

Medical Sciences RUG: GUIDE/FMS

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Quality assessment of education and research in Dutch universities was until recently carried out by the Quality Assurance department of the VSNU. In 2004 the activities of this department were transferred to QANU, which assumes responsibility for completion of the VSNU activities initiated before 2004.

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1. Introduction

1.1 The Dutch System for Quality Assessment of Research

This quality assessment of research is part of the assessment system for all Dutch university research, as organised by the universities in the Netherlands.

The aims of the assessment system are:

- Improvement of the quality of research through an assessment carried out according to international standards of quality and relevance;
- Improvement of research management and leadership;
- Accountability to higher levels of the research organisations and funding agencies, government, and society.

The assessment takes place at the level of research institutes and research programmes. The research institutes submit a description of the results that have been achieved in each research programme during the previous six years (including quantitative data about staff input, three key publications and a list of publications), a short outline of the 'mission' statement of each programme, and developments anticipated in the context of the research profile of the faculty or institute. Important elements of the assessments are the interviews, which the Review Committee conducts with the management and the programme directors, and the visits to the facilities.

This review of the research institute GUIDE/FMS was commissioned by the Board of Groningen University and organised by the independent organisation QANU (Quality Assurance Netherlands Universities).

1.2 The Review Committee

The Review Committee was appointed in June 2003 and consisted of:

- Prof. Dr. Joost Ruitenbergh, chairman, Vrije Universiteit Amsterdam
- Prof. Dr. Dirk Brutsaert, University of Antwerp
- Prof. Dr. Stan Kaye, Institute of Cancer Research and Royal Marsden NHS Trust, London/Sutton, UK.
- Prof. Dr. Johan Kips, Ghent University Hospital
- Prof. Dr. Jürg Reichen, University of Berne
- Prof. Dr. Eberhard Ritz, Heidelberg University
- Prof. Dr. J. Kathryn Wood, University of Oxford.

Drs. Roel Bennink of QANU was appointed secretary of the Review Committee.

A short curriculum vitae of each of the members is included in Appendix 1.

Independence

All members of the Committee signed a declaration and disclosure form to safeguard that:

- the panel members judge without bias, personal preference or personal interest, and
- the judgement is made without undue influence from the institute, the programme or other stakeholders.

Any existing professional relationships between committee members and programmes under review were reported and discussed in the committee meeting. The committee concluded that there was no risk in terms of bias or undue influence.

The committee regards the QANU-rules of conduct and the disclosure form a useful tool in safeguarding the independence of the committee.

1.3 Scope of the Assessment

This assessment covers the research of the part of the Groningen University Institute for Drug Exploration (GUIDE) that is embedded in the Faculty of Medical Sciences. (FMS). The period of assessment is 1997-2002, and recent developments have been taken into account as much as possible.

The part of GUIDE that is embedded in the Faculty of Mathematics and Natural Sciences is called the Groningen Research Institute for Pharmacy (GRIP). The research of GRIP is not covered by this assessment, but as part of the research of the University Centre for Pharmacy it is assessed by another committee (also chaired by Prof. Ruitenber) together with the research of the Utrecht Institute for Pharmaceutical Sciences (UIPS).

The Committee was asked to operate according to the *Standard Evaluation Protocol 2003-2009 for Public Research Universities*. This Protocol specifies the criteria for the assessment and the information that must be provided to the Committee.

1.4 Data provided to the Committee

The Review Committee has received a detailed self-evaluation report provided by the institute. For each programme, five key publications were specified in the report and copies of three of these publications were provided to the Committee.

The documentation included all the information required by the Protocol.

1.5 Procedures followed by the Committee

The assessments are based on the documentation provided by the institute, the key publications of each programme, the interviews and the tours of the facilities. The interviews took place during the site visit on March 1, 2004. Time was provided for visits to the experimental and instrumental set-ups and for poster presentations and discussions with PhD-students. The programme of the site visit is included in Appendix 2.

The Committee members have all read the Self Evaluation Report. The key publications of each programme were read by the first and the second reviewers of each programme, who independently gave a preliminary assessment, using the form provided in the Protocol. These preliminary assessments were compiled and sent to the members before the visit.

The preliminary assessments were discussed in the committee meeting on February 29, 2004, preceding the site visit. For each programme the preliminary scores were determined and a number of comments and questions were decided upon. The Committee also agreed upon procedural matters and aspects of the assessment as described in the following paragraphs.

At the formal dinner in Groningen, the committee had the opportunity to meet with the rector of Groningen University and representatives of the Faculty Board and the Institute management.

The interviews with the management and programme directors took place during the site visits on March 1, 2004. All interviews and discussions were held by the entire Committee, the tours

of the facilities were conducted in two separate groups.

After the interviews, the Committee discussed the scores and comments for each programme and determined the final assessment.

On the morning after the site visit a meeting with the institute management was arranged, in which the main findings of the Committee were reported. These findings were also reported in writing a few days later.

A draft version of the report was sent to the institute in May 2004 for factual corrections and comments. In June 2004 the comments were discussed with the committee chairman. This led to minor corrections and clarifications. The report was subsequently submitted to the Board of Groningen University.

1.6 Aspects and Assessment Scale

The Protocol requires the Review Committee to assess the research on four main aspects, namely:

- Quality (international recognition and innovative potential)
- Productivity (scientific output)
- Relevance (scientific and socio-economic impact)
- Vitality and feasibility (flexibility, management, and leadership)

The Committee points out that the score for Productivity is not completely separate from the score for Quality, because the Committee did not choose to use a purely numerical calculation as an indicator. Wherever possible on the basis of the data provided, the Committee took into account the impact and prominence of the journals and publishers.

The ratings used are: Excellent; Very good; Good; Satisfactory; Unsatisfactory.

Note: The ratings specified in the *Standard Evaluation Protocol* differ from the ratings specified in the VSNU-Protocol which was valid until 2003. From 1993 to 2003 the ratings were: Excellent, Good, Satisfactory, Unsatisfactory, Poor. This means that from 2003 a new rating “Very good” is added between “Excellent” and “Good”, and the rating “Poor” is abandoned.

When comparing scores this must be taken into account very carefully!

	VSNU 1992-2002	SEP 2003-2009	
5	Excellent	Excellent	5
		Very good	4
4	Good	Good	3
3	Satisfactory	Satisfactory	2
2	Unsatisfactory	Unsatisfactory	1
1	Poor		

2 The Institute GUIDE/FMS

2.1 Research policy

From the very comprehensive documentation provided it is evident that the research policy measures that were initiated after the last review, have been effective. There is a steady increase in the funding for GUIDE/FMS as a whole and most programmes show increases in all types of funding. Most of the funding in the programmes comes from projects obtained through competition in the 'derde geldstroom' (contract research). The income from the 'tweede geldstroom' (through the funding council NWO) also shows significant increases.

The policy measures that were taken include the appointment of research minded professors in selected fields, the start of a 'tenure track' system and an MD/PhD programme, the strengthening of the pre-clinical departments, large investments in up to date research facilities and generally a more research driven attitude.

The results in terms of publications, PhD theses and patents show a significant increase from 1997 to 2002. The academic publications rose from 345 in 1997 to 622 in 2002.

2.2 Mission & Strategy

The mission of GUIDE/FMS is to promote research into the pathophysiology of disease in order to establish new drug treatment options. In-depth studies into the pathophysiology of primarily chronic diseases are combined with advanced knowledge on the development of new drugs. The results of patient-oriented research are translated into new pathophysiological concepts, and vice versa.

The committee has investigated to what extent the separate research programmes of the Institute are actually involved in this complete chain of activities, ranging from the clinic to the drug development. This is a central issue from the perspective of the synergy within GUIDE/FMS, but also from the perspective of the fruitful cooperation with the pharmaceutical research in the adjoining research institute GRIP (Groningen Research Institute for Pharmacology). The committee found that in a number of programmes the drug exploration aspect is certainly present and that in those cases the expertise of the pharmacological researchers is well embedded. Good examples can be found in programmes 1 (Kidney), 4 (Lung, GRIAC) and 6 (Immunology, TRIO). In programme 4 the cooperation with Pharmacy is well established both through molecular pharmacology and through the development of animal models.

The actual drug development stages are most clearly present in programme 5 (Liver), in which case the development is not only targeted towards pharmacological goals, but also towards other industrial and nutritional domains. The committee is convinced that especially in this programme the close cooperation with GRIP has led to better medical understanding of the pharmacological needs, and has stimulated the pharmacological understanding of the relevant receptors for liver diseases. As such, this particular programme is another good example of the fruitful synergy between medical and pharmaceutical domains.

The committee felt that it could not adequately judge the full extent of that medicine/pharmacy synergy in each of the GUIDE/FMS programmes and in the total of the programmes of GRIP and GUIDE/FMS. It is true that in the documentation and in the interviews this topic was

raised, and the committee has taken this topic into account in the programme assessments as much as possible, but the committee feels that this topic deserves more specific attention.

Therefore, the committee recommends that the programmes and the Institutes conduct an additional analysis of the medicine/pharmacy synergy: what is the added value, what are the problems encountered, what are the organisational consequences? The next external review could then be organised in such a way that the medicine/pharmacy synergy can be fully evaluated.

Such an additional self-analysis also has strategic implications. The strategic view of GUIDE/FMS is to facilitate cooperation between their clinical and preclinical researchers and the biomedical researchers in the Pharmacy Department, in order to combine knowledge concerning the pathophysiology of a collection of related diseases with knowledge concerning drugs. The ultimate goal is to initiate and explore new concepts for treatment of disease. To what extent this strategy not only includes drug exploration but also the actual development of drugs or drug components, is a matter for careful consideration. If the answer is yes, a more coherent policy to that effect must be developed. That policy needs explicit support from both faculties concerned and from the University Board.

In any case a reduction of the structural and administrative complexity would seem helpful to reach the strategic objectives. In order to further strengthen the integrative trends, the committee would find it a logical step to consider placing GRIP and GUIDE/FMS under the authority of one Faculty.

2.3 Broader perspective

Pharmacoepidemiological research is an important element for the mission of GUIDE/FMS because it can provide insight into the gap between scientific evidence and practice, by identifying problems in drug use from the perspective of the doctors, the patients or the context. The size of programme number 3 (Pharmacoepidemiology and Drug Policy) is in itself insufficient to sustain a powerful influence towards the whole of the GUIDE/FMS research. In that sense it is understandable and commendable that programme 2 (Cardio) has carried out pharmacoepidemiological research within the programme itself and that the director of GUIDE/FMS has plans to attract two additional fte with this type of expertise.

Options to fuse programme 3 (Epi) with programme 1 (Kidney) and/or 2 (Cardio) or with programme 7 (Oncology) are feasible, but it should be borne in mind that the epidemiological expertise is important for the Institute as a whole. Maintaining a central facility for pharmacoepidemiological expertise, building upon the work of programme 3, would help to ensure that clinical trials lead to effective medication not only from a scientific perspective but also from a social and societal perspective. This is not just a matter of gathering data; there is a need for the development of scientific methodologies for evaluating the effects of medication in a broader sense, which can give unique added value for the clinical research. The research of programme 3 goes in the right direction but needs more critical mass. The existing embedment in the division Pharmacoepidemiology and Drug Policy (PEDP, which also has a department in the GRIP part of GUIDE) has apparently not been able to fully develop the right conditions for the potential added value.

2.4 Societal relevance

The relevance and appreciation of the research not only depends on the choice of the diseases, but also on the degree in which the research questions are formulated with reference to societal needs, as communicated through patient organisations, health institutions, governmental bodies, etc. Three programmes in particular have laid the groundwork to maintain interactions with doctors, apothecaries and patient organisations, namely Cardiology, GRIAC and Oncology. The other programmes also show high societal relevance, as evidenced by the results of the assessment of the socio-economic impact of the groups and subgroups, which is presented in the documentation. The Institute has carried out a self-assessment of the societal relevance of the programmes, using a method based on guidelines of the KNAW and on the methodology developed by SciQuest which was used in the review of GRIP. The Institute has modified this method to make it more manageable and to adapt the assessment to the area of medical research. Information was obtained by means of a stakeholder enquiry to evaluate the profile and the socio-economic impact in three domains: academic, industry and society. The overall result of the assessment of the societal impact of GUIDE/FMS shows strong embedment in all three domains. All groups not only fulfil the research targets set in their mission (which is predominantly scientifically oriented), but most groups are also strongly embedded in the societal and industrial domain.

2.5 Facilities

The committee considers the equipment and facilities an important asset of GUIDE/FMS. They are simply at top level, both in terms of the modernity of the technical infrastructure, and in terms of the level of skill and knowledge of the operating staff. Most importantly, the innovative research questions are geared towards optimal utilisation of the possibilities that the technical infrastructure provides, creating a true cutting edge situation.

Efficient use of the equipment is ensured by the fact that several groups share in the cost of purchase, maintenance and operation. The committee has noticed that the scientists agree that sharing the facilities also leads to interesting scientific confrontation and cooperation.

2.6 Research training

GUIDE/FMS and GUIDE/GRIP have a joint educational programme for PhD and MSc-students. This is a full fledged training programme for young researchers implemented through GUIDE. The PhD-students include AIO's, MD/PhD's, Clinical Researchers in Training (AGIKO's) and international trainees. The MSc-students include 'junior scientific master' and 'top-master' students. The programmes prepare these students technically and functionally for a career in an academic and industrial setting and are part of a structured educational process.

Core of the training is to let the student do in-depth hypothesis driven research. During a fixed period of time the students perform experiments and write scientific papers as part of the required preparatory work towards the defence of a thesis. In this period they are coached by an experienced researcher in a master-apprentice relation, they participate in regular research group meetings and attend 'master classes', seminars, symposia and congresses. In addition to this, the PhD students must attend courses to broaden their scientific view. Courses are either research related (methodology, pathophysiological or pharmaceutical concepts) or of a more general nature (e.g. courses in project management or entrepreneurship).

GUIDE is also responsible for the scientific training of top-master students in the framework of the top-MSc programme 'Medical Pharmaceutical Drug Innovation' which started in September 2003. After graduation most of these students are expected to enrol in a PhD-programme.

Finally, GUIDE is involved in the scientific training of medical students in the framework of the Junior Scientific Master programme, which can be followed by an additional 2-year curriculum leading to an MD/PhD-degree.

The committee has not fully assessed these research training programmes in the course of this review, but in the interviews and poster sessions that the committee has had with PhD-students, it became clear that the students are satisfied with the facilities, the organisation and the intellectual climate of their training. From the documentation provided it is evident that the research training is well organised. An Individual Training and Supervision Plan is made for each PhD student and their activities are registered in a log. Supervision is carried out by tenured staff. After one year an assessment of the progress takes place with promotor, supervisor and a personnel consultant. The PhD educational committee meets twice a year with the GUIDE management to discuss the training programme, evaluate existing courses and initiate new courses.

2.7 SWOT

The strength of GUIDE/FMS lies in the good quality research programmes aimed at a collection of related diseases. Especially the relationships between the diseases and between the research approaches provide a potential breadth and coherence with unique added value. This breadth can turn into a weakness if there are areas where sufficient depth cannot be attained. The management is aware of this, and has an open eye for structural opportunities and threats.

3 Assessments per programme

The Committee has carried out an assessment at the level of the programmes, as defined by the Institute. The documentation included descriptions and data not only at the programme level, but to some extent also at the level of subgroups or 'research lines' (up to four in the larger programmes).

The committee decided that complete assessments of all separate subgroups were not possible in the given time (a) because there is a large degree of integration in the programmes, and (b) because only the documentation presented at the programme level fully complies with the requirements of the Standard Evaluation Protocol (SEP). This is the reason why in the programme assessments scores are only provided at the programme level and not at the subgroup-level.

The committee has included remarks about subgroups in the assessment texts wherever this could add perspective to the overall picture.

The five point scale used in the assessment is described in the Standard Evaluation Protocol as follows:

- | | |
|-------------------------|---|
| 5 Excellent | Work that is at the forefront internationally, and which most likely will have an important and substantial impact in the field. Institute is considered an international leader. |
| 4 Very Good | Work that is internationally competitive and is expected to make a significant contribution; nationally speaking at the forefront in the field. Institute is considered international player, national leader. |
| 3 Good | Work that is competitive at the national level and will probably make a valuable contribution in the international field. Institute is considered internationally visible and a national player. |
| 2 Satisfactory | Work that is solid but not exciting, will add to our understanding and is in principle worthy of support. It is considered of less priority than work in the above categories. Institute is nationally visible. |
| 1 Unsatisfactory | Work that is neither solid nor exciting, flawed in the scientific and or technical approach, repetitions of other work, etc. Work not worthy of pursuing. |

Institute:	GUIDE/FMS, University of Groningen	
Programme 1:	Groningen Institute of Kidney Diseases	
Programme director:	Prof. dr. P.E. de Jong, Prof. dr. D. de Zeeuw	
Academic staff in 2002:	11.6 fte	
Assessments:	Quality	: Excellent
	Productivity	: Very good
	Relevance	: Excellent
	Prospects	: Very good

This research group has an excellent track record and has found wide-spread international recognition. Particularly the epidemiological study (PREVEND: Prevention of Renal and Vascular Endstage Disease) addressing the issue of incipient renal damage in the general population, including microalbuminuria, has broken ground and, as illustrated by the publication record, deservedly found international recognition. In addition, they have made an effort to characterise the renal effects of pharmacological blockade of the renin angiotensin system, mainly in focused clinical studies, as well as in some experimental studies, and have participated in major multicentre trials. This has placed the Groningen group, including a.o. Prof. D. de Zeeuw, in the top ten in this field. They have managed to play an internationally visible role through their numerous activities, educational and otherwise, in this field.

In the future, the PREVEND study holds great promise to obtain good results from the follow-up investigations. The most promising approach in the future will consist in closely cooperating with other disciplines. Of particular interest will be the aspect of cardiovascular risk attached to even minor renal dysfunction, a point which has been recognised only recently and to which the PREVEND study will certainly make major contributions. The link between minor renal dysfunction and the metabolic syndrome has also been recognised only recently and in this context it is particularly laudable that the group has acquired manpower (Gans and Wolfenbüttel) to cover these areas which predictably will play a major role in the PREVEND programme.

Such new lines of research (particularly the genetic programme, the cardiovascular risk profile programme, the issues of metabolic syndrome and microinflammation) will certainly enhance the impact of the study and the investigators are aware of this perspective.

From a public health perspective the study has considerable societal value, because early diagnosis and prevention is a rational strategy. The group has been very active in acquiring funds and funding appears to be adequate.

The studies focussing on pharmacological blockade of the renin angiotensin system in renal patients have led to much more rational use of this tool, particularly by defining proteinuria per se as a therapeutic target, and are thus of major public health importance as well. The novel

approach to define more clearly factors predisposing to response and non-response respectively, genetic and evaluation of antagonising systems, e.g. NO etc., are relevant.

Institute:	GUIDE/FMS, University of Groningen	
Programme 2:	Cardiovascular Centre	
Programme director:	Prof. dr. W.H. van Gilst, prof. dr. D.J. van Veldhuijsen (from December 2001), prof. dr. H.J.G.M. Crijns (until December 2001)	
Academic staff in 2002:	9.05 fte	
Assessments:	Quality	: Very good
	Productivity	: Excellent
	Relevance	: Excellent
	Prospects	: Very good

This programme is divided into three research lines, all focusing on heart failure:

- (i) clinical heart failure,
- (ii) experimental heart failure, and
- (iii) atrial fibrillation.

Despite the apparently somewhat divergent approach, the programme has strong and coherent leadership with a clear mission and goals. The goal is to develop new treatment strategies that will improve the prognosis of patients with heart failure, and ultimately to prevent or to formulate a cure for this lethal disease. The relatively small size of the programme favours coherence in the elaboration of these goals.

All three subgroups have published a substantial number of papers in the most prestigious peer-reviewed international journals, some of which with inter-group co-authorship.

Given the fact that cardiac failure constitutes the major epidemic of the coming decades, the relevance, both societal and academic, of this program has been and will still continue to be of the highest importance.

Moreover, bringing together the strengths, know-how, and expertise of these three research lines will further strengthen the entire GUIDE Institute of the Medical Faculty in Groningen.

Institute:	GUIDE/FMS, University of Groningen	
Programme 3:	Pharmacoepidemiology and Drug Policy	
Programme director:	Prof. dr. F.M. Haaijer-Ruskamp	
Academic staff in 2002:	1.95 fte	
Assessments:	Quality	: no score
	Productivity	: no score
	Relevance	: no score
	Prospects	: no score

The mission of this programme is to improve rational drug use by strengthening the link between evidence and actual practice. This is done by studying the continuous tension between scientific evidence, evidence based guidelines and actual prescribing practice. The research aims at developing tools and strategies for improving rational pharmacotherapy. One method is the use of dynamic databases for identifying gaps between evidence and practice. Randomised controlled trials, cohort studies and time series analyses are the quantitative approaches used. Comparative international studies enable the study of the impact of cultural context and the health care system.

Evaluation

In the opinion of the committee, this programme is so small that it should not have been submitted for review as a separate programme. The total senior staff was 0.3 fte from 1997 to 2001 and 0.4 fte since 2002. The total staff including PhD-students was 1.0 fte in 1997 and 1.95 fte in 2002. The activities have a high societal relevance, but they should either be broadened or incorporated in another group as a methodological approach. (See 2.3)

The committee has a positive general opinion about the research approach. There is an awareness that the patient can be an important agent of change. The doctors, patients and policy makers are regarded as target groups. The programme has close links and shares its main objectives with the pharmacoepidemiological programme of the Groningen Research Institute for Pharmacy (GRIP).

Institute:	GUIDE/FMS, University of Groningen		
Programme 4 :	Groningen Research Institute for Asthma and COPD (GRIAC)		
Programme Director :	Prof. dr. D.S. Postma and prof. dr. W. Timens		
Academic staff in 2002:	12.55 fte		
Assessment :	Quality :	Excellent	
	Productivity :	Very good	
	Relevance :	Excellent	
	Prospects:	Excellent	

The researchers have set themselves the ambitious goal to better understand two forms of obstructive airway diseases (asthma and Chronic Obstructive Pulmonary Disease COPD) that bear a significant health burden.

Four multidisciplinary research lines have been developed. These are centred around clear working hypotheses. The researchers have assembled the expertise and a broad range of research tools required to adequately address the hypotheses raised. The research lines are:

1. Epidemiological risk factors
2. Genetic background
3. Pathophysiology and pathogenesis of allergen-, environment- and smoke-induced disease
4. Assessment, modulation and intervention in disease severity and progression.

The researchers also take full advantage of the unique opportunities offered by the large catchment area (i.e. the northern provinces) but especially by the relatively isolated position of the region, thus allowing long term follow up of a genetically rather homogenous population.

The proposed research is of high societal relevance. Of note is that whilst being scientifically very active, the group also devotes much attention to local initiatives aiming at improving public health and involving the community in their research.

The internationally acclaimed quality of the programme director and staff members stands beyond any doubt. The sustained productivity in academic terms is very good.

As for any high-level multidisciplinary research project, it will be extremely important to maintain close attention to the coherence of research lines derived from the hypotheses that are formulated.

Institute:	GUIDE/FMS, University of Groningen	
Programme 5:	Centre for Liver, Digestive and Metabolic Diseases (CLDS)	
Programme director:	Prof. dr. P.L.M. Jansen (until 2003), Prof. dr. F. Kuipers	
Academic staff in 2002:	27.25 fte	
Assessments:	Quality	: Excellent
	Productivity	: Excellent
	Relevance	: Very good
	Prospects	: Very good

The group has two main lines of research, namely *liver transport and metabolism* on the one and *drug targeting* (in collaboration with the group of Meijer/Poelstra) on the other hand. In both domains, the group is excellent and internationally renowned and acknowledged as leaders in the field.

The programme director, Prof. Jansen, left Groningen University in November 2003 and was succeeded as CLDS-coordinator by Prof. Dr. F. Kuipers. His own line of research – metabolism – is very strong and of international stature. In the same research line the group of prof. D. Hoekstra, working on membrane biogenesis and lipid sorting, is also of excellent standing. Amongst other new or renewed research lines, two programmes will focus on the treatment of cholestatic liver diseases and intestinal development.

In the second line of work - drug targeting- the group depends heavily on the group of professor Dirk Meijer who will retire in 2005. Three professorships will together maintain the activities of this group.

The committee considers the planned approach – a combination of metabolite flux studies using stable isotopes with proteomics and genomics very promising. Of particular relevance is the fact that they have succeeded in downscaling their established *in vivo* methods from rats to mice thereby making possible the use of transgenic mice. In these studies as well as in the second line of research, targeting of nuclear receptors in control of glucose and fat metabolism and their interactions is again a very original and highly promising approach.

The publication output of the group is excellent with about one third of their publications appearing in the highest rating journals in the field, among others *Embo J*, *J Biol Chem*, *Gastroenterology* and *Hepatology*. Of particular note is that the group has generated more than one patent per year.

Most of the proposed research – in particular a better understanding of the control of glucose and fat metabolism and their interactions – is of high societal value since type II diabetes and non-alcoholic liver disease / steatohepatitis are emerging as a major health-burden.

Institute:	GUIDE/FMS, University of Groningen	
Programme 6:	Transplantation, Immunology and Inflammation (TRIO)	
Programme director:	Prof. dr. C.G.M. Kallenberg and prof. dr. M.J.H. Slooff	
Academic staff in 2002:	24.95 fte	
Assessments:	Quality	: Very good
	Productivity	: Very good
	Relevance	: Very good
	Prospects	: Very good

This programme is divided into four research themes, Transplantation, Autoimmune Disease, Infectious Diseases and Tumour Immunology. The themes have a common goal – the design of novel, more specific strategies for immunotherapeutic intervention and the prevention of disease.

Translational research is a major strength of the programme and should continue to be developed in order that the programme can take advantage of the clinical resources and facilities that are unique to Groningen.

In view of the importance of the transplantation research, prof. dr. M.J.H. Slooff, head of the department of Hepatobiliary Surgery and Liver Transplantation, was appointed to succeed as second coordinator of this programme in September 2002. Given the diversity of interests within this programme, this complementary expertise will provide leadership across the whole programme.

The diversity of the programme is both a strength and a weakness. The research priorities within each of the themes have been focussed to cover 3-4 topics. However, given the resources available and the ability to secure external and internal funding at an adequate level to support each theme in the future, it may be beneficial to consider restricting these further if the objective is to ensure that the programme as a whole and the individual themes achieve the highest possible standard in the future. A framework based upon concepts rather than topics (as presented to the committee during the interview) may be a good way to bring the different aspects of the programme together and to develop a coherent strategy for the future.

The group demonstrated good internal links within TRIO as well as cross programme links within GUIDE and to a certain extent GRIP. Strengthening internal links within TRIO to develop themes that cross the topic boundaries may give the programme additional value.

The programme has a consistent track record of publications and should continue to aim for quality rather than quantity. A series of patents have been filed during the review period.

Key funding has been obtained in the past year that will strengthen both the faculty and project base. A strategic review by the leadership in the light of these developments would be valuable.

Institute:	GUIDE/FMS, University of Groningen	
Programme 7:	Northern Netherlands Oncology Centre (NNOC)	
Programme director:	Prof. dr. E.G.E. de Vries and prof. dr. H.J. Hoekstra	
Academic staff in 2002:	46.25 fte	
Assessments:	Quality	: Excellent
	Productivity	: Very good
	Relevance	: Very good
	Prospects	: Very good

This programme is divided into four subprogrammes, and in different ways each has made an international impact.

(1) Cancer : genes, mutations and consequences

The group has performed important work on characterising individuals at risk of Hereditary Nonpolyposis Colorectal Cancer (HNPCC, also called Lynch syndrome, or Cancer family syndrome), and is now moving towards identifying low penetrance genes in this disease. This should take advantage of the stable founder population in the north of Holland. The group is pursuing studies in various aspects of genetic instability in cancer, including work on the role of molecular chaperones. While this could offer new opportunities in cancer therapy it is a particularly crowded area at present, and the competitive edge of this group is uncertain. Other studies have been focused on genes that regulate haematopoietic stem cell development, and this clearly overlaps with subgroup 2 below.

(2) Haematopoietic development and haemato-oncology

The group has examined mechanisms underlying normal and malignant stem cell functioning, and interesting observations on the role of transcription factors such as Stat-5 have been made. In the context of GUIDE in terms of new targets, the therapeutic implications of this work could be further considered with other groups.

The arrival of prof. dr. Ph. M. Kluin has resulted in expansion of the molecular pathology programme in lymphoma, particularly examining chromosomal translocations in malignant B cells. This will clearly have a positive impact.

(3) Translational oncology

The problem of drug resistance forms a particular focus, both in solid and haematological tumours, and the work on the death receptor pathway is particularly noteworthy. Innovative work on markers and imaging has been done, and the Groningen PET centre is a world leader. Tumour targeting (in collaboration with the Immunology Division) has been a major theme, and with their in vivo model, the group is well placed to make a further clinical impact, particularly using novel bispecific antibodies.

(4) Clinical studies

The Centre contributes well to single and multicentre clinical trials. The profile in germ cell and lung cancer is high, and long-term toxicity data have been carefully collected and are of considerable importance. Studies in gastric and rectal cancer, which demonstrate the roles of surgery and radiotherapy, have made an international impact and the importance is the recognition of the contribution of all treatment modalities.

Overall

The NNOC is a very good quality centre, with some excellent individuals working within it. The productivity in terms of scientific output is particularly noteworthy. Outstanding features are the PET centre (positron emission tomography), and the translational group working in tumour immunotherapy.

Interactions within GUIDE appear to be healthy; for the future it may be important to take full advantage of the opportunities presented to take potential new targets further towards new drug development, in conjunction with the Pharmacy school. Thought could be given to redefined project teams in this regard.

The NNOC is a large centre, and this makes it difficult to discern a strategic focus. To maximise the opportunities for progress across the full range of preclinical/translational/clinical projects, it may be worthwhile to consider smaller teams, concentrating on questions within a specific tumour type, combining expertise from different backgrounds.

APPENDIX 1 **Curricula vitae of the members of the Review Committee**

Prof. Dr. Joost Ruitenberg is professor for International Public Health at the Institute for Innovation and Transdisciplinary Research of the Vrije Universiteit Amsterdam. From 1989 until 2001 he was the general director of research of the Central Laboratory for Blood-Transfusion of the Dutch Red Cross (now CLB-Sanquin). From 1984 he was professor of Veterinary Immunology at the faculty of Veterinary Sciences, University of Utrecht and from 1985 he is a member of the Royal Academy of Arts and Sciences (KNAW). From 1962 until 1986 he worked for the Dutch National Institute for Public Health and the Environment (RIVM), from 1970 as head of the Laboratory for Pathology, from 1980 as director responsible for vaccine-production and research, and from 1986 as deputy director-general. He is a member of the Standing Committee on Infection and Immunity of the Health Council.

Prof. Dr. Dirk L. Brutsaert is emeritus Professor of the University of Antwerp, Belgium; presently Head of the Cardiology Department, Middelheim Hospital, University of Antwerp. He is President of the Royal Academy of Medicine of Belgium (KAGB) and Co-Chairman of the Working Group on Heart Failure of the European Society of Cardiology. He was director of the Laboratory for Human Physiology and Pathophysiology of the University of Antwerp.

Prof. Dr. Stan Kaye is Head of the Section of Medicine in the Institute of Cancer Research and of the Department of Medical Oncology in the Royal Marsden NHS Trust - Comprehensive Cancer Centre, London, UK. He is a medical oncologist, known for his work on drug development and drug resistance, and was Head of The Cancer Research UK Department of Medical Oncology at the University of Glasgow from 1985 to 2000.

Prof. Dr. Johan C. Kips, Department of Clinical Genetics, Ghent University Hospital, Belgium, is chairman of the Asthma Section of the European Academy for Allergology and Clinical Immunology.

Prof. Dr. Jürg Reichen is Professor of Medicine in the Faculty of Medicine of the University of Berne since 1986. Since 1994 he is Co-Director of the Department of Clinical Pharmacology, University of Berne, Switzerland and since 2001 chief of hepatology at the University Hospital in Berne, Switzerland. From 1994 to 1999 he was also co-director of the Department of Clinical Research and from 1998 – 1999 associate dean for research. His awards include the Prize of the Swiss Society for Internal Medicine (1987), the Prize of the Swiss Society for Gastroenterology (1987), the Cloëtta Prize (1995) and the Lucie Bolte Prize (2002). He is founding member of the Swiss Association for the Study of the Liver, and of the United European Gastroenterology Federation and a Fellow of the Academia Europaea. He is Associate Editor of the Journal of Hepatology and Trustee of Novartis (formerly Sandoz) Research Foundation. His main research interest is novel approaches to understanding and treating chronic liver disease.

Prof. Dr. Eberhard Ritz, is emeritus director of the Nephrology Department of the University Hospital, Heidelberg, Germany. He received the Science Prize of the German Hypertension Society, the Medal “Distinguished Investigator” of the National Kidney Foundation (USA), the Paul-Langerhans-Medal 2003 of the German Diabetes Society and of the John Peters award of the American Society of Nephrology. He is past president of the Gesellschaft für Nephrologie, past council member of the European Renal Association and currently vice president of the International Society of Nephrology. He was president of the “World Nephrology Congress” in Berlin, June 2003. He is editor in chief emeritus of Nephrology, Dialysis, Transplantation and currently associate editor of the Journal American Society Nephrology. He is honorary member of the French, Italian, British, Polish, Australian and Czech Societies of Nephrology.

Prof. Dr. Kathryn J. Wood is Professor of Immunology at the Nuffield Department of Surgery at the University of Oxford and a Visiting Professor at the University of Kyoto. She obtained her PhD in immunochemistry from the University of Oxford and has more than 20 years of experience in immunology and transplantation. She works in close association with the clinical team at the Oxford Transplant Centre to facilitate the translation of new therapeutic approaches in transplantation to the clinic. Professor Wood holds a Royal Society Wolfson Research Merit Award and is a Fellow of The Academy of Medical Sciences, UK. She is a member of the International Scientific Advisory Board of the Immune Tolerance Network of NIH and an Editor of the journal Transplantation.

APPENDIX 2 Program of the site visit of GUIDE/FMS

Sunday, February 29th

- 16.00-18.00 hrs.** Meeting of the committee (protocol and preparatory discussions; discussion of preliminary assessments)
- 19.00 hrs.** Dinner with the Rector Magnificus of the University, the dean of the Faculty of Medical Sciences, the director of GUIDE/FMS and a small selection of other persons from GUIDE

Monday, March 1st

- 8.30 – 9.20 hrs.** Meeting with the management of the institute (the director of GUIDE/FMS), in the presence of the Rector Magnificus of the University, the dean of the Faculty of Medical Sciences, and the director of GUIDE/GRIP
- 9.30 – 10.15 hrs.** Meeting with the coordinator of program 1 ‘Groningen Institute of Kidney Diseases’, Prof. Dr. Paul de Jong
- 10.15 – 11.00 hrs.** Meeting with the coordinator of program 2 ‘Cardiovascular Centre’, Prof. Dr. Wiek van Gilst
- 11.00 – 11.45 hrs.** Meeting with the coordinator of program 3 ‘Pharmacoepidemiology and Drug Policy’, Prof. Dr. Floor Haaijer – Ruskamp
- 11.45 – 12.30 hrs.** Meeting with the coordinator of program 5 ‘Centre for Liver, Digestive and Metabolic Diseases’, Prof. Dr. Folkert Kuipers
- 12.45 - 14.30 hrs.** Poster presentations of the various programs presented by PhD students and a short visit to selected facilities
- 14.30 – 15.15 hrs.** Meeting with the coordinators of program 4 ‘Groningen Research Institute for Asthma and COPD’, Prof. Dr. Dirkje Postma and Prof. Dr. Wim Timens
- 15.15 - 16.15 hrs.** Meeting with the coordinators of program 6 ‘Transplantation, Immunology and Inflammation’, Prof. Dr. Cees Kallenberg and Prof. Dr. Maarten Slooff
- 16.15 - 17.15 hrs.** Meeting with the coordinators of program 7 ‘Northern Netherlands Oncology Centre’, Prof. Dr. Liesbeth de Vries and Prof. Dr. Harald Hoekstra
- 17.15 – 17.45 hrs.** Meeting with PhD students
- 18.00 – 19.30 hrs.** Meeting of the committee

Tuesday March 2nd

- 9.00 – 10.00 hrs.** Meeting with the director of GUIDE: presentation of main findings