University of Oxford

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From the Chairman: Rodney Phillips MA MD FRCP FRACP FMedSci
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Dieter Wendelstadt
Chairman of the Syliva Lawry Centre Supervisory Committee
GENERAL CAPITAL GROUP
Beteiligungsberatung GmbH
Maximilianstrasse 11
D-80539 Munich
Germany

18th August 2008

Dear Mr Wendelstadt,

I have pleasure in submitting to you our final report on the Sylvia Lawry Centre for Multiple-Sclerosis Research.

Should you have any queries regarding the report please do not hesitate to contact me directly.

All best wishes

Rodney Phillips

External Review of the Sylvia Lawry Centre (SLC) for Multiple Sclerosis Research

Executive Summary

- The SLC has become a reference centre for the analysis of the long term natural history of patients with multiple sclerosis (MS).

- The SLC has demonstrated rigorously that widely accepted dogma about the evaluation of MS as a clinical disease is not sustained. Methods used to assess patient disability, the disease burden MS imposes and the efficacy of therapy have been shown to be flawed.

- Particular strengths of SLC include the evaluation of the natural history and interventions in MS; this expertise could be extended to other chronic diseases including neurodegenerative diseases.

- The scientific quality of work at the centre is good and at its best is very competitive internationally with great potential impact on health policy.

- Research awards for work at the SLC have been successful but the withdrawal of the Multiple Sclerosis International Federation core support severely restrained work at the Centre after 2005.

- Local, national and international collaborations have been very critical as means of achieving the scientific goals of the Centre. Both universities of Munich (TUM and LMU) are strong collaborators with SLC in respectively mathematics and statistics.

- The Director (Dr.M.Daumer) has demonstrated strong leadership particularly when the existence of the Centre was at stake.

- The SLC still faces a critical financial situation despite its laudable aims to assess, without bias, the expensive interventions proposed for MS.

- If the unique resource of the Centre are to preserved bridging funds are needed so that the new, admirable strategy of the Director can be enacted.

- This strategy as articulated is too broad. A more focussed plan which builds on the Centres' expertise is recommended.

Introduction

The Sylvia Lawry Centre (SLC), a not-for-profit charitable organisation under German law, was founded in 2001 to promote research and education in the fields of medicine and natural science, in particular in relation to multiple sclerosis (MS). The mission of the Centre is to improve human health by developing evidence based decision support tools for better clinical choices. To achieve this, the Centre aims to combine the physical sciences, with IT/biomedical engineering and medicine.

As part of efforts to increase the stability and long-term development of the centre, the Supervisory Board has requested an impartial and objective review of the organization, methodology and productivity of the SLC. This review is aimed at examining the achievements, contributions to new scientific knowledge and strategic directions in:

- Mathematics/physics/statistics;
- IT/biomedical informatics/biomedical engineering;
- Medicine/clinical trials.

Overall impression

Major strengths of SLC

1) The SLC has assembled the largest data base of the long term natural history and shorter term progress of placebo groups involved in clinical trials of therapy for multiple sclerosis (MS) in the world. At present this database encompasses 55 studies including major studies which have influenced the field. Of the 100.000 patient-years of data collected, more than a third covers around 25 years of individual observation in patients.
The team has shown that they can use this impressive base to verify or refute claims and conclusions made in much more limited studies involving short time frames, smaller patient groups and disability scores of limited predictive power. As a result of that position they have revealed, sometimes against accepted dogma, that some conclusions in the field are not sustained by the powerful evidence that they have collected. For example, serial MRI-scanning of patients with MS and the way of using this information to calculate aggregated disease burden does not correlate with disease progression.
2) Furthermore they have shown that the clinical measures for disability scoring in MS used for drug trials are a wholly inadequate tool to evaluate an intervention. The SLC and collaborating investigators has demonstrated that MRI measures which have been in wide use, have no added value when therapeutic efficacy is assessed.

These findings by SLC have had major consequences for the treatment and care of patients with MS.

3) The SLC has devised an impressive and sophisticated analytic approach which allows them to incorporate heterogeneous data sets and combine them in a useful electronic form. This allows the data to be used for very powerful comparative analyses. A particular strength of the Centre is that the approaches used for large scale MS analysis could very easily be extended to the evaluation of intervention in other chronic conditions where the durability of treatment is very difficult to assess. This is an area which the Centre might consider developing further as it is clearly where their track record is strongest.

Weaknesses of SLC

(1) The future research program as currently presented is too broad and would benefit from more focus on areas where the expertise of SLC is established and internationally recognized as outstanding.

Recently a critical need for funding created an imperative for the Director to enlarge the scope of the Centre's research activities. While completely understandable the review group felt that if core support could be re-instated (not an easy task) then some of the less strong projects could be dropped.

(2) The review group felt that the future academic exploitation of the powerful MS data base should be clearly demarcated. For example how would approaches by companies be dealt with compared with applications from academic groups? Likewise the legitimate aspirations of the company (Trium) should be better defined. The close relationship between the Company and the Centre may have had financial advantages but the review group felt that these links needed better definition. At interview the Director was asked detailed questions about this situation and his answers suggested high quality audit arrangements which conform to strict German law.

(3) Although SLC has been very successful in acquiring grants from the EU-framework programs and foundations (such as Porticus and Hertie foundation), the lack of core or infrastructure funding of the centre (which is not included in modest research grants) makes it very difficult for the Centre to make focussed future plans.

(4) The SLC is physically and academically isolated; this militates against local collaboration and partnerships in Munich which could be of great benefit. The Directors' zeal for independence is admirable but this need not prevent closer academic ties.

Strategic direction and future plans

The ambitions of the SLC team to extend their activities are laudable. But they would be well advised to focus initially on extending the methodology and expertise that they have in a logical and focussed manner. For example, their experience in using disparate data bases to much more accurately define the natural history of a chronic disease like MS could readily be applied to other chronic diseases. Obvious possibilities could be those which damage the nervous system slowly but progressively such as Parkinson's disease, Alzheimer disease and motor neuron diseases.
Another example of established expertise which could be pursued in more depth is the analysis of the validity and reproducibility of scanning data produced by technology such as MRI when used to monitor chronic diseases. Projects of this sort require significant financial investment. The centre must have an adequate core or infrastructure support to do this. The economic consequences of defining the limited utility of expensive tests are substantial and might provide a basis for asking for governmental support.
The motives and ambitions of the company (Trium) seem admirable and can potentially add to the way disability is measured in patients. However, those aims are distinct from the obvious academic potential of the centre itself and the two entities should be distinguishable in their objectives.

The Director outlined other, opportunistic projects involving the assessment of disability. The review group saw no reason to discourage these aims but the international competitiveness of this work might be questioned. Collaborations with groups such as the Mayo Clinic are an admirable way of gaining appropriate critical expertise.

Quality and quantity of clinically meaningful results

(See paragraph "Strengths of SLC")

Quality and quantity of scientific results

The Review Committee concluded that overall the scientific quality was good when compared internationally. The number of publications has significantly increased during the last years (from 4 in 2005 to 13 in 2007). Similarly the number of abstracts has strongly risen since 2005. Most articles have been published in international, peer-reviewed journals of which several have a high impact.

Local, National and International Academic and Clinical environment

At the local level TUM is a strong collaborator with the SLC notably in the area of statistics, learning from data analysis and computational modelling. Developing methods for patient monitoring, such as the fetal heart rate, is a joint project of SLC with the Dept. of Obstetrics at the TUM. The Ludwig Maximillians University of Munich and the SLC have signed a long-term framework agreement with the aim to foster scientific and clinical collaboration in research and teaching which involves the faculties for medicine and for mathematics, informatics and statistics. One of the joint projects is the modelling and prediction of the clinical course of MS. The Helmholtz Centre for Environmental Health in Munich which is interested in bioinformatics and biometrics, is also a partner of the SLC.
Together with a number of Universities in Germany (Göttingen, Leipzig) studies in the area of patient monitoring have been undertaken.

At the international level SLC created collaborations with a number of university research groups, hospitals and pharmaceutical companies so providing their invaluable patient databases. SLC has assisted some regulatory authorities (FDA, USA) in developing a data base ("Critical Path Tools"). The centre has organised a number of international workshops and scientific meetings in the area of MS-research and physical activity which were attended by experts and students from various parts of the world. Together with investigators in Cambridge (UK) the initiative was taken to create an International School for Technical Medicine and Clinical Bioinformatics to allow young scientists to attend courses in bioinformatics and related topics.

The Review Committee concluded that these collaborations have been extremely helpful and often vital as a means for the SLC to become a reference centre (and centre of excellence) in the analysis of long term disability. At present the collaboration with the Universities in Munich is largely informal. However, the Review Committee felt that these collaborations need to be stronger and be formalized.

The SLC may provide an important contribution to teaching of students. As was stressed by a representative of the pharma industry, they (and also the banking sector and insurance companies) have difficulty in recruiting students with an interest in modelling and data analysing. Together with universities SLC may help to fill this gap.

Leadership

In mid 2004 Dr Martin Daumer succeeded Professor Neiss as the Scientific Director and Chairman of the Board of the SLCMSR. Dr Daumer holds a PhD in Mathematics (1995) from the Ludwig Maximilians University (LMU) in Munich. He is visiting lecturer for "Telemedicine"at the Technical University of Munich (TUM) and for "Medical Informatics and Statistics/Biometrics"at the Heinrich-Heine University in Düsseldorf (Germany). He holds a number of US, European and German patents related to devices and methods to monitor patients. Furthermore he has been (co)author of about 40 scientific articles in peer-reviewed German and international scientific journals, several of which with a high impact factor.

During the time that he has been in charge of the SLC Dr Daumer has demonstrated that he has very strong organisational skills (see paragraph major strengths). He has shown that he and his team can combine heterogeneous data into an electronic form for comparative analysis. He established very fruitful collaborative studies with investigators in several countries. Furthermore he has been part of the development of devices (like the Actibelt).

The Review Committee agreed that it is largely due to the enthusiasm, perseverance, managerial skills and knowledge of Dr Daumer that the SLC has been very successful and has survived despite significant criticism from some organisations such as the International Multiple Sclerosis Society (see paragraph "Control of conflicts with pharma and academia").

Quality of staff

In 2008 the SLC employs 18 staff members of whom 3 are PhD and 12 have graduated in Mathematics, Informatics and Statistics. They showed a sincere interest and motivation for the project(s) they were involved in.
As a result of the collaborations with foreign institutes more than 15 guest researchers from various countries (North America, UK, Sweden, France) have since 2003 visited SLC to do research at the SLC.
Although the Review Committee did not have the opportunity to review all the staff, the overall impression is that Centre staff were well qualified for the work. Understandably many staff have no clinical background at all. A very useful outcome of closer links with medical specialists in Munich would be greater clinical input. But the review group acknowledged the Directors' wish to maintain impartiality. He should therefore select his collaborators carefully. A number of SLC staff were part-time employed by SLC, some worked also part-time for the company by Trium.

Adherence to ethical standards

The Review Group were not in a position to examine in detail the "ethics" of the Centre. However the Centres' core aims to impartially evaluate therapeutic intervention in chronic disease and so limit the use of useless treatments and tests is extremely admirable and could of itself be considered an "ethical" ambition.

Control of conflicts of interest with pharma and academia

The Review Committee was told that the outcome of the analysis of data collected by SLC regarding MS-trials was not always welcomed by clinicians and researchers working in this area. Some conclusions and dogma regarding the monitoring and treatment of MS patients have not been supported by work done at the SLC. These conclusions apparently triggered heated controversy and criticism has, in the past, been directed at the Centre. An earlier Review (2005) questioned if the SLC should continue to exist and suggested that the database be transferred to another country. We find these earlier conclusions surprising and not in accord with the state of the Centre in 2008. The SLC has published their very careful analyses of MS trials in highly ranked scientific journals which question the validity of some earlier conclusions in the field. This activity is in the great tradition of scepticism and scientific rigour. As their work questions the benefit to patients of expensive treatment and tests it deserves to be closely examined in its turn. Recent publications from the Centre will allow this debate to continue.

Funding

Originally a 5-years contract with a total volume of 5m€ from the Multiple Sclerosis International Federation (MSIF) was awarded to the Technical University Munich (TUM) and Trium Analysis Online. In 2001 representatives of MISF, TUM and Trium founded SLC as independent legal entity with long-term prospects for research and development for which the contract served. Funding by MSIF was ended mid 2007.
Historically SLC has also been funded by UKMS Society and the American MS Society (1 project). More recently UKMS, due to financial constraints has discontinued financial support to SLC. For a variety of reasons efforts to involve MS-Societies in other countries have up till now not been successful.
The total budget of SLC in 2007 amounted to about k€ 680, which was k€ 254 short to cover all the costs. In 2008 the estimated income is roughly k€ 500, which is about k€ 270 short to cover the estimated costs.

Funding is mainly provided by pharmaceutical companies (27 to 35%) and various foundations (51 to 60%).According to the Director it is estimated that about 2/3 of the total budget is spend on MS-research and 1/3 on activities related to research on mobility devices (like Actibelt).
These above figures show that the financial situation of SLC is quite critical and that there is an urgent need for additional and preferentially long term funding.

Recommendations

(1) The SLC is well placed to play a role in the evaluation of the nature and progression of disability created by chronic disease. It has a particular strength in the use of natural history data to assess the usefulness or otherwise of interventions. Depending on the vicissitudes of funding applications this proven strength should be pursued.

(2) Broadening these sorts of studies is admirable provided the aims of the Centre do not become too diffuse. If it were possible to extend the approaches used in MS to other chronic neurological diseases funding agencies might consider this an attractive direction to follow.

(3) The SLC-team should form suitable academic affiliations with the Universities of Munich. In case of TUM they should formalize the relationship that allows future partnership to flourish in the area of analysis of long-term diseases and monitoring of disability however measured. This could form part of TUM's strategy to gain appropriate state and federal funding in the critical area of aging and of dealing with the chronic disease burden in Germany.
To achieve this, it seemed to the Review Committee essential that the SLC elaborate and finalise agreements with TUM which protect the intellectual independence and detachment of the investigators. But it is essential that the centre is integrated with a partnership agreement that would allow joint grant applications and the involvement of responsibility of student enrolment to a natural academic home.

(4) The interest of national and international regulatory agencies for the evaluation and supervision of pharmaceuticals, like the European Medicines Agency (EMEA), in studies performed by SLC should be explored and may lead to governmental or European (structural) funding for SLC.

(5) It is also clear that the present location of the centre is unsatisfactory. To facilitate much closer liaison with trusted clinicians in the university hospitals in Munich and with colleagues from TUM with complementary interests in human disability, the centre should be located much closer to these elements.

(6) As the present financial situation of SLC looks critical it is urgent that additional long-term funding be found to keep the present expertise in data collection and analysis intact. Otherwise a unique and highly valuable approach to the evaluation of MS will be lost.

Annex I

Procedures of the Review

The Review Committee met on 24th July 2008 at the offices of the SLC in Munich and the following day at the Technical University of Munich (TUM), Campus Garching, Faculty of Mathematics and Computer Science.

Prior to the Review meeting the members of the Review Committee received preparatory information including the report ("Human Motion Project – HUMO") describing the achievements between 2001 and 2008 and the research plan 2008 – 2013, recent key publications and an overview of the finance budget 2008 – 2012.

At the start of the Review the Chairman briefly discussed the terms of reference and the review procedure.
Professor G.Ebers (Professor of Neurology, University of Oxford, UK, and member of the Scientific Advisory Committee of SLC) was invited *ex officio* which allowed the Review Committee to make use of his in depth knowledge of the background of MS clinical trials.
Dr Jayne Spink (Director of Policy and Research, Multiple Sclerosis Society, MS National Centre, London, UK) was invited to attend the meeting as an observer.
Dr Kenton Kaufmann (Director Bio-Engineering, Mayo Clinic, Rochester, Minn., USA) attended part of the Review as an observer.

It appeared that none of the members of the Review Committee (see Annex) had a conflict of interest.

The agenda of the Review (see Annex) included presentations by the Director and scientific staff members of the SLC, discussions with Professor Hoffmann (TUM) and Dr Daumer, and closed discussions of the Review Committee.

This first draft of report of the Review was written by the chairman and the rapporteur. The latter coordinated the final version with input from all the members of the Review while Dr Daumer was invited to make factual textual corrections where necessary.

Annex II

Members of the Review Committee

- Professor Rodney Phillips (Chairman), Professor of Clinical Medicine and Chairman The Peter Medawar Building for Pathogen Research, University of Oxford (UK).
- Professor Marek Niezgódka, Director of the Interdisciplinary Centre for Mathematical and Computational Modelling (ICM), University of Warsaw, Warsaw (Poland).
- Professor Reinhold Haux, Director of the Peter L.Reichertz Institute for Medical Informatics, University of Braunschweig and Hannover Medical Scholl (Germany).
- Professor Pim van Aken (rapporteur), (Em) Professor of Internal Medicine, Former Chairman of the Medical Research Council (ZonMW), Amstelveen, the Netherlands.

Annex III

Agenda of the Review meeting

(Copy of original agenda)

ACHIEVEMENTS 2001 – 2008
ONGOING WORK
RESEARCH PLAN 2008 – 2010

From an International MS Trials, Research and Resource Centre to an open international collaborative research platform to study human motion

24.07.2008

		Responsible	Time
	Agenda for Thursday, 24th July **Location: SLC, Hohenlindener Str. 1, 7th and 8th Floor**		
	Background, Achievements and Plans (room 8th floor)	Reviewers, Daumer	14:00 - 15:00
	Lounge 7th floor: Coffee, Introduction of Research Groups		15:00 - 15:10
	Presenting of different working groups/projects in the office rooms 7th floor (2 slots a 30 min)	SLC researchers, Reviewer subgroups	15:15 - 16:15
	Joint Summary Discussion – Open Points (Lounge 7th floor)		16:15 – 16:35
	Closed session Room 8th floor	Reviewers	16:45 – 17:45
	19:00 Dinner at **Halali** **Schönfeldstr. 22** **80539 München** **Tel: ++49 89 285909** Motto: HUMOP		

SLC Research Groups:

actibelt

Team: Kathrin Thaler, Franziska Bayer, Gerrit Kreuzer, Fabian Franzelin, Martin Slawski, Christine Gerges, Christian Lederer, Nadja Harner, Thomas Diederich

Topics:
Poster presentation
Online Demo,
Web Application,
Client Software
Online data analysis (OLAP)
Presentation of subprojects

EBDiMS – Evidence based Decision Support in MS

Team: Anneke Neuhaus, Martina Güntner, Nadja Harner, Simone Otten, Christian Lederer, Ralf Strobl

Topics:
Individual Risk Profile
Conversion to definite MS
Change in relapse rates,
MRI as an outcome in MS clinical trials,
Measurement of disability,
MSSS,
Staying Times,
London Ontario Database

Biostatistics and Bioinformatics methodology

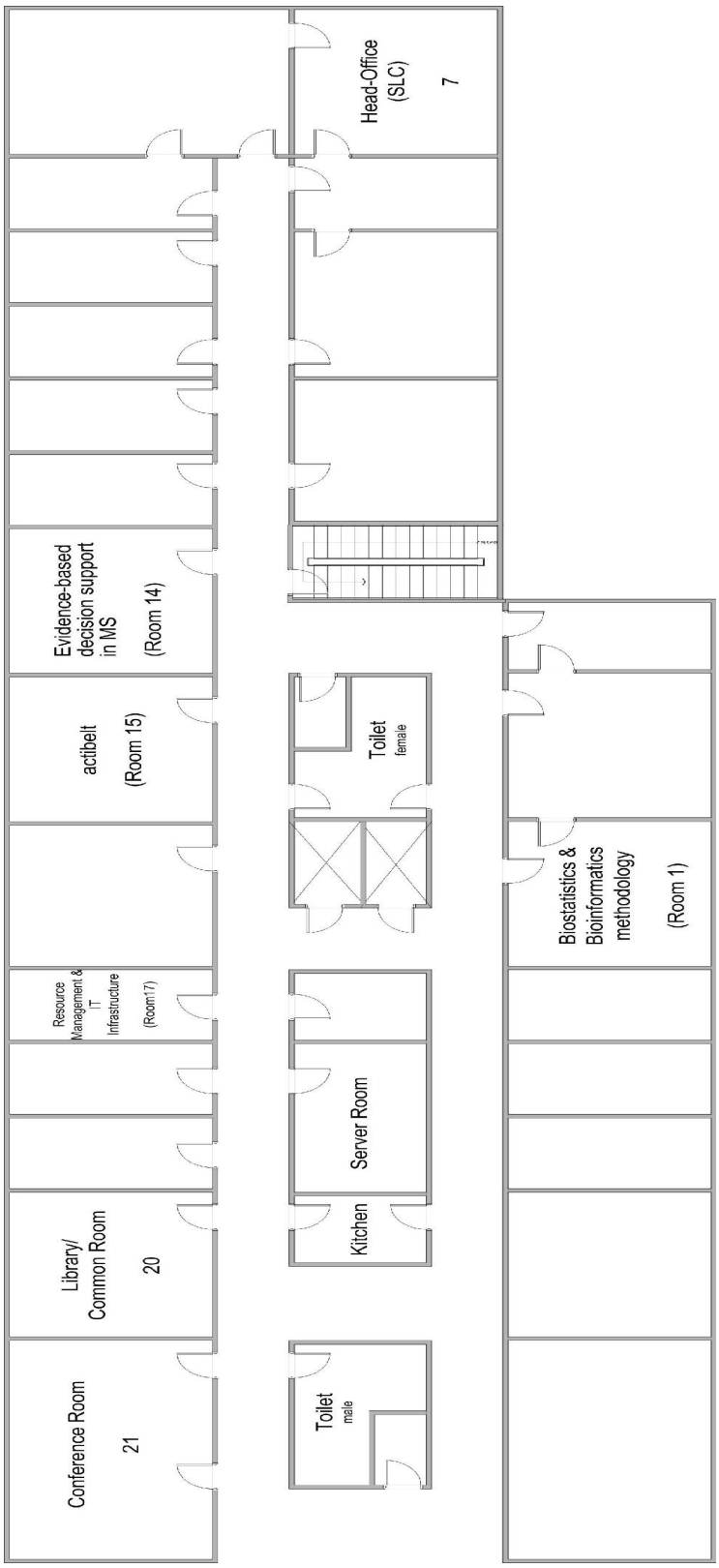
Team: Anne-Laure Boulesteix, Christian Lederer, Martin Slawski, Ralf Strobl, Anneke Neuhaus, Nadja Harner, Simone Otten

Topics:
Validation (policy, examples – BAQ)
Virtual Control groups (examples: Biopartners Bioferon, Novartis FTY720)
Synthetic datasets
Joint Modelling
Microarray (CMA)

Resource Management / IT infrastructure

Team: Simone Otten, Christine Gerges, Christian Lederer, Nadja Harner, Anneke Neuhaus, Michael Scholz

Topics:
Data Management (SOPs, Guidelines, Validation Policy)
Data Base Validation (Disease Management Project Schering, MRI OLAP)
Bloodomics OLAP
Server room
Security


Head-Office (SLC)
7
Evidence-based decision support in MS
(Room 14)
actibelt
(Room 15)
Toilet
female
Biostatistics & Bioinformatics methodology
(Room 1)
Resource Management & IT Infrastructure
(Room 17)
Server Room
Kitchen
Library/ Common Room
20
Conference Room
21
Toilet
male

TOWARDS THE

HUMAN MOTION PROJECT

EVIDENCE BASED DECISION SUPPORT FOR BETTER CLINICAL CHOICES

25.07.2008

MAYO CLINIC TUM LMU trium Analysis Online

Agenda for Friday, 25th July

Location: CAMPUS Garching, Boltzmannstr. 3

Meeting room of the Faculty for Mathematics/Computer Science - Room No. 00.10.011

		Responsible	Time
	Welcome and Overview Campus Garching	Hoffmann	8:30
	Steps towards the Human Motion Project	Daumer	8:45
	Evidence Based Decision Support in MS	Neuhaus, Ebers	9:00
	Physical activity as treatment and outcome measure in selected areas	Daumer	9:15
	- The Movement Disorder Society & The German Competence Networks in Parkinson and MS - Hardware, IT Platform actibelt - First results in clinical trials using the actibelt - Setup of an investigator initiated trial in Finland	Oertel, Hemmer Gerges Thaler Scholz	
	Coffee Break 10:30-10:45 - Option for closed discussion (room to be announced)		
	Validation and normal ranges in high quality data bases in obstetrics	Daumer, Boulesteix	10:45
	Support Vector Machines, pattern recognition and "acceleromics"	Castell, Slawski	11:00
	The Spring Mass Model: a realistic model for human gait	Daumer, Kreuzer	11:10
	Measures for short term variability – the analogy of light and gait	Lederer, Bayer	11:20
	Independent evaluation of pervasive computing - PerCoMed user acceptance	Rashid, Schlesinger	11:30
	Gait analysis facilities at the faculty of sports TUM – Sports & Space as drivers for innovations	Tusker	11:40
	Strategic Partnerships		11:50
	- The role of the SLC from a perspective of a pharmaceutical company - Mayo Vision 2020 and synergies Rochester - Munich	Looby Kaufmann	
	Plans for the future		12:10
	Lunch Break 12:15 – 12:45 - Option for closed discussion (room to be announced)		
	Campus Tour	Hoffmann	12:45
	- Leibniz Rechenzentrum and plan for super computing in Europe - CoTeSys / Intelligent autonomous systems / eyeseecam - Computer aided Medical Systems and Augmented Reality – use of actibelt for surgical workflow	Hegering, Hoffmann Beetz, Schneider Navab	
	Closed Session	Reviewers	15:00
	Round up	Reviewers, Hoffmann, Daumer	16:00-16:20

Reviewer Committee:

Rodney Phillips (chairman of the review committee)	CLINICAL TRIALS	Oxford, UK
Reinhold Haux	MEDICAL INFORMATICS BIOMEDICAL ENGINEERING	Braunschweig, GER
Marek Niezgodka	IT, MATHEMATICS, PHYSICS	Warsaw, PL
Willem G. van Aken (honorary secretary of the review committee)	MEDICAL RESEARCH POLICY AND MANAGEMENT	Enschede, NL
Jayne Spink	ex officio	Delegate MS Society, UK

Participants:

Wolfgang zu Castell	Helmholtz Zentrum München, GER
Rupert Lasser	Helmholtz Zentrum München, GER
George Ebers	University of Oxford, UK
Bernd Haslinger	Klinikum Rechts der Isar, Munich, GER
Bernhard Hemmer	Klinikum Rechts der Isar, Munich, GER
Karl-Heinz Hoffmann	TU München, GER
Kenton Kaufmann	Mayo Klinik, Rochester, USA
Nicolaus König	Marianne-Strauß-Klinik Kempfenhausen, GER
Michael Looby	Novartis Modelling and Simulation Group, Basel, CH
Nassir Navab	TU München, GER
Renate Oberhoffer	TU München, GER
Wolfgang H. Oertel	Uniklinik Marburg, GER
Holger Poppert	Klinikum Rechts der Isar, Munich, GER
Asarnusch Rashid	FZI Karlsruhe, GER
Stefan Schlesinger	Rhön Klinik Bad Neustadt, GER
Erich Schneider, Michael Beetz	TU München, LMU München, GER
Michael Scholz	Trium Analysis Online, Munich, GER
Ferdinand Tusker	TU München, GER
Dieter Wendelstadt	Munich, GER
Franziska Bayer	Sylvia Lawry Centre, Munich, GER
Anne-Laure Boulesteix	Sylvia Lawry Centre, Munich, GER
Martin Daumer	Sylvia Lawry Centre, Munich, GER
Fabian Franzelin	Sylvia Lawry Centre, Munich, GER
Christine Gerges	Sylvia Lawry Centre, Munich, GER
Martina Güntner	Sylvia Lawry Centre, Munich, GER
Nadja Harner	Sylvia Lawry Centre, Munich, GER
Andre Hauschild	Sylvia Lawry Centre, Munich, GER
Gerrit Kreuzer	Sylvia Lawry Centre, Munich, GER
Christian Lederer	Sylvia Lawry Centre, Munich, GER

Anneke Neuhaus	Sylvia Lawry Centre, Munich, GER
Simone Otten	Sylvia Lawry Centre, Munich, GER
Martin Slawski	Sylvia Lawry Centre, Munich, GER
Ralf Strobl	Sylvia Lawry Centre, Munich, GER
Kathrin Thaler	Sylvia Lawry Centre, Munich, GER

09.5.08

Outline for an Independent External Review of the Sylvia Lawry Centre for MS Research e. V.

To be approved by the SLC Supervisory Board
To be organised by the SLC Director
Supported by The Porticus Foundation and the MS Society of Great Britain and Northern Ireland

Key elements:
An impartial and objective examination of the scientific organization, methods and productivity of the Sylvia Lawry Centre `(SLC)`. (A previous external review, having been structured, conducted, in part, and subsequently assessed by individuals with financial and professional interests in the outcomes, begs for a fresh, thorough and authoritative follow up.) . Major supporters: Porticus foundation and the MS Society of Great Britain and Northern Ireland (UK MS Society). (The Hertie foundation has conducted an international external review of a major SLC project in 2007 with a positive outcome).
Scale: 4 reviewers, 2 day site visit 24/25 July 2008. 5-10 page written report.

Background:
The SLC is an independent scientific research organisation founded in 2001 to promote science, research and education in the fields of medicine and natural science, in particular in relation to multiple sclerosis; it is chartered as a not-for-profit charitable organization under German law. It builds on the idea of bringing together mathematics/physics with IT/biomedical engineering and medicine. The mission is to improve human health by developing evidence based decision support tools for better clinical choices.

The Supervisory Board of the SLC sees the need for an impartial and objective examination of the scientific organization, methods and productivity of the Sylvia Lawry Centre `(SLC)`. The Porticus foundation and the UK MS Society, as "investors" in the SLC– have been invited to join the effort to review the scientific status and progress of the Centre, in particular since the previous external review (2005), and the strategic direction and future plans. This is seen as an important step for efforts to increase stability and long term development of the SLC.

Scope of the review
The reviewers should cover the three main areas of the SLC:
- mathematics/physics/statistics,
- IT/ medical informatics/biomedical engineering,
- medicine/clinical trials.

The focus of the review should be on SLC achievements, contributions to new scientific knowledge to date and the strategic direction and plans for the future.

The reviewers will receive preparatory information 4 weeks before the 2 day site visit to the SLC – partly at the University Campus in Garching. The reviewers are expected to present a summary of their findings and recommendations to the SLC Director on the last day of the site visit and to send a final report to the SLC Supervisory Board before August 14. The SLC Director may comment on the draft report.

Selection criteria for the reviewers:
The reviewers should be internationally renowned, independent, senior scientists who will be able to comment on all aspects of the SLC operations. The reviewers should have no direct interests or links to MS or the SLC and should be available for a two day visit to the SLC in Munich at an agreed time in July.

The following reviewers – and their individual area of scientific expertise – have been selected after consultation with the Porticus foundation, the MS Society of Great Britain and Northern Ireland and the SLC's Scientific Advisory Committee:

- Rodney Phillips, Oxford; CLINICAL TRIALS
- Reinhold Haux, Braunschweig, Germany, MEDICAL INFORMATICS/BIOMEDICAL ENGINEERING
- Marek Niezgodka, Warsaw, PL – Director of the ICM in Warsaw, - IT/MATH/PHYSICS
- Pim van Aken, NL, CAD, "secretary" of the review committee,

Preparatory documentation:
- Historical context and support
- Research/business plan
- List of publications, abstracts, conferences
- List of completed and ongoing diploma/PhD theses
- Key publications & reviewer's comments
- Key reports for pharmaceutical companies
- Information about the SLC's data bases, procedures & policies
- Selection of running and submitted grant applications
- Staffing – CV of key researchers
- Financial overview (operational costs, external support, contractual income streams)
- Operational framework for handling requests for access to data and analyses
- Information about the validation of the data

Interviews during the review:
The review committee will have interviews with the Director of SLC, a limited number of staff members, selected representatives of the University (e.g. dean of some faculties of TUM/LMU) and a representative of a commercial (pharmaceutical) company which has (or still is) collaborated with SLC.

Outcome and dissemination of results
The outcome of the review will be a detailed report of 5-10 pages.
It should cover the following areas:

- Overall impression – major strengths, weaknesses & recommendations about strategic direction and future plans
- quality and quantity of clinically meaningful results
- quality and quantity of scientific results
- local, national and international academic & clinical environment
- leadership
- qualification of staff
- adherence to ethical standards
- control of conflicts of interest with pharma and academia

The report will represent the consensus of the independent external reviewers and will be provided by the Chair of the review committee to the SLC board, the SLC Scientific Advisory Committee and the representatives of the major supporters. The recipients will decide jointly about further dissemination and publication.

Roadmap:
- March 13: Informal agreement to support the external review from Porticus foundation and the UK MS Society (DONE)
- April 30: Selection of Reviewers and date for the site visit (DONE)
- July 24/25 site visit
- August 14: final report to SLC board

Costs: The cost of the review are expected to be around 15kE, including travel expenses for three reviewers, one night in a hotel, moderate honorarium for the professional services (400€ per reviewer).