institute as highly valuable assets and observes that GUIDE has developed excellent and innovative platform technologies.

These strong features confirm that the Institute indeed offers a highly productive, stimulating, dynamic, cutting-edge and collaborative research environment enabling its researchers to make major contributions to drug development and the advancement of personalized medicine where it matters. An excellent example of GUIDE's inter/multidisciplinary agility, its ability to adapt quickly to new and urgent developments affecting health care, was its response to COVID-19. Right after the start of the pandemic, GUIDE was able to direct part of its research activity quite swiftly towards COVID-19 related research with over 50 research studies ranging from drug targeting and

mechanistic studies, to investigations of the long-term effects of COVID-19 in patients as well as the general population.

In speaking to the different representatives of the Institute, the committee was impressed by how passionate researchers are about their work and the shared drive to improve drug treatment in such a way that it is tailored to the individual needs of patients. Researchers were very enthusiastic about all aspects of their working environment, and indicated that they feel supported in their endeavors and have the material and technical facilities they need to execute their research projects. They provided many prominent examples of inter- and multidisciplinary interactions between clinical and non-clinical researchers, and successful collaborations between pharmaceutical, medical and other sciences, within and outside the GUIDE and UMCG. The committee was very pleased to note how inventive researchers are in finding ways to achieve their goals, even when space and facilities are limited, and when faced with the challenges of the pandemic. Some researchers did note that changes in legislation (privacy requirements, for example) are making grant applications more and more complex and time-consuming. Additional support from GUIDE could help investigators navigate compliance and other requirements more efficiently and enhance overall success.

With regard to the organization of research within the programmes themselves, the committee observed that there are many great examples of how the programmes foster their specific research communities, with structural (weekly and/or monthly) meetings organized around particular themes and subjects (funding, grants, collaborations with industry), and with specified goals and aims. However, some programmes are more active than others, and the ratio between senior researchers, postdocs and PhD candidates varies considerably among programmes. This is a potential weakness, as it could negatively affect the opportunities of researchers and research initiatives within some programmes, particularly when it comes to the development and training of junior researchers who are dependent on the programme in which they are placed. Several ways to remedy this is to allow PhD's to actively interact with more than one group, and/or to stimulate PhD-supervision across programmes. In this way PhD's will be able to collaborate across disciplines and may profit from research expertise and support in different contexts. Also, learning from each other, and applying best practices with regard to community building, peer support, and PhD training could help to strengthen GUIDE as a whole.

Another, related, point of discussion was that though there is strong interaction across disciplines and departments within each individual research programme, the interplay between the 12 research programmes within GUIDE could be further strengthened and improved. The committee found that there are good examples of interactions between programmes (MHD has regular meetings with CAPE and TRIGR and BDDD, for example) but there is also a broadly shared desire for more structural synergy and interdisciplinary collaboration across programmes. GUIDE could play a role in creating opportunities like "creative hubs" for joint strategic thinking and working, and further support interdisciplinary and translational research, which is something that needs to be organized at the Institute level.

Finally, the committee supports the Institute's intentions to further strengthen immunology research, since it is key to many diseases and widely recognized as a domain that needs to expand. According to the committee, immunology represents a key cross-cutting theme, and it fully supports the efforts made and plans to further strengthen this research focus area and organize this more centrally within UMCG. The committee is happy to see that GUIDE has taken the recommendations of the previous evaluation to heart and initiated several improvements over the years (see *Viability*). Overall, a centralized approach to facilities and resources that serve various GUIDE programmes, as well as other UMCG/FSE Institutes, is to be advised. The committee recommends sustained, long-term support for biobanks and patient data, which provide precious material and information needed for innovative, relevant, and impactful research. Furthermore, centralized, state-of-the-art technical

facilities including an imaging center, an “omics” center, an organoid facility, a microbiome center, patient cohorts (such as Pharmlines) and an infrastructure for big data analysis are crucial for the high-quality research expected of the GUIDE programmes. Such investments will facilitate innovation and collaboration (see also *Viability*).

Position of GRIP within GUIDE

During the site visit, the committee paid careful attention to the position of the four GUIDE programmes in which GRIP researchers are active: BDDD (Biopharmaceuticals, Discovery, Design and Delivery), MCB: (Medicinal Chemistry & Bioanalysis), GRIAC (Groningen Research Institute for Asthma and COPD), PEGET (Real world studies in Pharmaco-Epidemiology, -Genetics, -Economics, &-Therapy). The committee observes that the integration of GRIP in GUIDE is without a doubt an enviable asset of the institution, since GRIP is strategically positioned to bridge the gap between bench and bedside. This is formalized by the position of the Deputy Director GUIDE who is also the Scientific Director GRIP. The integration of the 8 GRIP research groups within GUIDE is further strengthened by the recently added programme PEGET, which develops, validates and applies innovative methodologies and real-world assessments to study medication use and outcomes in clinical practice on the population and the individual level, sex/age differences in drug treatment and outcomes, and new interventions to improve medication use. Due to its new positioning, PEGET is able to link better with clinicians who are involved in the use of drugs and to shift towards new topics in drug therapy.

The committee is pleased to note that the support for GRIP investigators is substantial and that their participation in GUIDE allows them to make major contributions. In speaking with all the researchers involved, the committee learned that the GRIP research groups within GUIDE is considered to be a very strong asset, contributing to the interdisciplinary, multidisciplinary and translational scope and potential of research at GUIDE. The 4 GUIDE programmes in which GRIP researchers participate are very prominent and take the lead in certain fields, their link with UMCG and clinical researchers is clearly an added value to them, which allows them to develop research that is not possible in other contexts. Researchers from MCB, for example, indicated that they are very proud of their collaboration with clinicians in the hospital, which enables innovation and allows them to directly improve patient treatment through technology. Also, GUIDE benefits from GRIP with regard to the technology and expertise that they bring to the Institute. Researchers involved in the GRIP's research groups, in most cases non-clinicians, also work throughout the whole of the hospital and the laboratories at UMCG. GRIP researchers explained how there is ongoing movement and interaction between the UMCG and FSE locations, with a lot of meetings facilitating exchange and sharing of equipment. The PROMINENT programme, initiated by GUIDE, is another example of how FSE and UMCG researchers collaborate. The committee could establish that there is sustained and structural interaction and collaboration between fundamental/basic, non-clinical and clinical sciences, which is made visible by joint papers, grants and participation in programmes by UMCG and GRIP staff. For example, 46% of GRIP’s publications (which mostly involve non-clinical researchers) is the result of collaborations with UMCG researchers (who are mostly clinical researchers). Furthermore, other programmes in GUIDE are intensifying their collaborations with GRIP as well, something which the committee fully supports.

The committee can only applaud this strong and productive positioning of GRIP within GUIDE, which continues to prove itself as extremely successful; the committee fully encourages ongoing support for this enterprise facilitating an increased collaboration between clinical research and basic/fundamental sciences, as well as between as well as between BDDD, MCB, GRIAC and PEGET and other GUIDE programmes.

Output quality and funding

Overall, the research programmes at GUIDE are extremely productive and generate high quality basic and translational research. Objective evidence for the outstanding quality of research at GUIDE and its international standing is the consistent high level of productivity with regard to the number of impactful peer-reviewed publications and the large number of science and scholarship awards, as well as the high number of prestigious awards and prizes for individual researchers, such as the Spinoza prize in 2015. The Institute's publication profile is characterized by a significant number of top 10% papers, and a high, further increasing field weighted citation (FWCI) score in the period under review. GUIDE's contribution to the international field of research in drug treatment is evident from the high percentage of publications (58%) that are the result of collaboration with international partners and consortia. The committee was also very positive about the significant increase in the number of open access publications at GUIDE; 80% of publications were open access in 2020. This 20% increase over the period of 2015-2020 demonstrates that the Institute is indeed highly committed to the principles of open science.

The committee is very impressed by how successful the Institute has been in acquiring substantial external funding in the past years (in excess of 240 million euros, a total of 1214 grants) and its ability to acquire a high number of prestigious prizes and grants, including large Marie Skłodowska-Curie COFUND grants, which have significant impact on training for early career scientists (e.g., PRONKJEWAIL Horizon2020 (2016), ALERT Horizon2020 (2016), PROMINENT Horizon2020 (2017)). Furthermore, three EU-funded international training network (ITN) projects were coordinated by GUIDE researchers. In addition, GUIDE participated in another 11 ITNs, 12 EU IMI projects, and 2 Inter Reg projects. Between 2015 and 2020, prestigious personal research grants were acquired by GUIDE researchers, including two ERC Consolidator grants, five ERC Starting grants, two Vici grants, seven Vidi grants, and three Veni grants. The active leadership and participation in these projects are testament to the Institute's success in providing the necessary environment and infrastructure for its researchers to perform at an outstanding level and underlines the high international ranking of its research programmes.

Societal relevance

GUIDE is well positioned to contribute to societal relevance. Creating societal impact is integral to GUIDE's mission, vision and strategic goals, with a strong and explicit focus on personalized (drug) treatment, and a drive to develop treatments that are tailored to the needs of each individual patient. The scope and breadth of GUIDE's research programmes, the interdisciplinary teams, the strong interconnections between basic/fundamental, translational and clinical research, the partnerships with industry and public organizations, the productive platform technologies and valuable assets such as biobanks as well as patient cohorts and data ensure that GUIDE has vast potential to generate high societal impact. Indeed, in the period under review, the programmes have not only been able to impact drug treatment of patients in a great many ways, but also improve patient participation and communication in clinical research; enhance public awareness about medications (e.g., the influence of non-antibiotic drugs on the gut microbiome), the dangers of infectious diseases, and the benefits of vaccines; develop greener and more sustainable production of biologically active molecules; reduce the use of animals in disease and drug safety research; and spin-off numerous companies. These are just a few of the many excellent examples and case studies provided to the committee in the documentation and during the site visit of how GUIDE research has impacted and continues to create societal impact in many ways, good examples being research in sex differences in adverse drug events, or a tool (now used at the national level) that helps making decisions regarding drugs based on economic models, or innovations in prescribing drugs to elderly

people. The committee also highlights very interesting research presented in one of the case studies, in which circulating cancer biomarkers are used to explore heart failure in cancer patients.

GUIDE researchers are committed to engaging with the public through outreach activities, dissemination of their scientific findings and education. This engagement is also evident in the many productive collaborations with external stakeholders, with industry and national and regional healthcare organizations, governmental organizations, as well as patient advocacy groups, funders and local, national and international news agencies.

GUIDE stands out for its high number of clinical trials and patient cohorts, which form the valuable basis for innovations in drug treatment. In total, 373 clinical trials were started between 2015 and 2020 with GUIDE participation; 46 of these trials were headed by a GUIDE researcher and GUIDE researchers are involved in the registration, maintenance and supervision of 47 patient cohorts. The committee applauds the manner in which the GUIDE programmes engage with relevant patient/stakeholder groups in order to design and execute research and trials with maximum impact. The incorporation of patient participation and involvement in the design and execution of clinical trials is proof of its ambition to improve patient care. GUIDE is strongly embedded in the local region, the northern part of the Netherlands, and this allows the Institute to connect with patients in an effective manner. The importance of the patient's point of view and input has, for example, resulted in a research programme, set up by GRIAC, that trains both patient and researcher in communicating about the treatment and experience of disease, and aims to benefit from the patient's perspective; a programme that was awarded a Patient Participation Prize by the Dutch Lung Foundation in 2020. The committee encourages the Institute to support these initiatives focusing on patient participation and agency, and to find ways to share and implement best practices at the Institute level.

GUIDE is very strong in participating in developing various national and international guidelines and policies. This is an excellent indicator of societal relevance and impact, according to the committee, since this can make a significant difference for patient treatment locally, nationally and internationally. In recent years, 12 new tools, designs, models, systems, methods, guidelines, protocols, or websites, were made available to the general public. Over the past six years, 614 (national, European, and international) policy documents and guidelines mentioned output generated by GUIDE researchers.

The committee applauds the entrepreneurial drive within GUIDE, as well as the support and infrastructure that is offered to all researchers, PhD's included, for entrepreneurial initiatives. The Institute can make use of UG and UMCG facilities for entrepreneurship, such as the three incubator buildings as well as an extensive mentoring system via Northern Knowledge. Many aspects are offered in courses by the graduate schools (business plans, patenting, starting corporations) of UG and UMCG. The GRIP researchers involve companies or internal consultants in managing these trajectories, helping researchers set up good contracts. The interests of PhD candidates are carefully protected and monitored by arranging the terms in advance, such as intellectual property. The entrepreneurial orientation and support system has resulted in a high number of significant patents and start-ups. In total 43 patents were applied for over the past six years. Moreover, nine start-up companies were founded out of GUIDE (three UMCG and six GRIP) based on knowledge from the Institute, 12 research tools were developed, and royalty income totaled more than €21 million. Over the past six years, grants for 74 projects were awarded from regional sources (city, province or regional). This further emphasizes the important role that GUIDE plays in the local community by stimulating innovation, which leads to economic development.

Publications and partnerships are also a good indicator of societal relevance: many publications with industry and many public-private partnership projects started in the period under review, including regional partnerships. In total, 848 publications emerged from collaborations with co-authors from

industry, which is 11.7% of all Institute publications in total. In addition, 606 Public-Private (PPP) and Public-Public (P2P) partnership projects were started between 2015 and 2020, which amounts to over 50% of all projects; 74 of these projects involved regional partnerships (city, province, or regional). This indicator clearly shows not only the economic value of the work performed by the GUIDE researchers, but also how well the Institute succeeds in creating a network of partnerships which generate relevant research contributing to the ongoing improvement of drug development and treatment.

To further strengthen the structural and durable societal relevance of its research, the committee advises ensuring a clear vision and shared reflection on societal impact, making clear what it aspires to, and setting clear goals and making explicit expectations. At present, the committee found that each programme defines societal impact differently, and that even between researchers there are differences regarding interpretation. A shared vision on the types of public outreach, activities, and engagements that are most impactful would be helpful in setting goals for the future.

Viability

The leadership vision and strategy for personalized and precision medicine is an important pillar for the future development of GUIDE. In the period under review, GUIDE has shown itself to be forward-looking, agile, self-reflective and proactive in taking measures to ensure that it is able to achieve its mission and goals. The Institute's increased focus on personalized and precision medicine for the following period will serve as a strong basis for, and give momentum to, further research development.

The Institute has been successful in the review period in its ambition to serve as a facilitator of collaborative opportunities in the broad spectrum of research in drug development and treatment. The restructuring of the programmes and the introduction of a Management Team with dedicated responsibilities has contributed to further focus and structure of GUIDE. Furthermore, innovative research and effective collaborations between preclinical and clinical units, investment in clinical trials, patient cohorts and platform technologies, the strong focus on patient involvement and participation, the contributions to health care guidelines and policies, the Institute's international collaborations, as well as with partners in industry and regional and national health care (research) organizations all contribute to the present and future viability of the Institute. Importantly, the positioning of the GRIP research groups within GUIDE allows for unique opportunities for sustained and productive exchange between fundamental/basic, translational and clinical research. The connection between UMCG and FSE is key to the Institute's profile and therefore, integral to its present and future viability.

The committee explored the relationship between GUIDE and the departments it interfaces with, as well as the interconnections between the research programmes themselves. On the whole, the ambitions of the Institute and the UMCG departments appear well-aligned, and overall seem to share the same interests and goals when it comes to infrastructure, facilities, funding and recruitment. Whilst there is good synergy between the various departments and the Institute, this alignment can be fragile and dependent on the investment of specific PI's and department heads. The committee recognizes that this potential fragility may be due to the current organizational structure at UMCG. The committee recommends improved strategic planning, co-ordination and communication at a more central level to ensure alignment and transparency. This may also aid in guiding project development and personnel deployment.

As mentioned in the section on research quality, the interplay between the 12 research programmes within GUIDE could be further strengthened and improved. While there are many good examples of

exchange and collaboration between programmes, the committee thinks that a more structured facilitation of cross-fertilization should be organized at the Institute level. For example, thoughtfully designed meetings engaging all levels of staff could further enhance shared ownership of the research directions. The structuring of ongoing cross-fertilization of research between programmes is also crucial when it comes to the acquisition of large grants and funding, which more and more require close interdisciplinary and multidisciplinary collaboration of many different groups and scientific approaches.

GUIDE is clearly contributing to talent development through well-established career tracks centered on early career researchers (ECRs). The quality of PhD's is high and the overall support for PhD's is good, with GUIDE-specific courses and support, as well as its own PhD-student council. The committee is pleased to note that bursary PhD candidates have found a way to organize themselves and advocate for their rights, and that they feel supported by their supervisors. PhD candidates are aware of where they can go for support and questions, and they feel heard by their supervisors and mentors.

However, there is some concern around high numbers of PhD candidates, the long duration of the PhD trajectory, and the potential inequality resulting from differences between employed PhD's and PhD's funded by bursaries. The committee was left with the impression that the Institute PhD system, both at the UMCG level and at the Institute level, may require careful consideration and review in order to achieve its optimal balance and full potential within the Institute as a whole. In its conversations during the site visit, the committee learned that the Institute is aware of the challenges and that different measures have been taken at both levels to remedy this. The committee learned that the reason for delay of PhD trajectories within GUIDE is often due to the fact that PhD candidates are working part-time on their research, in addition to clinical work. PhD candidates who are struggling receive extra support through GSMS, GSSE or their supervisors to help them execute their research project. Extra funding is sought by the PI if a PhD student is not able to finish in 4 years. The committee concludes that GUIDE would benefit from overarching, coherent guidelines for PhD recruitment, support, and career guidance that match with the Institute's research strategy.

Of those interviewed, the committee was happy to note that junior and senior researchers at the Institute feel supported by their peers and supervisors and that they receive personal mentoring and are stimulated to find their own research path. They feel well-supported in grant applications (support offered at UMCG-level and by colleagues). Mentoring schemes and role-models are present. The committee appreciates that GUIDE actively invests in talent management and encourages the Institute to continue to improve its management of talent and the nurturing of careers of junior researchers (PhD's as well as postdoctoral researchers) supporting them in identifying possible career paths that are available, whether this be in academia, industry, or other domains in society.

For the committee, a consistent key to success is the embedding of the post-graduate research community as high value partners that energize programme development. The committee observes that the decreased funding and low number of postdoctoral scholars relative to the high number PhD candidates could impact the quality of PhD training. The committee noted the long time to degree for some PhD candidates (5-6 years). Based on the available information, the committee concluded that that many PhD candidates do additional work after the nominal 3-4 years of their PhD programme and may be kept 'dependent' for a longer period of time than necessary. The committee recommends assigning more funds and positions to the postdoctoral career phase. The committee would like to stress that mentorship should go beyond the individual supervisor and that it is important that postdoctoral researchers receive the support they need to make the next step in their careers. Whilst individual cases of good practice around support are apparent, the committee

recommends that procedures and practices are put in place for all and that it is not dependent on individual good practice.

Investment in cross-cutting domains as well in important facilities and infrastructure is key to the viability of the Institute. As described in the section on research quality, the committee welcomes the Institute's intentions to further strengthen immunology research. In response to recommendations from the previous committee, GUIDE has appointed two scientific leaders in the field of Immunology and Ageing, a very innovative field. The Institute has continued preparations for a centralized Translational Immunology Facility that serves several GUIDE programmes. The facility has suffered delays due to COVID-19. In the meantime, central facilities focused on specific techniques (flow cytometry facility) and support for centralized processing of biological samples (cell banking and immune monitoring facility) have been initiated. These interim facilities can be used by all immunologists. The committee sees these as important first steps towards a definite lab space that can integrate all immunologic activities with larger capacity within the new laboratory facilities planned for the UMCG. The committee is also pleased to note that GUIDE is taking steps in anticipation of the retirement of senior PI's and is investing in the acquisition of new researchers in this important domain. High profile candidates are currently being recruited to fill positions in mucosal immunology. The committee fully supports these proactive measures that will benefit the viability of GUIDE as a whole.

Good facilities and infrastructure in general are critical to the viability of the Institute. Core-funding for facilities and infrastructure is provided by UMCG, and is based on the wishes and needs of the programmes. The committee recommends sustained, long-term support for the biobanks, patient data and large population cohorts, which form the precious material of innovative, relevant and impactful research, as well as for centralized inter-programme platforms (such as for PK/PD, systems biology, imaging, fibrosis as well as centers for microbiome and medication adherence), which facilitate innovation and collaboration. This also holds for large multi-user infrastructure initiatives such as the imaging center, (gen)omic center, organ on a chip/organoids center, data banking, MS-center, (biotech) drug production facility, Phase I unit, cohorts, AI, and an infrastructure for big data analysis.

Viability also depends on the continued structural and financial support for the research efforts. Based on overall research funding, the viability of GUIDE is sound, with acquisition of substantial funding from a large variety of sources. Significant funding comes from charity as well as from grants received from industrial partners and governmental institutes. This portfolio of funding sources helps mitigate policy changes in governmental programmes or economic changes that affect national charities. A point of concern with regard to the financial viability of GUIDE is a reduction in funding from industry and other external sources over the last two years. The effects of the pandemic on income for charities might be one explanation, but the downward trend may also be attributed to new co-funding programmes in the Netherlands, which draw direct industry funding away from research programmes. According to the committee this does not pose a threat to the viability of the Institute in the short term but advises that consideration should be given to identifying specific areas of expertise among GUIDE staff, both in research and education, that might meet the needs of industry.

The committee emphasizes the importance of succession planning. Staff composition shows a relatively large fraction of senior researchers and many of these PI's will be retiring in the near future. The Institute is aware of this and is in the process of taking measures to ensure continuity in programme leadership. The committee supports this and encourages proactive succession planning and change management.

To conclude, GUIDE has been successful in its ambition to serve as a facilitator of collaborative opportunities in a broad spectrum of research in (drug) treatment, in line with UMCG and FSE vision and strategy. In contributing to talent development, in facilitating innovation and collaboration, and in preparing succession planning, GUIDE seems to be ready for the future.

4. Recommendations

Research quality

- The committee fully supports the efforts that are made and planned to strengthen and centralize immunology research, which is a key research area for many diseases and recognized as a domain that needs to expand.
- The committee appreciates that GUIDE actively invests in talent management and encourages the Institute to continue to improve its management of talent and the nurturing of careers of junior researchers (PhD's as well as postdocs) by supporting them in identifying possible career paths that are available, whether this be in academia, industry or other domains in society.
- GUIDE would benefit from overarching, coherent guidelines for PhD recruitment, support and career guidance that match with the Institute's research strategy.
- Changes in legislation are making grant applications more and more complex and time-consuming. Additional support from GUIDE could help investigators in applying for grants and navigate compliance and other requirements more efficiently.
- The interplay between the 12 research programmes within GUIDE could be further strengthened and improved. There is a shared desire and need for more structural interaction and cross-fertilization, which should be organized at the Institute level. Thoughtfully designed meetings engaging all levels of staff is needed to further enhance shared ownership of the research directions and collaborative enterprise.

Societal relevance

- To further strengthen the structural and durable societal relevance of its research, the committee advises ensuring a clear vision and shared reflection on societal impact, making clear what the Institute aspires to, and setting clear goals and making explicit expectations.

Viability

- The committee recommends that GUIDE considers long-term support of the Institute's critical assets of biobanks and patient data as well as of centralized, state-of-the-art technical facilities which contribute towards innovation and collaboration.
- A point of concern with regard to the financial viability of GUIDE is a reduction in funding from industry and other external sources over the last two years. According to the committee this does not pose a threat to the viability of the Institute in the short term but advises that consideration should be given to identifying specific areas of expertise among GUIDE staff, both in research and education, that might meet the needs of industry.
- The committee emphasizes the importance of succession planning. Staff composition shows a relatively large fraction of senior researchers and many of these PI's will be retiring in the near future. The committee supports the measures taken to ensure continuity of leadership and encourages proactive succession planning and mission-driven change management.