QANU Research Review
Pharmaceutical Sciences UIPS

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FOREWORD

This report follows the Standard Evaluation Protocol 2009-2015 (SEP) for Research Assessment in the Netherlands that was developed by VSNU, KNAW and NWO. The purpose of this report is to present a reliable picture of the research activities submitted for this review and to give feedback on the research management and quality assurance.

The review Committee was supported by QANU (Quality Assurance Netherlands Universities). QANU aims to ensure compliance with the SEP in all aspects and to produce independent assessment reports with peer review Committees of international experts in the academic fields involved.

QANU wishes to thank the chairperson and members of the review Committee for their participation in this assessment and for the dedication with which they carried out this task.

We also thank the staff of the units under review for their carefully prepared documentation and for their co-operation during the assessment.

Quality Assurance Netherlands Universities

Mr. Chris J. Peels
Director

Dr. Jan G.F. Veldhuis
Chairman of the Board

1. THE REVIEW COMMITTEE AND REVIEW PROCEDURES

Scope of the assessment
The Committee was asked to perform an assessment of the research of the Utrecht Institute for Pharmaceutical Sciences (UIPS). This assessment covers the research in the period 2004 - 2009.

In accordance with the Standard Evaluation Protocol 2009-2015 for Research Assessment in the Netherlands (SEP), the Committee's tasks were to assess the quality of the institute and the research programmes on the basis of the information provided by the institute and through interviews with the management and the research leaders, and to advise how this quality might be improved.

The 'discipline protocol' for this assessment specifies that the main objective is twofold:
to evaluate the quality of the individual research programs in order to enhance quality,
to contribute to the accountability of the research carried out during the period under review.
The assessment should also contribute
to the further improvement of fundamental and strategic research in the field of pharmaceutical sciences aiming for a high international level
to the development of concepts of therapeutic targets potentially leading to better and safer drugs and vaccines.
The evaluation of the research management at the institutional level (UIPS) should include leadership and management processes, research policy and strategy, people management and human resource policy, funding policy and appreciation by external peers. In addition, proper attention must be given to appreciation by society (societal value of research) and to postgraduate education and training programs. The evaluation should be carried out in view of the multidisciplinary context of pharmaceutical research.

Composition of the Committee
The composition of the Committee was as follows:

Prof. Douwe D. Breimer, Leiden University, chairman of the Committee
Prof. Ralph A. Bradshaw, University of California, San Francisco
Prof. Stephen J.W. Evans, University of London, London School of Hygiene & Tropical Medicine
Prof. Alexander T. Florence, University of London, Centre for Drug Delivery Research
Prof. George F. Koob, The Scripps Research Institute, La Jolla
Prof. Adam Nelson, Astbury Centre for Structural Molecular Biology, University of Leeds.

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

Roel Bennink of the Bureau of QANU (Quality Assurance Netherlands Universities) was appointed secretary to the Committee.

Independence
All members of the Committee signed a statement of independence to safeguard that they would assess the quality of the Institute and research programmes in an unbiased and independent way. Any existing personal or professional relationships between Committee members and programmes under review were reported and discussed in the committee meeting. The Committee concluded that there were no unacceptable relations or dependencies and that there was no specific risk in terms of bias or undue influence.

Data provided to the Committee
The Committee has received detailed documentation consisting of the following parts:
Self-evaluation report of the units under review, including all the information required by the Standard Evaluation Protocol (SEP) and the results of the citation analysis performed by CWTS
Digital copies of three key publications per research programme.

Remarks about the data provided
The Committee found the self-assessment report a very well-prepared, attractive and informative document. The presentations by the management and the programme directors were also very informative and the discussions were open and interesting. Requests for additional information were honoured without any hesitation.

Procedures followed by the Committee
The Committee proceeded according to the Standard Evaluation Protocol (SEP). Prior to the Committee meeting, each programme was assigned to two reviewers, who independently formulated a preliminary assessment. The final assessments by the Committee collectively are based on the documentation provided by the Institute, the key publications and the interviews with the management and with the leaders of the programmes. The interviews took place on 4 and 5 November 2010 (see the schedule in Appendix C) in the premises of UIPS.

Preceding the interviews, the Committee was briefed by QANU about research assessment according to SEP, and the Committee discussed the preliminary assessments. The Committee also agreed upon procedural matters and aspects of the assessment. After the interviews the Committee discussed the scores and comments. The texts for the committee report were finalised through email exchanges. The final version was presented to the Faculty for factual corrections and comments.

The final report was presented to the Board of Utrecht University and was printed after their formal acceptance of the report.

The Committee used the rating system of the Standard Evaluation Protocol (SEP). The meaning of the scores is described in Appendix B.

2. INSTITUTE ASSESSMENT

University: **Utrecht University**
Faculty: **Faculty of Science**
Institute: **Utrecht Institute for Pharmaceutical Sciences**

QUALITY

1. The institute

Description

The mission of UIPS is to carry out high-quality basic and strategic research in the Pharmaceutical Sciences, specifically to perform conceptual research focused on the discovery, development and use of drugs and medical food components. In addition, UIPS trains future research scientists in the field of Pharmaceutical Sciences.

The research focuses on processes around discovery, development, and use of drugs and medical food components using molecular and technological principles from the Natural Sciences. The research is primarily inspired by, but not limited to, disorders of the central nervous system and the immune system.

Strategic research questions	Expertise and programmes
Which mechanisms underlie the diseases under study?	*Pharmacology* involves investigating the basic mechanisms underlying diseases, which are mediated by the central nervous system and the immune system including its pharmacological manipulations via drugs, biological and medical food components.
Which biological (macro) molecular and cellular complexes play a role?	Researchers in *Biomolecular Mass Spectrometry and Proteomics* investigate the underlying mechanisms of action and side effects of drugs at the protein level, focusing on cascades of molecular processes and analysis of post translational modifications.
Which biologically active molecules are involved?	*Chemical Biology* involves studying molecular approaches to the design, synthesis and characterization of bioactive and biomimetic molecules and their use as chemical tools to study and influence biological processes. *Medicinal Chemistry* involves synthesizing, analysing (*Biomolecular Analysis*) and studying molecules that are active at disease-related targets.
Which delivery form is required to achieve the optimal concentration of a drug in the target location in the body?	*Pharmaceutics* is based on the delivery and targeting of drugs, by integrating Chemistry, Formulation, Biopharmaceutics and Cell Biology.
What are the effects of newly developed as well as existing drugs and medical food components in the population and in the individual?	This field of expertise has two main focal points: 1) large cohorts of patients (*Pharmacoepidemiology*) 2) the individual patient (*Clinical Pharmacology* and related bio-analysis).

During the period of review 2004-2009 UIPS coordinated six research programmes. Since the reorganization of 15 May 2010 UIPS has been restructured in order to focus on five programmes. This transition is illustrated in the following overview.

2004-2009	After 15 May 2010
- Immunopharmacology (Prof. J. Garssen/Prof. F.P. Nijkamp) - Psychopharmacology (Prof. B. Olivier)	- Pharmacology (Prof. B. Olivier; Prof. J. Garssen)
- Medicinal Chemistry and Chemical Biology (Prof. R.M.J. Liskamp)	- Medicinal Chemistry and Chemical Biology including Pharmaceutical (Biomolecular) Analysis (Prof. R.M.J. Liskamp)
- Pharmaceutics (Prof. W.E. Hennink)	- Pharmaceutics (Prof. W.E. Hennink)

- Biomedical Analysis (Prof. A.J.R. Heck), with three subgroups:
  - Biomolecular Mass Spectrometry and Proteomics (50/50 with Chemistry; Prof. A.J.R. Heck)
  - Pharmaceutical Analysis (Prof. G.J. de Jong)
  - Drug Toxicology (patients in Slotervaart Hospital, Prof. J.H. Beijnen/Prof. J.H.M. Schellens)
	- Biomolecular Mass Spectrometry and Proteomics (50/50 with Chemistry; Prof. A.J.R. Heck)

- Pharmacoepidemiology and Pharmacotherapy (Prof. H.G.M. Leufkens)	- Pharmacoepidemiology and Clinical Pharmacology including Drug Toxicology (Prof. H.G.M. Leufkens; Prof. J.H.M.Schellens, Prof. J.H. Beijnen)

The self-assessment report states that the research of UIPS is ideally positioned in the Faculty of Science to work on basic scientific problems and to translate new findings into potential solutions to urgent societal medical needs, which are addressed in the Faculties of Medicine and Veterinary Medicine.

Internal evaluation of the research is carried out via a planning/control cycle. UIPS management audits the internal research on an annual basis, evaluating the scientific quality of the tenured staff in terms of publications and external grants and funds acquired, making adjustments where necessary.

To intensify the Pharmacy-Chemistry collaboration within the Science faculty and the Pharmacy-clinical collaboration with the UMCU, new Chairs are planned in Chemical Neurobiology, Cellular and Translational Chemical Biology and Clinical Pharmacology.

Assessment
The Committee agrees with the strategic focus of UIPS on conceptual research focused on the discovery, development and use of drugs and medical food components. A valuable element in the strategy is that such research should be carried out in close collaboration with the societal field, including industry.

The Committee agrees with UIPS that the **positioning of the Institute** provides great opportunities. This not only applies to the position in the Faculty of Science (associated with basic research) and the close contacts with the Faculties of Medicine and Veterinary Science (associated with clinical research), but also to the link with Industry via Nutricia Research and to the link with public health via the RIVM in Bilthoven.

The complex relationships between basic research, preclinical research, clinical research and the actual production of drugs and health products, provide a good basis for UIPS as an Institute to create added value. Excellence in the research programmes or the opportunities provided by the proximity of related groups and organisations are in themselves not sufficient conditions to realise such an added value. The Committee is convinced that UIPS is aware of this and is continuously searching for ways to stimulate and facilitate **collaboration across internal and external borders**, both conceptual and practical. The Committee has attempted to focus this review on elements that may be helpful for this search.

The Committee has noticed that the statement in the UIPS mission that the research is primarily inspired by disorders of the central nervous system and the immune system, does not fully reflect the actual research in the programmes. Several elements of the drug discovery research rightly have no obvious links with any specific diseases, for example in pharmaceutics. In the view of the Committee, concentration of efforts should be based on a **shared focus on elementary problems to be tackled,** rather than being primarily associated with a specific disease. UIPS has good technology and methodology that can be applied to relevant problems; the challenge is to find the best groups and systems to link up with, based on complementarity of expertise.

The potential for more **translational research** seems an excellent starting point for this search. This allows UIPS to strengthen the research policy that aims to build bridges with human and animal medicine. The ultimate aim is to produce research results that can be used for the benefit of health.

In order to succeed in building bridges, UIPS must continue to find and strengthen aspects that make the Institute more than the sum of its parts. The 'programme committee' consisting of the

programme directors will not only have to agree on this, but they must also have the authority to **select and monitor research activities that support these cohesive aspects**. [1]

At the moment little money seems to be available for flexibility and **strategic research decisions**. This effectively limits the cohesive power of the leadership, because grants are acquired by the programmes and the Institute has hardly any money of its own. Nevertheless, the Committee believes that UIPS will have to increase the concerted efforts towards three kinds of collaboration:

- ***Collaboration within UIPS.*** UIPS has provided information to the Committee about the number of PhD-projects that are co-supervised from two or more programmes. That number is currently limited but is expected to increase. The Committee believes that increased collaboration between the programmes may provide strength for acquiring larger scale funding. UIPS could identify cross-programme strategic themes (grand challenges) with that goal in mind. These collaborative prioritised areas could be supported through the allocation of studentships from the UIPS Strategic Pool.[2]
- ***Collaboration with other departments within Utrecht University.*** There is a good level of such collaboration as evidenced by the proportion of collaborative PhD-students between 2004 and 2009. The strategic alliance in Utrecht Life Sciences is intended to forge links between education, research and entrepreneurship in the domain of the Life Sciences in the Utrecht area. This will also require clear views on prioritisation, complementarity and synergy.
- ***Collaboration with other groups in the Netherlands or abroad***. Some excellent examples of such collaboration were already presented in the documentation for this review. A common goal seems to be to facilitate a more integrative approach to drug discovery.

The strategic challenge for UIPS is to use these collaborations to create and maintain cohesion, and to prevent fragmentation. The Committee supports the intention to intensify the Pharmacy-Chemistry collaboration within the Science faculty and the Pharmacy-clinical collaboration with the UMCU, but the Committee feels that the centre of gravity of the Institute should remain in the pharmaceutical sciences. The new chairs planned to support these collaborations will play a crucial role in this respect, but the strategic challenges range more widely and involve many partners on several levels.

The Committee believes that the discussion on the future direction and the sharing of expertise aimed at increased interaction within UIPS will have to be intensified and aligned with strategic planning within the Utrecht network. Strong and inspiring leadership is required to achieve this, which represents a real challenge to the current leadership.

2. Academic reputation

Description
The self-assessment report gives an overview of personal grants in the review period, which illustrates the quality of the academic staff. Included are eight VENI, VIDI or VICI grants, one NWO top grant and several local, national and international awards.

[1] The Committee has learned that UIPS has regular **research retreats** involving all PIs to promote collegiality and interactions between programmes. These retreats are held twice a year. This seems to be a very valuable instrument in the strategic efforts towards synergy and cohesion. The aim should be to identify cross-programme grand challenges.

[2] The UIPS Strategic Pool funds 15 PhD students and allows to support and explore potential new or high-risk research directions and to match external finance for projects.

Table: Scientific collaboration and impact (1999-2008)

	P	C	C+sc	CPP	Pnc	CPP/ JCSm	CPP/ FCSm	JCSm/ FCSm	Self Citations
No collaboration	419	5,692	6,935	13.58	16%	1.18	1.28	1.09	18%
National	135	15,384	19,052	11.39	17%	1.04	1.19	1.14	19%
International	806	11,483	14,658	14.25	15%	1.15	1.37	1.19	22%

The self-assessment report mentions a number of programmes that are run with extensive external funding:

- NPC2 (Netherlands Proteomics Centre),
- Fondation Leducq (transatlantic collaboration on Proteomics)
- MediTrans (Targeted Delivery of Nanomedicine-FP6)
- IMI (IMI/PROTECT (Pharmacovigilance)
- Eu2P (Pharmacotherapeutic Education) and EU-Pact (Pharmacogenetics, coordinated by UIPS scientists)
- Danone alliance
- GSK alliance
- PsychoGenics Inc.

Assessment
Both the personal observation of the committee members and the examples provided in the self-assessment report, confirm the prominent position of UIPS-researchers in their respective fields on the national and international stage. The programme directors are among the leaders in their fields and are well-known from their publications and from their participation in conferences and other networking activities. From an international perspective, the reputation of UIPS as a research institute has secondary importance in this respect; in most cases the academic world will associate the individual researchers with Utrecht University, rather than with UIPS. The Committee does not regard this as a disadvantage or a weakness. In the view of the Committee, the added value of UIPS as an Institute is to provide a stable platform for individual and collective excellence, by means of coordination, cohesion and a common sense of direction.

UIPS has secured one major European Research Council (ERC) grant to date (Raymond Schiffelers, Microvesicle-inspired drug delivery systems, 2010). ERC grants provide a significant opportunity for individuals to build and lead research teams (especially interdisciplinary teams) to define and address major research problems. These grants are focused on academics at very specific stages in their careers; competitive individuals to lead these grants can be easily identified and then vigorously supported through careful management of other duties. In addition, assiduous mentoring is particularly important for applicants for ERC Starting Grant to ensure that the wider, strategic impact of the proposed research programme is clear to the broad scientific panels.

3. Quality and scientific relevance of the research

Description
In the period 2004-2009, UIPS adopted a publication strategy which was not just based on impact factors, but rather on the intention to publish in the top 25% of journals in a particular field. The percentage of papers in the top 10 and 25% journals in the relevant field has increased significantly since 2004.

	2004	2005	2006	2007	2008	2009
UIPS	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)
Top 10%	64(25%)	91(31%)	105(36%)	100(33%)	100(29%)	100(26%)
Top 25%	151 (60%)	189(65%)	210(73%)	220(73%)	220(63%)	262(68%)
Total #	**253**	**290**	**289**	**302**	**347**	**385**

The citation analysis carried out by CWTS shows that most articles receive above-average citations in the journals they appear in, and are cited more than the average articles published in the respective fields covered by the research groups. Most publications are in the field of Pharmacology and Pharmacy, but publications in other areas have even more impact. Output in 'non-core' areas (e.g. Organic, Multidisciplinary, Analytical, Polymer and Physical Chemistry, Rheumatology, Oncology, Endocrine & Metabolism, Cardiovascular and Respiratory fields) scores relatively high. Output in 'core' areas scores relatively low, but better than average. In the view of UIPS this indicates the high quality of the basic and pre-competitive research carried out: publications about novel findings in the basic fields of Biology, Chemistry and Medicine are well cited. Publications about the applications and validation of these novel findings in the Pharmacy field have a lower impact but still better than average. In the coming six years the target is to increase the field normalised impact, as measured by CPP/FCSm, to more than 1.5.

Assessment
The quality and scientific relevance of the research programmes is assessed in the programme sections of this report. Generally speaking, the Committee assesses the quality as very good to excellent. This means that some of the research is world leading and makes a substantial impact in the field, while most of the work is at least internationally competitive. The Committee regards this as an achievement to be proud of.

In the view of the Committee, the research management and the facilities at the level of the Institute are in line with the quality of the programmes. The management has excellent instruments for monitoring and feedback towards the programmes, including explicit performance indicators and targets.

The bibliometric data provided in the self-assessment report show a good performance. The Institute management makes a well-reasoned use of these indicators and aims at a higher impact level in the coming years.

4. Resources

Description
The table below summarizes the research capacity. The total number of staff is steadily increasing. This can be attributed mainly to the increase in PhD students. In 2009 UIPS had 158 PhD students (75.56 FTEs). On average, the tenured staff had a research task of 35%, the non-tenured staff (post-docs) 90% and the PhD students 70%. The ratio of tenured operational research staff to PhD students is currently 1 to 6, not counting external PhD students.

The total teaching load of all staff members is 45 FTE. The number of new Pharmacy students each year is 225.

Table: Research staff at the institutional level in FTE

	2004	2005	2006	2007	2008	2009
Tenured staff	25.21	26.28	24.97	24.20	25.96	26.21
Non-tenured staff	22.71	25.31	28.19	30.13	30.59	26.67
PhD students	56.42	59.93	59.35	59.31	63.55	75.56
Total research staff	**104.34**	**111.5**	**112.51**	**113.64**	**120.10**	**128.44**

Supporting staff	24.44	28.58	28.18	24.22	23.74	21.51
Total staff	**128.78**	**140.08**	**140.69**	**137.86**	**143.84**	**149.95**

UIPS has defined a "recruitment potency", which is the ratio of research grants and contract research (second and third flow of funds) to direct funding (first flow of funds) in FTE. It was above 3:2 in 2009. The ratio of the three flows of funds was 1 : 0.35 : 1.22 in 2009.

Table: Research staff in FTE per flow of funds

	2004	***2005***	***2006***	***2007***	***2008***	***2009***
Direct funding (1)	46.90	50.36	43.92	42.40	46.05	49.70
Research grants (2)	18.30	25.31	22.97	19.15	16.67	17.38
Contract research (3)	35.80	34.95	44.52	50.77	54.72	60.79
Total	**101.00**	**110.60**	**111.41**	**112.32**	**117.44**	**127.87**
Recruitment potency	***1.15***	***1.20***	***1.54***	***1.65***	***1.55***	***1.57***

Table: Funding and expenditure in €1.000.000

	2004	***2005***	***2006***	***2007***	***2008***	***2009***
Funding in €1.000.000(%)						
Direct funding (1)	6.66(45%)	7.21(54%)	7.16(52%)	7.52(58%)	6.93(49%)	7.28(46%)
Research grants (2)	2.75(19%)	3.27(24%)	1.03(7%)	1.21(9%)	0.99(7%)	2.01(13%)
Contract research (3)	3.06(21%)	2.79(21%)	5.57(40%)	4.09(32%)	6.20(44%)	6.40(41%)
Other (4)	2.22(15%)	0.12(1%)	0.05(0%)	0.14(1%)		
Total funding	**14.69**	**13.40**	**13.81**	**12.96**	**14.13**	**15.69**
Earning capacity	***0.65***	***0.83***	***0.92***	***0.69***	***1.04***	***1.16***
Expenditure						
Personnel (1)	4.58 (32%)	4.73 (39%)	4.61 (36%)	4.68 (34%)	4.73 (28%)	4.97 (34%)
Other costs (1)	2.76 (19%)	2.08 (17%)	1.94 (15%)	1.01 (7%)	2.74 (16%)	1.47 (10%)
Personnel (2)	0.97 (7%)	1.55 (13%)	1.11 (9%)	0.90 (7%)	0.89 (5%)	1.12 (8%)
Other costs (2)	2.98(21%)	1.03 (8%)	0.19 (2%)	0.21 (2%)	0.35 (2%)	0.42 (3%)
Personnel (3)	1.74(12%)	1.57 (13%)	2.80 (22%)	2.88(21%)	3.21 (19%)	3.64 (25%)
Other costs (3)	1.36 (9%)	1.26 (10%)	2.13 (17%)	3.90 (29%)	4.71 (28%)	2.92 (20%)
Total Expenditure	**14.39**	**12.23**	**12.79**	**13.58**	**16.63**	**14.53**

The earning capacity is the ratio of research grants and contract research (second and third flow of funds) to direct funding (first and fourth flow of funds) in €. On average it is around 1:1 and it has been increasing steadily since 2004. The ratio of personnel to other costs is on average 61:39. This includes the national facilities of the Netherlands Proteomics Centre (NPC).

UIPS aims to increase the ratio of human resources versus other costs to 70:30 (excluding national facilities), while in the meantime increasing recruitment potency from 1.5 to 2.

The institute is adequately equipped with a wide variety of basic and sophisticated experimental facilities and has open access to the shared Utrecht Life Science facilities, including e.g. MRI, and NMR technologies and animal imaging.

Assessment
The Committee concludes from the numerical data provided that UIPS is generally in a healthy state. The number of PhD-students is high and growing. The number of personnel, the teaching load and the ratio of personnel costs to other costs are well within normal bandwidths, on the understanding that the vacant positions will be filled as soon as possible. The targets set by the UIPS management are challenging. The research facilities have high relevance for the research, not only within UIPS but also locally, nationally and internationally.

[PhD Training: see separate chapter at the end of this report]

PRODUCTIVITY

6. Productivity

Description
The output increased to more than 3 refereed articles per research FTE in 2009. The number of PhD theses fluctuates over the years.

Table: Research output

	2004	2005	2006	2007	2008	2009	Total
Academic publications	266	333	314	332	354	393	1992
- refereed articles	257	327	313	328	351	388	1964
- other articles	1	0	1	0	1	1	4
- book chapters	8	6	0	4	2	4	24
- chapters in professional books	8	15	15	14	12	5	69
Monographs	1	2	0	1	0	1	5
PhD theses	25	23	34	31	20	36	159
Professional publications and output	157	167	222	189	139	152	1026

Assessment
The Committee finds the productivity policies and the actual output quantity fully satisfactory.

SOCIETAL RELEVANCE

7. Societal Relevance

Description
Several societal stakeholders were interviewed to comment on their collaboration with the research groups. The questions were based on a survey that was taken during the previous QANU assessment in 2003. In the self-assessment report, the results of the survey were presented in the chapters of the individual programmes.

UIPS was actively involved in setting up a variety of start-up companies such as PsychoGenics, Emotional Brain, Enceladus and others with an STW valorisation grant (e.g. Cristal Delivery). UIPS also actively participates in major research networks with industrial partners, e.g. with GSK, Danone, DSM, TI Pharma, BMM, CTMM, OctoPlus and PamGene.

Assessment
In the view of the Committee, the UIPS research is a very good example of a successful combination of basic research with potential and practical implications for important societal issues. The relevance not only lies in the general importance of health issues, but especially in the very concrete contributions to such issues that are made on the basis of the research findings and by the efforts towards productive interaction with stakeholders in society, such as the pharmaceutical industry, pharmacists, patient organisations and the general public.

There is however the concern that the apparent disconnect between UIPS and the important and extensive education programme in the training of pharmacists to become highly qualified professionals, is not given sufficient attention. Most UIPS scientists contribute to this education programme (it is in fact their primary teaching assignment), but clear affinity and commitment did not become apparent in the interviews with the Committee. Valuable research alliances such as those with Chemistry should not diminish the central importance of the undergraduate pharmacy cohort, in the view of the Committee.

VITALITY AND FEASIBILITY

8. Strategy

Description
UIPS is part of the Life Sciences focus at Utrecht University but formulates its own research strategy, which is aligned to the Department and Faculty strategy. The strategy is continuously discussed and reported to the Vice Dean of Life Sciences within the Science Faculty.

Every month a meeting between UIPS management and programme leaders is held. The programme leaders are responsible for the coherence and quality in the respective programmes; they are also responsible for the content and implementation of the research strategies and for the introduction of new scientific views and technologies in the education of future drug researchers.

As an institute UIPS is an attractive partner for external consortia and granting agencies because of its high external visibility. Although UIPS is built on separate research groups, the added value of the institute has proven its value. Because of its organizational structure, UIPS as a whole generates sufficient capacity and intellectual power to partner large external programmes; moreover, it also functions as a safety net capable of dealing with unexpected problems that arise in the research groups.

The Department applies a "tenure track" system with post-tenure review evaluations for new academic positions with personal career pathways on the basis of externally acquired personal grants (Vidi, Vici and ERC). UIPS offers all staff members the possibility to acquire Basic and Senior Qualifications in Research. Selected staff members follow courses in Academic Leadership.

The self-assessment report contains an elaborate and informative SWOT-analysis, based on discussions with internal and external experts.

Assessment
In the view of the Committee, the Institute has shown a good ability to react to changing internal and external circumstances. The Committee has seen several examples of clear evidence for this. In the coming period, this flexibility and anticipation of expected changes will be extremely important on several levels. The main challenge will be the alignment of the UIPS strategy with a multitude of external partners, both within the Utrecht Life Science area and in wider circles of collaboration.

The Committee is somewhat uncertain about the relationship of UIPS with the Department of Chemistry. Considering the strong position in Pharmaceutical Sciences in the Netherlands and internationally, the Committee does not support the formation of an Institute for Pharmaceutical Sciences and Chemistry. The identity of Pharmaceutical Sciences is an asset and strong itself and should not be diluted.

The apparent tension between the professional training of Pharmacists and the position of UIPS as a research institute seems to have caused some occasional disconnection which requires attention.

There are concerns regarding the financial situation, especially with regard to the number of permanent staff; the vacant new positions will have to be filled in order to maintain the

impressive earning capacity and research quality. This will have to be brought to the attention of the Faculty and the Executive Board of the University.

The Committee shares UIPS's plans for increasing the share of funding from NWO and ERC; additional effort will be needed to be successful there as well. The Committee believes that UIPS has considerable opportunities for increased collaboration between the programmes. The current number of projects that are co-supervised from two or more programmes is limited. Increasing such collaboration may provide strength for acquiring larger scale funding.

The gender issue requires a specific policy, in the opinion of the Committee. Especially at a senior level more female staff must be recruited and policy measures must be taken to achieve this, also in view of the fact that half of the student population is female, which means that there is good potential.

10. Robustness and stability

Description
UIPS scientists cover a wide range of scientific expertise, including chemists, biologists, pharmacists and physicians. The institute is adequately equipped with a wide variety of basic and sophisticated experimental facilities and has open access to the shared Utrecht Life Science facilities, including e.g. MRI, and NMR technologies and animal imaging.

UIPS regards an equal proportion of internal and external funding as the optimal situation, with a ratio of 70% for human resources and 30% for research infrastructure (excluding housing and national facilities).

Recent policy adjustments include:
An increased focus on core areas in pharmaceutical research (in particular, the action, delivery and use of drugs) based on an intensified basic (neuro/immuno) science approach
- Selection of investigators with an established track record in scientific quality and acquiring external funding. These investigators (PI's) form the core of *UIPS* research and create an intellectual environment to which new top-talented scientists can be attracted

Intensifying the Pharmacy-Chemistry collaboration within the Science faculty and the Pharmacy-clinical collaboration with the UMCU. New Chairs are planned in Chemical Neurobiology, Cellular and Translational Chemical Biology and Clinical Pharmacology
Intensified exchange between research and education
The creation of a new research-oriented Bachelor's programme, called the College of Pharmaceutical Science, starting in September 2010, which will deliver new generations of researchers through the Master's programme in Drug Innovation.

UIPS has developed a number of new policy instruments designed to further improve the quality of research and the PhD training programme, such as:
The UIPS Strategic Pool with 15 PhD students to support and explore potential new or high-risk research directions and to match external project funding
An investment budget for matching external funds to encourage research groups to acquire external funding for purchasing equipment, to encourage interactions between research groups and to create facilities for general use
A programme for continuing education of academic staff including sabbatical leave.

According to the self-assessment report, UIPS will evolve into a research institute of the Departments of Pharmaceutical Sciences and Chemistry. In the presentation during the site-visit,

the UIPS management stated that UIPS will develop into a Pharmaceutical Research Institute of the Science and Medical Faculties of Utrecht University, based on the strategic plan 2020.

The self-assessment report describes the following measures:
Analytical research will be strengthened by resituating two groups.
Medicinal Chemistry and Chemical Biology will be strengthened with world leading biology expertise in the field of Chemical Neurobiology as a joint venture between Chemistry and Pharmaceutical sciences.
Further strengthening of Pharmacology, including closer links with the clinic, is anticipated notably by creating and further development of an in-vivo whole animal expertise centre.
The Biomolecular Mass Spectrometry and Proteomics group needs high-level expertise in Cell Biology in order to maintain its leading position worldwide.
Further strengthening and focusing of the Pharmacoepidemiology group is anticipated, including Clinical Pharmacology (with respect to links with the clinic).

The basic pharmaceutical research is under pressure by the teaching responsibilities inherent to the professional Master Pharmacy, also because the associated Pharmacy Practice research is not funded by mandatory practical internships (like the Medical and Veterinary Sciences).

Recently, the financial situation of the Departments of Pharmaceutical Sciences and Chemistry, but also the Faculty of Science has deteriorated very seriously, so maintenance and investment in new equipment is at risk. This also applies to investments in the next generation of faculty. In addition, lab and office space in the new building on the Leuvenlaan will be reduced.

The Board of Utrecht University has allocated special funds to stimulate the collaboration between the Medical Centre (UMCU), Chemistry and Pharmaceutical Sciences. The programme on Drug Innovation is part of the UU Focus & Mass initiative.

Assessment
The Committee assesses the viability of the Institute, in terms of resource management, available infrastructure and innovative capacity, as very good. However, the current financial situation seems to endanger several elements in the strategy of the Institute, such as the strategic pool of PhD-students and possibly the new chairs planned. This poses challenges for the UIPS leadership and for the programme directors. In a wider sense, elements in the regional, national and international network may be affected. The Committee believes that the structure and quality of the Institute provide a good basis to handle these challenges. Alignment with strategic perspectives of the Faculty of Science and Utrecht Life Sciences, as well as UMC Utrecht, will be all the more important to face these challenges. As indicated before, this requires strong pro-active leadership within and on behalf of UIPS.

Regarding the long-term plan for UIPS to develop into a Pharmaceutical Research Institute of the Science Faculty and the University Medical Centre (UMCU) of Utrecht University, the Committee was not in a position to form an opinion. In itself this would seem a very good prospect, but careful alignment and well-phased development measures must be considered, including the maintenance of pharmaceutical sciences as a strong identity.

3. PROGRAMME ASSESSMENTS

Programme 1:	**Pharmacology**	
Programme director:	Prof. B. Olivier	
Research staff 2009:	17.7 fte in Immunopharmacology and 13.6 fte in Psychopharmacology	
Assessments:	Quality:	4/5
	Productivity:	4/5
	Relevance:	4/5
	Viability:	4

Description

The Immunopharmacology group (headed by Nijkamp/Garssen) and the Psychopharmacology group (headed by Olivier) merged in May 2010.

The ***Immunopharmacology*** research aims at a better understanding of immune-related diseases using basic physiological, pathophysiological and translational research approaches. The following topics are studied:

- The relationship between immune cells, neurons and their mediators in the development/maintenance and inhibition of immune-related diseases
- The mechanistic action of immunomodulating activities of medical food concepts in the pathogenesis of immune-related diseases
- Epigenetic phenomena in the development of the immune and metabolic systems.

The ***Psychopharmacology*** research aims to understand CNS-related disorders at a broad multidisciplinary and translational level, where Pharmacology, Molecular Biology, Behaviour, Physiology, Neurochemistry, Neurophysiology and Neuroanatomy are integrated. The following topics are investigated:

- Brain mechanisms involved in the treatment of stress-related disorders by using multidisciplinary (*in vivo* and *in vitro*) approaches.

Developing, optimizing and applying animal and human models for stress-related disorders
Causes, consequences and prevention of recreational drug use, addiction and alcohol hangover.

Extra investments will be put into developing ***Neuroimmunopharmacology*** combining technology and methodology from both fields in order to boost cooperation between the two research groups

Assessment

Quality

The research on animal models of psychiatric disease is some of the best in the world and the leadership of Dr. Olivier outstanding. The Committee supported the plans to see more of a marriage of the two fields in future goals to exploit the expertise in both areas. Some changes in organization as proposed (neuroimmunopharmacology) could facilitate such integration. In this light, the Committee felt that common overall conceptual goals would be useful. This is particularly important in that an active process will be needed to merge the two relatively disparate domains which the Committee felt would be difficult despite the enthusiasm expressed by the team leaders. New areas the Committee urged the team to emphasize included bridges to translational work in the areas of biomarkers and human laboratory models. Resources are excellent. Some concerns were raised about the commitment of Dr. Garssen to UIPS per se given his strong involvement in Nutricia and his emphasis on the possibility of even further

involvement. Clear delineations of potential conflicts of interest should be elaborated and monitored.

Productivity
Publications are steadily increasing with all faculty members and high quality journals are well represented. Perhaps some more emphasis could be placed on high-profile reviews to increase the profile of the programme. Neurosciences and pharmacology/pharmacy generally have higher productivity numbers. Some of the publications in the immunopharmacology area are of the highest quality and are improving in citations. The Committee encourages the continued focus on publication on high quality, high impact journals.

Relevance
The relevance to society is very strong with a strong translational potential. The benefit of the strong relationship to industry (Nutricia) is the obvious relevance to society at large. In addition, Pharmacology has a strong commitment to teaching and the graduate programme and their expertise is vital to the training programme.

Viability
Collaborations are good and staff are excellent. More effort could be put into translational work including human laboratory models to facilitate translation, integration of immunopharmacology with neurosciences/pharmacology including development of viable biomarkers. The programme seems robust under the direction of Dr. Olivier but more young people need to step up and take more responsibility for aspects of the programme. More emphasis should be put on obtaining tenure track positions for young faculty. The commitment from industry looks strong but the commitment of research positions from the University should also be pursued. The move towards pharmacological research on the influences of food constituents creates a unique national and international niche that can be exploited by the combined talents of the immunological and psychopharmacological marriage.

Conclusion
The research on animal models of psychiatric disease is among the best in the world and the programme leadership is outstanding. The Committee supported the plans to see more of a marriage of the fields of psychopharmacology and immunopharmacology in the future in order to exploit the expertise in both areas. Such a merge may result in a unique niche of research. However, an active process will be needed to merge the two relatively disparate domains.

Programme 2:	**Medicinal Chemistry and Chemical Biology**	
Programme director:	Prof. R.M.J. Liskamp	
Research staff 2009:	18.47 fte	
Assessments:	Quality:	4
	Productivity:	4
	Relevance:	4/5
	Viability:	4/5

Description

The research aims at understanding, modulating and exploring the biomolecular interactions of targets that are involved in infection, cancer and CNS disorders, by designing and synthesizing molecular constructs. Protein-protein and carbohydrate-protein interactions play a central role in all cellular processes. Research objectives are:

1. the design, synthesis and evaluation of new anti-microbial peptide constructs for prevention and treatment of infections;
2. the design, synthesis and evaluation of new multivalent carbohydrate constructs for monitoring and prevention of infections;
3. the design, synthesis and evaluation of new multivalent molecular constructs e.g. those involved in crucial interactions with carbohydrate-binding proteins or for imaging purposes;
4. the design, synthesis and evaluation of new protein mimics as synthetic vaccines and synthetic antibodies;
5. the development, exploration and application of microarrays for evaluating important carbohydrate-protein and protein-protein interactions to be used for developing new molecular constructs as e.g. new anti-infective agents or kinase inhibitors;
6. the exploration of peptide based bio-nanomaterials;
7. developing chemical methods, molecular building blocks and methodology required for these molecular constructs including peptoid and peptidosulfonamide peptidomimetics, (modified) peptides dendrimers, carbohydrates, chemical ligation and C-C-coupling reactions.

Assessment

Note: The quality, productivity and relevance of the Biomolecular Analysis groups are not assessed here, as this area was not under the management of the programme during the review period.

Quality

The programme's research is of a high scientific quality and is highly distinctive. The research programme is built on strong expertise in synthetic chemistry and biophysical methods, and this generic expertise has allowed a wide range of problems to be addressed: for example, the development of novel dentritic anti-infectives, protein surface mimetics, and bisubstrate inhibitors of protein kinases. The programme publishes in some of the leading journals of organic chemistry and chemical biology, and the quality of papers is very high. The group should not be overly modest about their most significant research outputs which are certainly appropriate for publication in the highest impact journals in chemistry and chemical biology (for example *J. Am. Chem. Soc., Angew. Chemie* and *Nat. Chem. Biol.*); the group should strive to publish their best research in these journals.

Productivity

The programme is productive, and exploits the resources at its disposal effectively. The productivity of the group could be further improved through prioritisation of its research themes, and through targeting (albeit limited) opportunities for longer term research funding. The programme has key expertise in biophysical chemistry and – uniquely within Utrecht University – chemical synthesis: this expertise is indispensable in many collaborative research programmes.

The programme, and UIPS in general, would benefit from strengthening the links with other programmes, including longer term, cross-programme grand challenges.

Relevance
The group's research is highly relevant to society in a number of ways. First, research into novel anti-infectives, is not widely undertaken elsewhere (either in academia or industry); and has potential to have a great impact in developing countries. Second, undergraduate and masters students at Utrecht benefit tremendously from a rigorous training in chemistry and biophysical techniques. Third, the programme leads admirable outreach programmes, both for scientists in Africa and for the general public.

Viability
The excellence of medicinal chemistry and chemical biology research is based on distinctive and strong expertise in synthetic chemistry and biophysics. The group is highly viable because excellent research leadership is provided by several academic staff, including Liskamp. These generic capabilities will allow the programme to address a broad range of scientific problems. The group will be able to continue to build on its strong record in securing external research grants (second stream funding). The programme should prioritise the research themes that may lead to longer term research funding.

This group would particularly benefit from the identification of cross-programme grand challenges, which would allow UIPS to benefit more strongly from the programme's distinctive expertise in chemical synthesis and biophysics. Development of strategic research themes within UIPS, with contribution from the medicinal chemistry and chemical biology research programme, could lead to new large scale, externally-funded research programmes.

The established link with the Max Planck Chemical Biology research school provides superb opportunities for PhD students within the programme to engage with other leading chemical biology research groups in Europe.

The programme is an appropriate home for the Biomolecular Analysis group. The programme should take active steps to ensure that the Biomolecular Analysis group can forge links both within the programme and with scientists with complementary expertise in UIPS. The instigation of research retreats could help the Biomolecular Analysis group to build these crucial links.

Conclusion
The Medicinal Chemistry and Chemical Biology programme is easily the most prominent group in this field in the Netherlands, and is competing with the leading groups within Europe. Its research is highly distinctive, both with respect to other academic groups and to the pharmaceutical industry, since it focuses on the design, synthesis and evaluation of molecules that lie outside conventional small molecule chemical space.

Programme 3: **Pharmaceutical Analysis**
Programme director: Prof. G.J. de Jong
Research staff 2009: 7.5 fte

The mission of this group is to explore, design and apply innovative analytical-chemical methodologies, thus providing new prospects for solving urgent analytical issues in the pharmaceutical and biomedical field. In-depth understanding of disease and drug action relies on the availability of tools allowing both global and targeted analysis of biological fluids. The research concentrates on advanced separation technologies, combining them with mass spectrometric techniques. The main research areas are drug profiling, characterization of (potential) protein pharmaceuticals and mimics thereof, and metabolomics, with particular attention to advanced sample pretreatment, efficient separation and selective detection.

In the restructured UIPS (as of 15 May 2010), the Pharmaceutical Analysis group (de Jong/Somsen) has been anchored as the Biomolecular Analysis group to the Medicinal Chemistry and Chemical Biology group.

The Committee had a brief discussion with Prof. de Jong, in which he expressed concern as to the future of pharmaceutical analysis. This issue was subsequently discussed with Dr. Somsen in the context of Medicinal Chemistry and Chemical Biology in which the Biomolecular Analysis group is now integrated, which the Committee views as a constructive move.

Prof. De Jong believes that the termination of the chair in Pharmaceutical Analysis could increase the distance between pharmaceutical teaching and research. In the opinion of the Committee, this point certainly deserves attention. The Committee has learned that UIPS has decided to shift the focus from analytical methodology towards biomolecular analysis, not only to increase the coherence in the research programme, but also on the basis of developments in pharmaceutical practice.

The Committee was not asked to assess this (sub)programme separately and there was no expert in this particular field in the Committee, but it became clear that the new embedding and focus of the group are intended to maintain and consolidate the high level of quality.

Programme 4:	**Pharmaceutics**	
Programme director:	Prof. W.E. Hennink	
Research staff 2009:	32.7 fte	
Assessments:	Quality:	5
	Productivity:	5
	Relevance:	4
	Viability:	4/5

Description

The mission of this group is to perform basic research in Biopharmacy, Pharmaceutics and Pharmaceutical Technology. The transfer of the results of this research into new and improved delivery systems for biologically active substances will be actively pursued. The research focuses on the design of carrier systems for biologically active substances (drugs/proteins/antigenic/genetic material) to be released at the right site and within the right time frame. The research has the following topics:

1. delivery systems based on synthetic biodegradable polymers and hydrogels suitable for the controlled release of biopharmaceuticals (proteins, peptides, antigens)
2. non-viral gene transfection systems which deliver plasmid DNA or siRNA into the target cell
3. nanomedicines based on lipids, proteins, peptides or synthetic polymers suitable for the targeted delivery of low molecular weight drugs (particularly anti-inflammatory agents, kinase inhibitors, cytostatic agents)
4. polymeric scaffolds based on biodegradable polymers for tissue engineering applications
5. formulation-related immunogenicity of recombinant proteins.

Assessment

Quality

The group ranks very highly internationally. It is led by a strong team which has continued to enhance its already strong reputation world-wide. It is grounded in multidisciplinarity, spanning the range from technology, chemical sciences, polymer science and molecular and cell biology, essential for the real progress the teams have made in drug delivery and targeting. Research covers not only advanced delivery and targeting systems but also the potential immunogenicity of constructs. While diverse the central focus is pharmaceutical a fact which contributes to its success. All this has been achieved through tapping internal expertise, judicious appointments and selected external collaborations. The group has been successful in gaining funding from a variety of highly competitive sources in the Netherlands and Europe. There is much evidence of exciting new approaches in drug targeting, for example to tumour tissues, being explored through harnessing the spectrum of disciplines in the group.

Productivity

The research output, which has contributed to the reputation of the group, is impressive in quantity and quality, internationally competitive, appearing in high impact journals in the fields of chemistry, polymer science, biochemistry and molecular biology, toxicology and biophysics, and not least in specialised pharmaceutical science journals. The work thus has wide exposure not only to other academic researchers but also to those in industry who might use their technologies. The policy for publication is appropriate, evidenced by citations; the philosophy of preliminary patent protection of relevant work is realistic and sensible.

Relevance

The ultimate relevance of drug delivery and targeting is without question in the pharmaceutical sciences and pharmacy, even though the work undertaken is mostly at the preclinical stage. The societal impact is potentially high, not solely because of the work *per se* , but because the centre of expertise embedded in the University is an important attractor for pharma industry large and

small. It is some time since any of the group have written for professional journals and hence their expertise, aspirations and potential is perhaps not transmitted as widely as it deserves to pharmacists in practice in the Netherlands and further afield. The transmission of the group's expertise and enthusiasm and its ability to prognosticate is important to undergraduate and postgraduate students of pharmacy. Second to their research, the most valuable societal contribution the group could make would be to ensure that pharmacists are expert in this uniquely pharmacy-centred discipline, and that more are encouraged to study for higher degrees. This sentiment applies to other groups within UIPS as well.

Viability

The group is aware of the challenges facing science funding in the short and longer term. It is however well placed to withstand change and has plans for a new Chair as a result of their contemplation of future needs. There are strong young professors making their own unique contributions. The group has a pivotal role to play within UIPS and is central to the mission of pharmaceutical sciences. To maintain this, future alliances must be chosen with care to ensure the central focus remains as it is. These interactions might not only be with other laboratory sciences but with groups such as pharmacoepidemiology where the knowledge of the pharmaceutics group could be utilised.

Conclusion

The overall impression, both from the visit and from a knowledge of the work seen on the international stage, is of a highly committed and successful group pursuing valuable and ground-breaking work.

Programme 5:	**Biomolecular Mass Spectrometry and Proteomics**	
Programme director:	Prof. A.J.R. Heck	
Research staff 2009:	16.6 fte[3]	
Assessments:	Quality:	4/5
	Productivity:	4/5
	Relevance:	4
	Viability:	4

Description
The mission of this group is to develop mass spectrometry-based enabling technologies for the structural and functional analysis and characterization of proteins and proteomes, based primarily on the sequence of the human genome. The group focuses on developing new enabling tools, and applying them (often in collaboration) to significant research questions, leading to biologically relevant information.
Specifically, their research goals are to:

1. develop and implement innovative mass spectrometric-based methods for the more efficient and detailed characterization of proteins in relation to their biological function
2. perform comprehensive quantitative analyses of proteomes, including the identification and quantification of post-translational modifications
3. develop novel macromolecular mass spectrometric-based methods to analyze intact proteins and protein complexes and their dynamics with a focus on folding and transcriptional complexes and viruses
4. perform studies in proteome biology, whereby choices are made based on the optimal use of the newest methods to address the most relevant biological and biomedical research questions, with a focus on stem cell biology and molecular systems biology
5. play a pivotal role in the Netherlands Proteomics Centre, and related international initiatives
6. play a pivotal role in (inter)national initiatives in Structural Biology such as the Bijvoet School and INSTRUCT.[4]

Assessment

Quality
This is an important group to the Netherlands, in general, and UIPS, in particular. It is arguably the top proteomic laboratory in the country and has extensive technological skills covering an array of approaches with the primary emphasis on mass spectrometry (MS). It is involved in a number of national/international collaborations/consortia and they are well-recognized internationally. However their interactions locally (particularly within UIPS) appear to be more curtailed. The group has 20 MS instruments (a very impressive number) and is using them for whole proteome analyses, post-translational modification studies, and structural biology applications. They are also developing enabling technologies (some of these being more important and innovative than others). The group is very heavily weighted to students and post doctoral fellows (total: 34), which by any criterion is a large group and directing the research of this many young scientists was viewed as a real challenge for Prof Heck and his two junior assistants. This was reflected in the opinion that not all the research projects were of equal weight or importance. They presently receive very good support from a variety of sources but the

[3] According to the self-assessment report, a better of approximation of the research input would be 28.9 fte, based on a fixed formula rather than an estimate of the operational research capacity.

[4] Professor Albert Heck jointly heads the INSTRUCT Associate Centre for Mass Spectrometry together with Professor Carol Robinson of Oxford University. Part of the European Strategy Forum on Research Infrastructures (ESFRI), INSTRUCT receives subsidies from the European Union's Seventh Framework Programme. The INSTRUCT programme focuses on collaboration between various different fields of expertise within structural biology, including mass spectrometry, electron microscopy and crystallography.

maintenance of such a large, technology-heavy operation demands a continuous high level of funding that represents a future challenge (see Viability).

Productivity

Over the past six years, the group has published between 30 and 50 papers a year. On average, a little less than half of these have appeared in first tier (defined in the self-assessment report as the top 10 % - by this definition it would include about 600 journals in all of biology/chemistry), which is a very good but not truly outstanding record. This is certainly competitive on an international basis but would probably not place the group in the same tier of world-wide leading proteomic laboratories. It appears to have graduated 1-2 students/yr with most finishing in 4-5 years, which is consistent with the large current student enrolment in this group.

Relevance

Proteomics, as an applied technology, has enormous potential, particularly for the identification of new diagnostics (biomarkers) and drug targets. Unfortunately it has not as yet lived up to expectations (that were probably rashly over-exaggerated when MS advances first propelled the field into the forefront). This group is not presently directed to either pursuit. Some of their studies, e.g. the stem cell and cardiovascular studies, have some real translational potential but otherwise the group's efforts are mainly in the basic biomedical science area. However, proteomics is a young field and it is growing rapidly. The extensive commitment to providing future scientists skilled in this area, exemplified by the large number of trainees, will in the long run have very important and positive societal impact, particular as some of the early hype for proteomics is realized.

Viability

The review committee recognized that Prof. Heck is an able and highly qualified group leader but it was concerned with the lack of senior colleagues to help him in student instruction and laboratory operations. Although the possibility that Prof. Heck might leave or be unable to continue, for some precipitous reason, was viewed as remote, the lack of clearly identified back-up leadership was considered to be of serious concern. It was the strong recommendation of the review committee that the senior scientist position that had been previously awarded to Prof. Heck's group and later withdrawn be restored as quickly as possible. Similarly, the fiscal requirements of this operation are substantive and it was noted that the long term support for the Netherlands Proteomics Centre (of which this group is the central lab) was apparently not clear. It was felt that some attention to developing a more secure fiscal base for the operation, perhaps through fee for service arrangements, was required.

Conclusion

The overall impression was that this is a well-established and recognized proteomics laboratory, which has made significant contributions and promises to continue to do so. It is structured more like a big research group (with 34 students/post-docs) than a hierarchy of investigators (as in other UIPS groups) and would significantly profit from having senior lieutenants to help direct the research and lab operations. It seems poised to break into the top ten of such laboratories world-wide if it can maintain its support and momentum, and sharpen its research focus, which would be of great importance to both Utrecht and the Netherlands.

Programme 6:	**Pharmacoepidemiology and Clinical Pharmacology**	
Programme director:	Prof. H.G.M. Leufkens	
Research staff 2009:	19.75 fte	
Assessments:	Quality:	4/5
	Productivity:	5
	Relevance:	5
	Viability:	4

Description

The mission of this group is to contribute to a better understanding of the sources of variance in drug response in users of medicines, with the goal to increase the benefit-risk ratio of therapeutics for individual patients and for public health in general. The research integrates various disciplines, dimensions and phases of a product life cycle in order to learn about drug effects and their determinants both before and after initial marketing approval of the product. The integration involves basic science, translational and general medicine, clinical pharmacology, pathophysiology, and epidemiology, but also regulatory decision making and policy analysis.

Assessment

Quality

The research quality is very high in the field of Pharmacoepidemiology. The work is generally published in the top journals in this field and some work has been published in good general medical journals of very wide influence. The work of both Professors Leufkens and Egberts is highly respected. The UK-based General Practice Research Database is perhaps the most respected single resource for Pharmaco-epidemiology in the world, and Dr Van Staa's contributions there are wider than is shown by his own publications.

The research work presented at International meetings has consistently been excellent, reflected in the prizes awarded. The work of PhD students and Post-doctoral fellows has been found to be the highest quality from any group in the world attending the major meetings devoted to Pharmacoepidemiology.

The research covered has included work in studying particular drug effects, general methodology applied to the specific problems encountered in pharmacoepidemiology and the implications of wider clinical and regulatory relevance. The staff have high profiles in research and in European regulation, and given their size, have a disproportionately important influence worldwide.

The Committee felt that this field required strong connections with clinical practice and the quality aspects of this were high. It is important to focus on the issues of public health relevance. To further improve the quality will require full-time leadership in Pharmacoepidemiology, while maintaining the excellent links with clinical practice and regulatory authorities. The influence of this group on regulatory matters has been very strong and has encouraged application of best science in decision making.

Productivity

The volume and impact of the published work has, given the small number of staff, been very high. The output of the PhD students has been particularly good, and the graduates of the PhD programme have continued to make very important contributions to research and to drug regulation.

In contrast to other areas of UIPS, this group must rely on non-industry funding for most of its activities. It has been making efforts recently to do this and the best prospects are in collaboration. The changes in requirements for the sources of funding make it difficult to generate the necessary funding. This group has wide collaboration both within and without The Netherlands, and this should be continued and pursued with vigour. Public European funding depends on this but requires major effort to obtain it. Research infrastructure to allow for the

major effort to obtain public funding must be in place, even when success is not 100%. The collaboration must continue to be with those facing real-life clinical problems.

Relevance

The relevance of the work of this group is very high indeed. Safety of medicines is a high societal priority and demonstrating absence of harm (not always "exciting" in science) is an important aspect as well as finding new harms. The group has good links with clinical practice both in hospitals and in pharmacy practice. As noted, their involvement in regulation of medicines in Europe has had a major impact and continues to be very influential. Their activity may not be as well known in The Netherlands in the lay or scientific media as is justified by its importance. Excellent work is done and it is reasonable to ensure that this excellence is communicated widely.

Viability

It could be argued that this is the only area where there is a slight weakness, partly at least because of the strength in the Group's external activities. The vision for the future is excellent, and having vital contact with regulatory and clinical practice militates against close involvement within UIPS. There is no evidence that the wider involvement has had a deleterious effect on staff or PhD students, but the strength in depth of full-time academic leadership is not as great as is desirable. Consideration should be given to appointing at a very senior level to ensure that continuity is guaranteed. The group could be vulnerable if either Leufkens or Egberts moved on. (There is no suggestion that this is a possibility, but the vulnerability is there).

Conclusion

This group is one of the top ten if not the top five world wide. They do excellent scientific work which is grounded in real world problems and has notable impact on the regulatory world, especially in Europe. Their output, the camaraderie within the group at all levels seems to be excellent. Inevitably within a relatively small group it depends on good leadership of a few people. This is present, but the good involvement outside UIPS means that it would be good to have a full time senior level appointment to increase the depth of this strong group.

Programme 7: **Drug Toxicology**
Programme director: Prof. J.H. Beijnen, Prof. J.H.M. Schellens
Research staff 2009: 3.2 fte

The group is involved in research in different phases of anticancer drug development. This concerns:
Clinical and translational research
Bioanalytical method development and implementation in clinical and preclinical pharmacological studies
Utility and cost-effectiveness of anticancer drugs.

During the period under review the group consisted of two part-time professors and two assistant professors. The group was part of the Biomedical Analysis group. The group will form the Clinical Pharmacology group in the Pharmacoepidemiology and Clinical Pharmacology division.

The Committee did not assess this group as a separate entity, but included it in its assessment of Programme 6. It would like to note however that the connection with the National Cancer Institute which these part-time chairs represent, is a strong asset for UIPS. Both Prof. Schellens and Prof. Beijnen are leaders of highly relevant and very productive research programmes representing research excellence in their own right. Their incorporation into the Pharmacoepidemiology group is considered to have great potential.

4. PhD-TRAINING

Description
UIPS offers its PhD candidates a four-year educational programme in pharmaceutical research, preparing them for a doctoral thesis. The PhD programme Drug Innovation is open to candidates with a Dutch or equivalent MSc in Life Sciences (e.g. Pharmaceutical, Chemical or Biomedical Sciences). Each research group selects its own PhD candidates.

Depending on the research project the PhD student is entering, he/she should have the required theoretical and lab skills background. Depending on the field of research within the context of drug innovation, educational programmes will be tailored with respect to basic student competency, drug innovation education, supplementary Chemical Biology courses, as well as participation in master classes (part of the International Seminar Programme), conferences, meetings, etc. The PhD students receive their research training within the research groups of UIPS, e.g. (weekly) research colloquia, research project meetings, research lectures.

UIPS participates in the Graduate School of Life Sciences (GS-LS) at Utrecht University and is responsible for the PhD programme in Drug Innovation. To protect the quality of the training and supervision of PhD students, the GS-LS introduced a uniform 'Training and Supervision Agreement' (TSA) for all students who follow a regular PhD track within the school as of January 2007. The 'TSA' specifies the rights and duties of the PhD student and his/her supervisors with respect to education and supervision during the PhD track. Education and training for PhD students is provided within the individual programmes and by the Faculties of affiliation.

Each PhD student is required to earn 20 credits from the ECTS (European Credit Transfer System) during his/her PhD period. A minimum of 8 credits must be gained within the PhD programme to which the student has been admitted and a minimum of 4 credits should be gained on courses that provide training and education in general and professional skills. PhD students are allowed to attend courses required for their research that are offered by the other PhD programmes of the GS-LS. The GS-LS guarantees the quality of training and supervision by monitoring the quality of the courses and the progress of the PhD students. Four times a year, a delegation of the PhD students and the *UIPS* management meet.

The *UIPS* International Seminar Programme invites international experts to teach at Utrecht. On recommendation of PhD students, keynote speakers are also invited to Utrecht. These monthly seminars keep the PhD students up to date on the latest trends in pharmaceutical research and related areas. These lectures have recently been combined with master classes.

The table below lists the success rates of standard PhD students. The average duration was 4 years and 8 months. On average 72% graduated within 7 years and UIPS expects this number will increase. On average 7% graduated within 4 years and 7% discontinued their studies.

Table: Standard PhD candidates, status on 1-1-2010

Enrolment			Success rates				Total		
	Male/female	Total	Graduated in 4 yrs	Graduated in 5 yrs	Graduated in 6 yrs	Graduated in 7 yrs	Graduated	Not yet finished	Discontinued
2001	6/6	12	0	7(58%)	1(8%)	3(25%)	11(92%)	0	1
2002	12/9	21	4(19%)	12(57%)	5(24%)	0	21(100%)	0	0
2003	15/11	26	0	12(46%)	4(15%)	2(8%)	18(69%)	4	4
2004	14/11	25	3(12%)	9(36%)	4(16%)	0	16(64%)	8	1
2005	9/8	17	0	7(41%)	0	0	7(41%)	9	1

External PhD students do not necessarily finish in 4 years. The number of non-standard PhD students is estimated as follows.

Table: Distribution of standard and non-standard PhD theses

	2004	2005	2006	2007	2008	2009	Total
Standard	11	17	18	25	15	23	109
Non-standard	14	6	6	6	5	12	50
Total	25	23	24	31	20	36	159

On average there is almost 1 non-standard or external PhD student to every 2 standard PhD students. UIPS estimates that there were 158 standard and 66 non-standard PhD students in 2009.

A survey was made of the employment statistics of PhD students within a year after graduating. The results are shown in the table below.

Table: Employment statistics within one year after graduation

	2004	2005	2006	2007	2008	2009	Total
Category							
Natl Academia/Res. Inst./Health services	13	8	7	15	9	19	71
Intnl Academia/Res. Inst./Health services	4	5	8	4	1	1	23
Government	0	2	0	1	1	0	4
Industry	7	5	8	9	8	12	49
Unknown	1	3	1	2	1	4	12

The success rate of the PhD programme is around 80%. All PhD students are discussed annually with the programme leaders and it appears that problems most often arise in Year 4 of the programme.

Assessment

The Committee found the PhD-students very articulate, positive and generally optimistic about finishing their theses within 4 years. They feel very much at home at UIPS. The Committee found that the poster session showed immense enthusiasm by the PhD's; they are well resourced and have an encouraging desire to continue in research.

The Committee challenged the PhD-students to express concerns with respect to their working environment, facilities, resources and/or supervision, but all seem to be perfectly in order. The only minor point of attention mentioned was the need for a welcoming introductory programme for PhD students coming from abroad.

Appendix A: Curricula vitae of the committee members

Douwe D. Breimer, chairman of the Committee, is Professor of Pharmacology at Leiden University since 1975. He graduated in pharmacy at the University of Groningen (1970) and obtained his PhD in pharmacology at the University of Nijmegen (1975). He was Director of the Leiden/Amsterdam Centre for Drug Research (LACDR) for ten years, (1990 – 2000), he was vice-president of the National Research Organization NWO (1995-2000) and chairman of the Section on Medicine of the Royal Netherlands Academy of Arts and Sciences (1996 – 2000). He was Rector Magnificus (2001-2007) and chairman of the Executive Board (2005-2007) of Leiden University. He is vice-chairman of the Supervisory Board of Delft University of Technology, member of the Supervisory Board of the Catholic University of Leuven and member of the Governing Body of University College Cork. He holds honorary doctorates of the universities of Uppsala, Gent, Budapest, Montreal, Tokyo, Pamplona and London.

Ralph A. Bradshaw is Professor of Chemistry and Pharmaceutical Chemistry in the Department of Pharmaceutical Chemistry, University of California, San Francisco (UCSF) and Deputy Director of the Mass Spectrometry Facility, UCSF. He is Professor Emeritus of the Department of Physiology and Biophysics, College of Medicine, University of California, Irvine. He was the founding Editor-in-Chief of Molecular & Cellular Proteomics and currently serves as its Co-editor. In 2004/05 he was Parke-Davis Exchange Fellow, Department of Biochemistry, Cambridge University. In 1997-2006 he was Professor at the Department of Physiology and Biophysics, and at the Department of Anatomy and Neurobiology, College of Medicine, University of California, Irvine. His research interests are related to the structure/function relationships of proteins. For many years, the research focused on eukaryotic signal transduction and co/post-translational processing of protein N-termini. More recently, there is a strong interest in the use of proteomic analyses, particularly those supported by mass spectrometric approaches.

Stephen J.W. Evans is Professor of Pharmacoepidemiology at the Medical Statistics Unit of the London School of Hygiene & Tropical Medicine (LSHTM), University of London. He holds degrees in Physics, Chemistry and Medical Statistics, and worked in statistics and computing at The London Hospital and Medical College for 25 years. He is a co-opted member of the Pharmacovigilance (Drug Safety) Working Party at the European Medicines Agency and on the WHO Global Advisory Committee on Vaccine Safety. He is President of the International Society of Pharmacoepidemiology for 2010/2011.
He teaches courses in pharmacoepidemiology and pharmacovigilance and contributes to the DL MSc in Clinical Trials. In research his main interest is safety of medicines. This concerns assessment of safety and risk in a general sense, but particularly in trials and epidemiological studies, especially in databases.

Alexander T. Florence is emeritus Professor of Pharmacy at the Centre for Drug Delivery Research, The School of Pharmacy, University of London. He was Dean of the School from January 1989 until April 2006. Before joining the School, he was Professor of Pharmaceutics and head of the Department of Pharmaceutics at the University of Strathclyde. He is editor-in-chief of the International Journal of Pharmaceutics and was founding co-editor with Professor Vincent Lee of the Journal of Drug Targeting. He received the GSK International Achievement award in 2001, the Høst Madsen award from FIP in 1997, the Scheele Prize of the Swedish Academy of Sciences in 1993 and the Harrison Memorial Medal of the Royal Pharmaceutical Society of Great Britain in 1986. He is a former President of the Controlled Release Society. His main research interests are in pharmaceutical nanotechnology: understanding the behaviour of nanoparticulates in pharmaceutical and biological systems.

George F. Koob is Professor and Chair of the Committee on the Neurobiology of Addictive Disorders at The Scripps Research Institute, and Adjunct Professor of Psychology and Psychiatry at the University of California, San Diego. He is the United States Editor-In-Chief of the journal Pharmacology, Biochemistry and Behavior, Director of the NIAAA Alcohol Research Center at The Scripps Research Institute, and Consortium Coordinator for NIAAA's multi-center Integrative Neuroscience Initiative on Alcoholism. His current research is focused on exploration of the neurobiological basis for the neuroadaptation associated with drug dependence and stress. This includes the characterization of behavioural functions in the central nervous systems for stress-related neurotransmitters/neuroregulators. He has won six excellence in teaching awards and two Professor of the Year awards. He is Director of a National Institute on Alcohol Abuse and Alcoholism post-doctoral training programme and serves on the Executive Committee for the Neuroscience Program at the University of California, San Diego.

Adam Nelson is Professor of Chemical Biology and Director of the Astbury Centre for Structural Molecular Biology (ACSMB), University of Leeds. He is Programme manager of the MSc Chemical Biology, University of Leeds, and Deputy Programme Manager of the Leeds Wellcome Trust 4-year PhD programme. The ACSMB is an interdisciplinary research centre, bringing together over fifty academic staff from four faculties who share the common goal of understanding life in atomic detail.
His research interests focus on the application of synthetic organic chemistry to biological problems. This includes the development of new strategies and methods for asymmetric and stereoselective synthesis, which is applied in the synthesis of biologically active molecules and natural products. The applications range from the evolution of new enzymes for synthetic chemistry, to the discovery of new modulators of protein function. His research and publications cover the areas of chemical genetics, directed evolution, diversity-oriented synthesis, natural product synthesis, new strategies for asymmetric synthesis, stereochemically diverse libraries.

Appendix B: Explanation of the SEP criteria and scores

The four main criteria for assessment are: Quality, Productivity, Relevance, and Vitality & feasibility. The assessment at the institute level primarily focuses on strategy and organisation, whereas the assessment at the level of the research group or programme primarily focuses on performance and activities of researchers and the results of their work (output and outcome).

Quality	The level or degree of excellence of the research, compared to accepted (international) standards in that field. The scope of the term 'research' is not limited to the research results. Research management, research policy, research facilities, PhD training and the societal relevance of research are considered integral parts of the quality of work in an institute and its programmes.
Productivity	The relationship between input and output, judged in relation to the mission and resources of the institute.
Relevance	Social, economic and cultural relevance. Aspects to be considered are: ▪ *Social quality*: efforts of the institute or group to interact in a productive way with stakeholders in society ▪ *Social impact*: how research affects specific stakeholders or procedures in society ▪ *Valorisation*: activities aimed at making research results available and suitable for application in product, processes and services. Remarks can also be made about relevance for the academic community, but the assessment should be on societal relevance.
Vitality & feasibility	The ability to react adequately to important changes in the environment. Also vision for the future.

The meaning of the scores on the five-point scale is as follows:

5 Excellent	Research is world leading. Researchers are working at the forefront of their field internationally and their research has an important and substantial impact in the field.
4 Very Good	Research is considered nationally leading. Research is internationally competitive and makes a significant contribution to the field.
3 Good	Research is considered internationally visible. Work is competitive at the national level and makes a valuable contribution in the international field.
2 Satisfactory	Research is nationally visible. Work adds to our understanding and is solid, but not exciting.
1 Unsatisfactory	Work is neither solid nor exciting, flawed in the scientific and/or technical approach, repetitions of other work, etc.

Appendix C: Schedule of the site-visit

Wednesday 3 November 2010

17:00-17:45	Welcome and short introduction of the research programme of UIPS by the Director of Research of UIPS, Prof. Berend Olivier
17:45-18:45	Discussion in the committee
19:00-21:00	Drinks and dinner with UIPS management.

Thursday 4 November 2010

9:00-9:30	Faculty, Department, UIPS management (Prof. Moerdijk, Prof. De Boer, Prof. Olivier, Prof. Hennink, Dr. Moret)
9:30-10:30	**Pharmacology** (Prof. Olivier, Prof. Garssen, Prof. Folkerts)
10:45-11:45	**Medicinal Chemistry and Chemical Biology** (Prof. Liskamp, Prof. Pieters, Dr. Somsen)
11:45-12:15	Prof. De Jong, Pharmaceutical Analysis
12:15-13:00	Lunch for Committee
13:00-14:00	**Pharmaceutics** (Prof. Hennink, Prof. Storm)
14:15-15:15	**Biomolecular Mass Spectrometry and Proteomics** (Prof. Heck, Dr. Scholten)
15:30-16:30	**Pharmacoepidemiology and Clinical Pharmacology** (Prof. Leufkens, Prof. Egberts)
17:00-18:00	Drinks and PhD poster presentations
18:30	Dinner for Committee only

Friday 5 November 2010

9:00-9:30	PhD-training programme (Dr. Henricks, Dr. Moret)
9:30-10:15	Group interview with PhD-students
10:15-11:15	Lab tour
11:15-13:30	Committee meeting and lunch
13:30-14:00	Brief oral report of major findings to UIPS-management
14:00	Departure