



Annual Report 2005-2006



Basic science to better sight

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Executive Summary

The annual report as required by the Department of Health is submitted in electronic format and is very restrictive in its presentation and format. The focus is on (1) change, as measured by major changes in the strategic direction of individual programmes (or new programmes); (2) input as measured by non-commercial external grants and use of internal support funding and (3) output as measured by publications and impact on clinical practice.

The development of the Joint Research Strategy with the Institute of Ophthalmology (IoO) and changes in the funding arrangements for R&D Support resulted in maintenance of the same programmes reported in 2005. Future changes will therefore be better able to reflect the agreed strategy and the new funding arrangements.

- Age Related Macular Degeneration
- Cataract and Refractive Surgery
- Community Eye Health
- Diabetic Retinopathy and Retinal Angiogenesis
- Gene Therapy
- Glaucoma
- Ocular Immunology
- Ocular Repair and Regeneration Biology
- Ocular Surface Disease
- Paediatric Ophthalmology and Ocular Motility
- Stem Cell Research
- Vision Impairment and Rehabilitation
- Vitreoretinal Surgery
- Predictive Oncology

A summary of our progress with managing this portfolio is given followed by the financial tables. There is a summary of the achievements within each programme together with a list of all publications that were generated by the programme in the year. Finally, the report covers a forward look at the strategic direction of the research portfolio and the main objectives for 2006/7.

Summary

1. Introduction

The research and development annual report 2005-6 follows the same format as in previous years; it is divided into three parts. The first part looks at the activities of the R&D department and updates these from previous reports taking into account the changes that have occurred over the past twelve months. The second part consists of the programmes of research as reported to the Department of Health. This year we have prefaced the material that has been sent to the Department of Health as part of the Trust's annual report by a list of achievements that impinge on clinical practice relevant to the individual programmes. The third part looks at the impact the proposed National Institute of Health Research (NIHR) will have upon R&D in the Trust and its partner and academic collaborator the Institute of Ophthalmology.

2. Joint Research Strategy

2.1 The Moorfields Eye Hospital NHS Foundation Trust and the UCL Institute of Ophthalmology share a common mission statement to improve the eye care and visual health of the nation. Consequently much of the research work that is carried out on the combined site is shared. The whole process can be summarised as 'basic science to better sight'. A significant proportion of research at the Institute does not have specific clinical problems in mind but investigates modalities and mechanisms. A significant proportion of research undertaken by the Trust will not necessarily have involved work at the Institute of Ophthalmology (it may have involved other academic partners such as the City University or the London School of Tropical Medicine and Hygiene) or it will have been carried out without an academic or industry partner. However, between these two extremes much research would start in the laboratory with a clinical problem in mind and end with the patient as the early introduction of new therapy, for example 'proof of principle', first into man studies. This passage which includes all the regulatory hurdles that need to be passed, is known as translational research. The Trust together with the Institute of Ophthalmology has set up a specific committee (the Translational Research Committee) to prioritise, financially support and facilitate translational research on site.

2.2 The Translational Research Committee reports directly to the Joint Strategy Board and in turn receives information from the respective institutions own research boards. (the relationship of these various committees and their composition has been set out in Appendix 1).

2.3 The changes to research and development brought about by the government strategy document "Better Research for Best Health" have resulted in the Trust to applying for Biomedical Research Centre status. As part of this application the Trust with the Institute of Ophthalmology have recognised a number of themes of research. The work covered by each theme fits into the definition of translational research set out above. The themes that have been identified constitute the strongest areas of joint research current on the site and form the backbone of a joint research strategy for the site. These themes are, age related macular degeneration, diabetes, glaucoma, ocular surface disease, paediatrics, community eye health with rehabilitation. It will be noted that a number of the programmes of research reported annually to the Department of Health (electrophysiology, gene therapy, ocular immunology, ocular repair and regeneration biology, retinal degeneration-surgical strategies, stem cell research, vitreo-retinal surgery and ocular oncology) have been subsumed into the above themes.

3. Research Governance

3.1 The Trust has developed robust measures to demonstrate compliance with the highest standards of Good Clinical Practice (GCP) and research governance

according to all statutory legislation and recognised standards of practice. Regular training sessions in GCP are undertaken and the R&D Office anticipates an inspection by the MHRA within the coming months. All these issues required continuous evaluation of our standard operating procedures (SOPs), policies and procedures together with development of comprehensive monitoring arrangements to demonstrate compliance.

3.2 The partnership between the Trust and the UCL Institute of Ophthalmology and the development of research programmes within the joint research strategy has necessitated the establishment of a shared research governance infrastructure. This is made up of a Joint Research Governance Strategy Group (chaired by Phil Luthert), the well established weekly Trust Research Governance Committee (chaired by John Dart) and the Institute Research Governance Committee (tbd). All committees have cross representation with staff from both organisations. The terms of reference for all committees includes issues related to the Human Tissue Act, the Moorfields Eye Bank, Cells for Sight Laboratory and management of both human tissue and bloods.

3.3 The Central Office for Research Ethics Committees (COREC) has been very supportive and the merger between Moorfields and the Whittington Ethics Committee is working well. The committee are not registered to accept clinical trial proposals due to insufficient turnover but these applications are directed to one of the four in London that qualify. Multicentre trials also go to dedicated MRECs. An Implementation Plan has recently been published for “Building on Improvement – implementing the recommendations of the ad hoc advisory group on the operation of NHS ethics committees”. Over the next two years this plan aims to increase the ‘professionalism’ of the RECs through improved training and introduce different levels of review according to need. This will reduce the workload and streamline the service appropriately.

4. Intellectual Property Management Strategy

4.1 Building on the development of in-house skills in IP management we have focused our exploitation efforts on a small number of projects. The contract with Medius Associates has expired and developments within UCL have led to an agreement for joint management support with UCL Biomedica. Each organisation has a separate arrangement with UCL Biomedica but the joint IP is managed accordingly.

4.2 The IP strategy group needs to be re-convened following changes within the UCL Institute of Ophthalmology. However, a ‘pipeline’ of innovation is taking shape and we are currently focusing our activities on achieving ‘proof-of-concept’ funding for those projects closest to potential clinical application. Negotiations are underway with a number of different ‘Joint Venture’ organisations. A successful portfolio of projects that are at different stages of this ‘pipeline’ will, in the future, offer both stability and re-investment opportunities as the income from successful products can be re-invested.

4.3 The IP strategy group will continue to focus on the early identification of IP through training and education of investigators in IP issues, the identification and development of a potential pipeline of innovation and an exploration of all avenues of exploitation and investment. The current focus is developing networks of potential investors and partners and the development of business plans for our leading IP.

5. Clinical Trials Unit, Phenotyping Unit and Reading Centre

5.1 Clinical Trials Unit

5.1.1 The CTU continues to attract new business, providing investigators/sponsors with a clinical trial service of the highest quality.

5.1.2 The overall objectives of the Clinical Trials Unit remain:

- To support the Trust's overall R&D strategy.
- To provide an environment which will optimise the Trust's provision of a quality research product and ensure compliance with the requirements of trials legislation and best practice by ensuring all staff involved with clinical trials undergo the mandatory GCP training the R&D Department have put in place.
- To be self-funding and generate income both directly and indirectly through a combination of quality clinical research and quality management.
- To provide a 'ring fenced' high profile focus for quality clinical trials of medical devices and drugs
- To protect the Trust's financial position (research income) by enhancing the level of external sponsorship (Department of Health, Medical Research Council, Charity, Industry) and complementing the Trust allocation of R&D Support funding from the NHS.

5.1.3 The CTU will be accredited this year as part of the European Vision Institute Clinical Trials Sites of Excellence (EVI.CT.SE)

5.2 Phenotyping Unit

5.2.1 The Phenotyping Unit has established routine phenotyping for patients from a range of services within the Trust, including outreaches. This information facilitates the determination of an ideal course of management and supports identification and monitoring of trends in the disease process. It also facilitates the identification of suitable clinical trial patients

5.3 Reading Centre

5.3.1 The Reading Centre continues to attract studies from external sources as well as the Trust and the Institute of Ophthalmology. It has collaborated on several major external projects and has produced publications / presentations for international meetings and journals. It also continues to provide support for innovative studies all over the world. The Reading Centre is one of three centres identified nationally for grading angiographic images for the DoH funded PDT (PhotoDynamic Therapy) Cohort Study for patients with age-related macular degeneration.

5.3.2 Exchange visits with the Wisconsin Fundus Photograph Centre in the USA provide external quality control and peer-review.

5.3.3 A diabetic retinopathy screening, training and quality control service is provided through the Reading Centre which complies with the National Service Framework for diabetes. The Reading Centre has also been chosen as the lead centre for the EVI.CT.SE.

6. **The National Library for Health (NLH) and Eyes and Vision Specialist Library (EVSL)**

6.1 The Eyes and Vision Specialist Library was launched on World Sight Day, October 13th 2005. The contract between the R&D department and the NHS National Library for Health (NLH) for its development was extended in April 2006 for a further 2 years.

6.2 The EVSL is an online library accessible 24/7 to any generalist or specialist health professional involved in eye health care. The purpose of the library is to find, organise, and facilitate access to the best currently available evidence on eye health in order to support and inform clinical care in NHS England. It is one of 30 specialist libraries commissioned by the NHS National Library for Health.

- 6.3 Since launch, 300 records have been added to the EVSL collection according to quality and content protocols. About 1000 resources are currently available, drawn from nationally procured content and guidance from specialty specific organisations.
- 6.4 Hits to the EVSL are currently 2500 a month and rising steadily in line with our communication strategy.
- 6.5 The Management Group has spent some time post launch reviewing EVSL processes and updating protocols. Specifically, a new competency based topics list and a new content providers list has been agreed by the External Reference Group (ERG). Also as the NLH requires EVSL content to be of quality, the EVSL quality appraisal tool has been evaluated and a report presented to the ERG and NLH.
- 6.6 Having identified the core quality knowledge resources prevalent within eye health at launch, the management group have changed focus to capturing incident knowledge, broadening the scope and depth of topics covered, identifying knowledge gaps and promoting the library. This has involved establishing collaborative practice with our stakeholder groups. For example, the EVSL is now collaborating with Cochrane Eyes and Vision Group to identify knowledge gaps and mutual priority topics, has attended or had representation at the annual conferences of all eye health professional bodies, and has held EVSL training sessions with Joint Library staff for Moorfields nurses.
- 6.7 The EVSL has contributed to the wider NLH development by reporting on specialty needs eg recommendations for national electronic journal procurement and EVSL RSS feed and specialty “my Library” template submissions and has established working relationships with other Specialist Libraries eg EVSL promotion of the Diabetes SL Diabetic Retinopathy National Knowledge Week.
- 6.8 As part of the extended contract, the EVSL is preparing for a Glaucoma National Knowledge Week (NKW) to be held in October. The purpose of a NKW is to provide and promote a collection of updates on knowledge already in existence (eg to update from the position of the last major guidance) or on emerging technology or understanding.
- 6.9 The Do Once and Share (DOAS) programme – part of the Knowledge, Process and Safety Directorate of Connecting for Health – has the main objective of defining and developing national clinical care pathway templates. The DOAS Glaucoma project based in the R&D department started in November 2005 with duration of 6 months. Within this time the team have researched and produced the first evidence based cross professional body consensus national clinical care pathway and a supporting core national dataset. Once codified, the pathway and dataset will contribute to the national electronic care record.
- 6.10 The objectives for the Eyes and Vision Specialist Library for the year ahead are to :
- Include resources from all new content providers
 - Add new topics and images to the EVSL
 - Promote the library to a wider audience and increase hits to the website
 - Prepare and disseminate an Age Related Macular Degeneration NKW
 - Respond to wider NLH developments eg incorporating new NLH wide services to the EVSL

7. Certification of Visual Impairment

- 7.1 The department has taken a keen interest in the epidemiology of eye disease for many years as good quality data can and should, not only inform health policy but give information about incidence and causes from which priorities for prevention, treatment, management and research can be identified.

- 7.2 The R&D department has secured a grant from the Guide Dogs for the Blind Association (GDBA) and agreement with the DoH and Welsh Assembly Government, for MEH, in collaboration with the RCOphth, to act as the repository for the epidemiological data collected during registration for visual impairment in England and Wales. This will enable analysis in real time for trends in visual impairment and its causes. This comes after successfully analysing this data from the OPCS data of 1999. We have established a Certifications Office and employed two new members of staff who manage receipt of the Certificates of Vision Impairment and put these paper forms into electronic format ready for statistical analysis.
- 7.3 We have established a Steering Group who will supervise management and reporting of CVI data. This group comprises members of the DoH, RCOphth, Vision2020, GDBA, RNIB and the ADSS Sensory Group.
- 7.4 We are continuing our commitment to the development of an electronic CVI and have updated our software in line with the changes made to the CVI in September 2005. We are now approaching neighbouring Trusts with a view to testing the ECVI at external sites. We are setting up an electronic newsletter which will enable rapid dissemination of analysis results to all interested stakeholders.
- 7.5 Our current objectives at the end of the year are:
- To have commenced testing the ECVI system at a neighbouring Trust.
 - To have written the first report on data gathered with the new registration form for visual impairment and make comparison with the 1999 analysis.
 - To have developed an electronic newsletter that will facilitate widespread dissemination of analysis results.

8 The Ophthalmic Research Network

- 8.1 The Ophthalmic Research Network has been in operation for over 5 years now and during this time was highly commended as best accessible health related information system in 2001 in the Healthcare IT effectiveness awards. The website contains all kinds of information related to Ophthalmology such as Research projects, Publications, Guidelines, Patient Information and more.
- Designed as a support network for the 5 year plan for Ophthalmology
 - Highly commended as best accessible health related information system in 2001 Healthcare effectiveness awards
 - Large collection of information – over 1000 pages
 - Inventive design, useful features - view 'what's new' on PubMed for a research area
 - Internet usage and internet capabilities have both grown significantly
- 8.2 The department is supporting the development of a network of academic eye units called the Ophthalmic Research Network.
- The UK Clinical Research Collaboration (UKCRC) is a partnership of organisations working to establish the UK as a world leader in clinical research, by harnessing the power of the NHS
 - The UK Clinical Research Network (UKCRN) is working on behalf of the UKCRC to create a UK-wide clinical research infrastructure
 - UKCRN consists of six topic specific networks and one general research network that covers everything else
 - MEH and the IoO are proposing to become a virtual network for ophthalmology, as part of the general network
 - ORN website would support this 'virtual' network

8.3 The new website, the ORNw will act as a resource linking academic eye units, primarily in the UK, to create an up-to-date record of current opinion in ophthalmic research, development in projects and research outputs.

- Structured, clean and professional. Acting as a tool for the user
- Techniques such as animation can be used but will not play any major role in the site. Alternative methods will also be provided
- Consistent layout to keep users interest in the site, using style sheets and carefully considered fonts, line spacing and line height
- Navigation to be the single most important aspect in the redevelopment

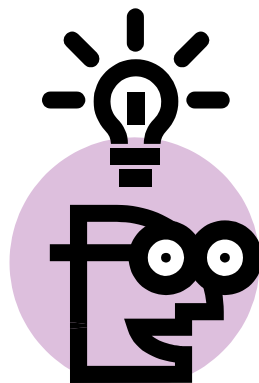
The new website will be focused on research and the network of academic eye units. We will still link to information on Guidelines and Patient Information but this will be taken from the Eyes and Vision Specialist Library, to ensure that the latest information is always featured.

The website can be viewed by visiting <http://www.site4sight.org.uk> and new concepts can be viewed at <http://www.site4sight.org.uk/concept3> and <http://www.site4sight.org.uk/concept6>

Example pages can be found at Appendix 2

Programme 1

Age-Related Macular Degeneration



Age-Related Macular Degeneration

1. Development of new therapies for the treatment of exudative AMD

Trials of PDT (Photodynamic therapy) and Macugen have continued during the year. However, all currently licensed therapies for exudative AMD have a low chance of restoring lost vision and have a high cost per QALY (Quality Adjusted Life Years). Therefore a need to find better therapies is vital. The drug bevacizumab in uncontrolled trials suggest a much greater chance of restoring vision than any other therapy available. In addition it is potentially very inexpensive compared to all other current therapies. A randomised controlled trial to evaluate bevacizumab in the management of exudative AMD has been commenced. If the results of the trial support the uncontrolled trial outcomes data then this drug has the potential to revolutionise the management of exudative AMD, result in a reduction in blindness in the commonest cause of vision loss in the over 50 population and achieve a significant cost saving to the NHS.

2. Prevention of late AMD

Work has continued to achieve an understanding of inflammatory events and their relationship to AMD by evaluating various measures to help understand gene-environment interaction. The EPIC Cohort is helping in the development of strategies to prevent vision loss from AMD.

3. Evaluation of functional response to AMD.

Research has focused on the achievement of a better understanding of macular and cortical function in response to exudative AMD as this may lead to more effective rehabilitation and better patient selection for therapeutic intervention. There have been two projects evaluating aspects of function.

- a. Evaluating cortical plasticity in relation to central vision loss in AMD. Collaboration with Gary Rubin - (MRC funding)
- b. Evaluation of structure and function of the Macula in AMD - in order to select optimal therapy for a particular patient. This is a long-standing project focusing on electrodiagnostic tests to see if they can evaluate the viability of the retina in patients about to undergo therapy for exudative AMD

4. Improved NHS referral pathways - to improve outcomes in patients requiring treatment for wet AMD

In response to delays in the normal NHS referral pathways (confirmed by our own audit) that result in irreversible visual loss for patients with exudative AMD before being seen at a treatment centre, I have developed a rapid referral pathway for patients with AMD. This uses specifically written software allowing angiograms and retinal photographs of patients with sight threatening exudative AMD to be sent to Moorfields directly from the imaging equipment in local centres. This facilitates a response the same day with the aim of achieving a more accurate and rapid referral of patients for treatment before more serious vision loss occurs.

1) Summary of programme area and objectives

1. Priorities

- i. To develop programmes of research focusing on mechanisms, diagnosis and therapies in ARMD funded by non-commercial external organisations
- ii. To develop a collaborative relationship with the Pharmaceutical Industry to undertake joint Preclinical and Phase I/II clinical trials.
- iii. To increase the programme of Phase III trials in ARMD

2. Rationale

It is anticipated that there will be a dramatic increase in studies and research funds available to investigate the mechanisms, improve diagnosis and evaluate new therapies, including biological treatments, gene therapy and stem cell research in ARMD over the next 5 to 10 years. It is therefore appropriate to seek to expand the Medical Retina Clinical Research Profile in these areas in the short and medium term. The major emphasis will be on in house externally funded non-commercial research examining new therapeutic approaches to ARMD. In addition we intend to consolidate a collaborative relationship with the pharmaceutical industry to undertake Phase I/II collaborative studies. Finally, a significant expansion of our Phase III clinical trial work programme is envisaged to ensure the hospital remains at the forefront of delivering novel therapies, particularly in exudative ARMD (eARMD)

Short Term Research

Symptoms, presentation and referral

Develop further epidemiological studies to improve information about the incidence and prevalence of AMD

Medium Term

Prevention and surveillance

Establish an AMD specific disease register.

Phenotyping, information and communication

Continue the collection of phenotyping data in the Phenotyping Unit

Genetics, genotyping and risk factors

Continue the molecular genetic studies of patients with AMD using blood collected from our patients, and their siblings. Segregate according to their phenotype using photography, fluorescein angiography and autofluorescence imaging. Spouses of patients free of AMD provide a comparison group.

Develop more reliable source of AMD donor tissue, appropriately consented

Continue, in parallel, histological studies undertaken to document the variation of age-changes at the macula, compatible with the concept that several genes are involved in conferring risk of visual loss.

Interventions -surgery, medical, radiological

Clinical trials to evaluate novel, and improvement of existing treatments in AMD focusing on using common outcome measures, risks and benefits that are relevant to patients:

Photodynamic therapy

Intraocular administration of tissue plasminogen activator, other clot lysis agents and anti-angiogenic, anti-scarring agents

Long Term Research

Diagnosis, investigations and pathology

Elucidation of novel therapies including gene replacement therapy

'Blue skies' Research

Diagnosis, investigations and pathology

Investigate the role of trace elements in drusen formation

Research into the genes and proteins underlying the disorder offers the most promising hope for development of novel treatment strategies

This programme incorporates the neuro-ophthalmic research focused on AMD

(The Department of Health rated this programme in 2005 as *Strong*)

2) Changes made in response to feedback from the Department of Health

Last year we identified a surgical programme of activity for treating age-related macular degeneration(ARMD) from within the ARMD programme and offered it as a stand alone programme. The feedback from DH rated the programme as moderate and the comments suggested that the DH did not feel that this was sufficiently robust to stand alone. In addition, although maintaining its strong rating, the comments on the ARMD programme noted that there had been a significant reduction in projects, external funding and publications. It was therefore agreed to revert to a single programme for the treatment of age-related macular degeneration. This now includes the following objectives:

Research Priorities

- To fund and complete a two centre (at least) prospective trial in 360 retinal translocation for end stage ARMD following the good outcome of the pilot.
- To consolidate clear-cut clinical features that define optimal patient selection for ARMD surgical procedures.
- To calibrate the clinical fixation strategy developed for the translocation pilot and currently used to select patients for surgery.
- To establish a follow-on study of RPE - choroidal

transplantation that is based on the patients with good outcome in the current pilot study

- To aim to participate in and or establish a prospective clinical trial for RPE – choroidal transplantation in the treatment of ARMD and other macular diseases
- To create a clear strategy to take the project of transplantation of artificial RPE cells created in the IOO to the level needed for a clinical trial.

2B

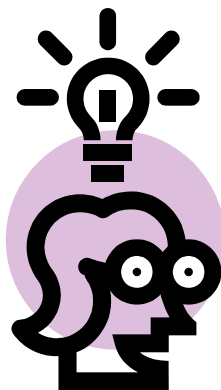
Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	12	12
4) Number of peer-reviewed publications (financial year 2005/06)	26	26
5) Number of higher degrees directly funded by NHS R&D Support Funding (unspecified year type)	0	0
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.	
7) Examples of impact on health services or policy	<p>Age-related macular disease (AMD) accounts for over 50% of blind registration in the UK and 75% is due to choroidal neovascularisation. Treatment of this complication has been disappointing in the past but our programme has contributed to great advances in therapy including PDT (approved by NICE) and Macugen (reduces vascular growth and results superior to PDT for certain patients) which has been approved by the FDA and European drugs agency. Cost to PCTs is an issue but there are early indications that Avastin may be even more effective and would also be more affordable for more patients.</p> <p>Translocation surgery has been shown to restore near normal vision to a proportion of cases of age related macular degeneration who are already blind or significantly partially sighted. Visual recovery, with excellent levels of reading and distance vision, is greater than expected by careful selection of patients using a Moorfields algorithm. Expansion of this technique in our research programme has made this treatment available to a greater number of patients in this otherwise untreatable</p>	

group.

Programme 2

Cataract and Refractive Surgery



Cataract and Refractive Surgery

1. The Cataract Service has recently completed an industry-sponsored randomised controlled trial comparing visual function between two competing designs of intraocular lenses. This will provide valuable guidance regarding the best option of lens designs for clinical practice as well as providing a careful assessment of the quality of vision following cataract extraction.
2. A second randomised controlled trial helped clarify guidelines regarding the surgical management of astigmatism during cataract surgery – a common clinical problem.
3. A large retrospective case-controlled study further defined the impact of posterior capsule tear during cataract as a risk factor for pseudophakic retinal detachment, which has clinical implications for cataract training.
4. The role of non-steroidal agents in the prevention and treatment of cystoid macular oedema following cataract surgery has been the subject of a major systematic review which has helped establish guidelines for clinical management.
5. In collaboration with the anaesthetic department, a randomised controlled trial was performed evaluating patient satisfaction following either sub-tenon or topical anaesthesia.
6. The Refractive Service has conducted a systematic review of the evidence for safety and efficacy of LASIK or PRK for the treatment of myopia. This has helped resolve the controversy surrounding the relative merits of these two surgical modalities. A large case series of LASIK procedures has provided up-to-date information on the risks involved in LASIK.

1) Summary of programme area and objectives

Cataract Surgery

The scope of the cataract research strategy covers all aspects of disease progression and will contribute to the evidence base following a pathway from genomics / proteomics through diagnosis / treatment to rehabilitation and care in the community. The focus on the patient pathway facilitates the application of many different disciplines to the understanding of the mechanisms and processes underlying progression of the disease and finding solutions to problems associated with them. The evidence base has been organised in the same way and gaps or weaknesses in the existing knowledge can then be targeted. Prioritisation is patient orientated and takes into account the need to balance the search for novel clinical treatments that might be applied relatively quickly against the basic science research that will produce new generations of disease management in the future. The joint site facilitates the identification of clinical problems, research into mechanisms of disease, an environment for the trial of new therapies and their introduction into clinical practice.

The short, medium and long term benefits of this programme will be:

- Reduction in the waiting times for surgery and PCO correction
- Improved intraocular lenses and a reduction in presbyopia
- Identification of risk factors, causes and mechanisms of cataract formation that will lead to preventative treatments

Refractive Surgery Priorities

- To publish accurate multi-surgeon outcome data for contemporary refractive surgical procedures.
- To feed back information confidentially to contributing surgeons enabling them to ensure that they are in step with pooled data.
- To quantify the visual impact of technical advances and changes in treatment protocols.
- To publish comparisons of refractive surgery outcomes with visual function for equivalent patient groups who have not undergone refractive surgery.
- To correlate subjective visual outcomes (data from questionnaire instruments) with objective indices (e.g. Acuity, contrast sensitivity, wavefront indices).

100,000 cases of refractive surgery are performed in the UK annually. Technical development, improved patient selection, and improved strategies for the treatment of complications have combined to raise safety for LASIK, the dominant refractive surgical procedure, to a level approaching that for a ten year period of contact lens wear. But public confidence has been badly damaged by newspaper coverage of a recent preliminary report from the National Institute of Clinical Excellence examining refractive surgery outcomes as a public health issue. The NICE report and a subsequent parliamentary review highlighted 3 weak areas:

1. Audit procedures are poor or non-existent in most clinics.
2. Quality of life based outcome measures have been largely ignored.
3. Follow up in most studies is relatively short.

In line with the priorities outlined above, we would anticipate utilising our patient base, expertise in quantifying visual outcomes and IT resources to demonstrate best practice in refractive surgery.

(The Department of Health rated this programme in 2005 as *Strong*)

2) **Changes made in response to feedback from the Department of Health**

2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	8	8
4) Number of peer-reviewed publications (financial year 2005/06)	13	13
5) Number of higher degrees directly funded by NHS R&D Support Funding (unspecified year type)	0	0

6) **Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating**

In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.

7) **Examples of impact on health services or policy**

The findings of a study focusing on adverse events following phaco surgery led to the development of formulae which indicate patients at higher risk of complications. Patient safety is therefore improved because these patients can be diverted to surgeons with the most experience.

Moorfields Cataract Service contributed several hundred patients to the recently completed prospective European Trial of prophylactic treatments for the prevention of cataract surgical infection (endophthalmitis) which demonstrated, for the first time, a difference between therapies. This will have a major impact on standards of care with intraocular injection replacing topical antibiotic therapy. This will reduce costs as well as improve outcomes by potentially halving the rate of infection which currently runs at 250-500 cases per year in the UK.

Use of our large patient database has been enhanced by recording all cataract surgical procedures and their outcomes prospectively on our electronic patient record system. This permits real time audit of outcomes in relation to clinical risk factors and surgical risk factors feeding into quality of care. Similar studies here have evaluated intra-ocular lens power measurement and its precision to produce guidelines for improving these. We have also provided data on other risk factors for complications of surgery to inform providers and

patients and assist in risk containment.

Trials of new models of intraocular lens have been, and are being conducted. The first trial examined the effect of new lens optics to establish whether the anticipated benefits are real. This independent assessment can then be incorporated into the cost benefit analysis for NHS users who need to order implants for 250,000 cataract procedures annually. Objective assessments include assessment of visual function using LogMar vision charts, contrast sensitivity, together with forward light scatter and validated patient questionnaires developed in the Institute of Ophthalmology.

100,000 cases of refractive surgery are performed in the UK annually. The NICE issued guarded guidance regarding the procedure which highlighted the facts that outcomes of these therapies are a public health issue, that audit procedures are poor or non-existent in most clinics, that quality of life based outcomes have been ignored and that follow up studies are short. Approximately 4000 refractive surgery operations are performed annually at Moorfields and we have been producing some high quality data to address these problems.

Programme 3

Community Eye Health



Community Eye Health

1. We have completed a large randomised controlled trial of beta-radiation for glaucoma surgery in South Africa. The results show a clear clinical benefit from the use of adjunctive beta-radiation in terms of success of glaucoma surgery. The report of this trial has been accepted for publication in the BMJ.
2. Our glaucoma team at Ealing won first prize in the Allergan Glaucoma Achievement Award based on our research program investigating ways of improving glaucoma detection in the community. Our public health campaign for glaucoma awareness in the Indian Community has been created and is about to be launched on television, radio and in posters.
3. Seven community optometrists have been trained and passed the first examination in a project investigating their integration into glaucoma care teams. This project will look at the cost-effectiveness, safety, acceptability and other aspects of running glaucoma clinics in the community.

1) **Summary of programme area and objectives**

Setting

The primary purpose of all of our efforts at Moorfields is to improve the eye health of the population. To this end it is vital that we are involved at the community level.

Priorities

- To establish an integrated eye care service involving optometrists, GPs and other primary health care workers in one team approach aimed at improving the ocular health and health care in the community.
- To establish outcomes reflecting the ocular health of the community.
- To demonstrate measurable improvement in the ocular health of community.

Short term research

Prevention and monitoring

- Diabetic retinopathy screening by trained optometrists and other models is being investigated.
- Symptoms, presentation and referral
- Improvement of case detection of glaucoma by optometrists.
- Investigation of the impact of health education on public health knowledge and health seeking behaviour is underway.

Healthcare delivery

- The commonest ocular problems in the community are often simple ocular surface disorders (blepharitis, conjunctivitis and dry eye). Co-management of ocular surface disease in the community between ophthalmologists, optometrists and GP's is to be assessed
- Assessment of safety, cost effectiveness and acceptability of various models of delivery of cataract services
- Telemedicine for providing specialist ophthalmic advice on site to accident and emergency departments who otherwise have to refer such patients to alternative Hospitals for sub-specialist opinions.
- Telemedicine advice to GP surgeries directly
- Investigation of better communication with Asian patients by use of touch screen technology.

Medium term research

Outcome assessment

- Comprehensive audit of refractive surgery outcomes adopting a broad definition of visual function pre and post surgery with outcome measures including validated questionnaire instruments and objective measures in addition to high contrast visual acuity.

Symptoms, presentation and referral

- Improve specificity of referral of patients from the community setting into hospital care.
- Expansion of the programme that led to improved detection of glaucoma in the Ealing community to the other outreaches. Community optometrists, GPs and hospital A&E departments will

all be part of this forming an integrated whole. This will involve improved glaucoma and diabetic eye disease detection and therapy.

Healthcare delivery

- Investigation of the impact, safety, cost-effectiveness and practicality of integrated eye care services for glaucoma and ocular surface disease.
- Investigation of integration of overall eye care services with general practices.

Follow-up and continuing care

- Effective home devices and aids for visual rehabilitation.
- Improved education using patient leaflets and videos for the management of chronic conditions such as blepharitis.
- All of this activity is compatible with the Vision 2020 initiative for the prevention of avoidable blindness in our communities in the UK and will be focused with particular attention on those parts of the community at most disadvantage.

(The Department of Health rated this programme in 2005 as **Strong**)

- 2) **Changes made in response to feedback from the Department of Health**

2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	7	7
4) Number of peer-reviewed publications (financial year 2005/06)	12	12
5) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	1	1
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.	

7) Examples of impact on health services or policy

Clear demonstration of improved glaucoma detection in the community by collaborative work with optometrists. We have doubled the number of cases of glaucoma detected in the community. This is important as early treatment can prevent visual loss.

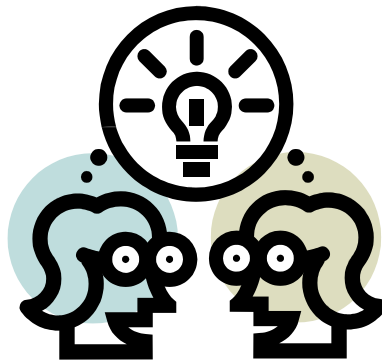
Identification of key barriers to access to available health care for the Indian and Pakistani communities. We have developed an advertising campaign specifically for this community in order to raise awareness of eye disease and are addressing ways of overcoming the barriers identified.

Regular communication and progress towards the creation of a uniform and integrated eye care service involving all providers. Ten community optometrists have now received a dedicated training package with qualification exam with a view to establishing more service within the community.

Extensively investigated the use of telemedicine in provision of specialist opinion locally. The safety of decision making has been established and our next step is to assess utilisation and practicality within an A&E situation.

Programme 4

Diabetic Retinopathy and Retinal Angiogenesis



Diabetic Retinopathy and Retinal Angiogenesis

1. Different models of diabetic screening have been evaluated and as a result we have now initiated an optometry led Diabetic Retinopathy Screening and Low Vision service. We will be appraising this and optimal intervals for diabetic retinopathy screening
2. We have recently audited the determination of diabetic retinopathy and hypertensive control in patients eligible for diabetic screening to assess the best approach.
3. We continue to evaluate the role of sequential OCT imaging in the diagnosis and response to treatment of diabetic macular oedema. The Moorfields Macula Protocol which provides a sensitive assessment of macular function using fine matrix mapping, microperimetry, electrodiagnostic evaluation and autofluorescence imaging will be applied to diabetic patients undergoing future evaluation of novel treatments.
4. The Reading Centre is moving towards automated grading of images for assessment of sensitivity and specificity.
5. We have completed a prospective randomised trial of intravitreal triamcinolone in diabetic macular oedema. This showed no significant benefit to this intervention and the use throughout the UK is now restricted.
6. The role for pars plana vitrectomy has been established in selected cases of diabetic macular oedema unresponsive to conventional laser therapy.

1) **Summary of programme area and objectives**

Disease of the retina due to complications arising secondary to retinal vascular disease include common disorders such as diabetic retinopathy and retinal vein occlusion.

Short Term Research

Prevention and surveillance

- Evaluation studies of screening for diabetic retinopathy
- Assessment of most efficient delivery of diabetic screening and ophthalmic management in the UK.

Follow up and community care

- NSF targets and health promotion for diabetics in collaboration with PCTs
- Identify optimum screening intervals in collaboration with PCTs

Medium Term Research

Prevention and Surveillance

- Evaluation of health-related quality of life and costs associated with prevention or progression of diabetic retinopathy

Diagnosis and Phenotyping.

- Develop services within the Phenotyping Unit to work towards automated grading of retinal images.
- Optical Coherence Tomography and retinal thickness Interventions – medical and surgical.
- Clinical trial to assess of the effectiveness of treatments such as vitrectomy/membrane peel.
- RCT on the role of vitrectomy in the treatment of diabetic macular oedema.
- Clinical trials of surgical approaches to cannulation of retinal vessels and delivery of new agents to them.
- Clinical trials of new therapeutic principles focusing on patient-oriented outcomes.

Long term Research

Interventions – surgical and medical

- Prospective trials on the use of anti-angiogenic agents as adjuncts to vitreoretinal surgery for eyes with severe diabetic retinopathy.
- The role of growth factors such as VEGF and the angiopoietins in diabetic retinal angiogenesis and macular oedema focusing on key molecular targets for pharmacological therapeutic intervention.
- Chorio-retinal anastomosis, either by laser or surgical means to bypass CRVO will be further examined and systemic and intravitreal clot lysis agents refined and reassessed.
- Comparison of surgery to other emerging treatments in terms of risk, cost, qualitative and technical assessments of outcomes Blue Skies Research.
- Characterisation of molecules involved in neovascularisation occurring in diabetic retinopathy and vein occlusion.
- Molecular targets for pharmacological therapeutic intervention.
- Inhibition of intracellular molecules upregulated by VEGF, eg Protein Kinase C, will undergo more investigation before introduction as medical treatments.
- Viral vector introduction of VEGF receptors and other growth factor

antagonist genes.

- Elucidation of novel genes and chromosomal loci causing monogenic retinal disease.
- Elucidation of population genetic polymorphisms influencing the susceptibility to diabetic retinopathy.
- Evaluation of gene function, protein structure, chemistry and interaction in cell systems and animal models.
- Prothrombotic tendencies and systemic risk factors for development of strategies that will reduce disease incidence.
- Inflammatory response causing neovascularisation.
- Elucidation of novel therapies including gene therapy, modulation of cell apoptosis, catalysis of harmful gene mutations in vivo and retinal cell transplantation.

(The Department of Health rated this programme in 2005 as **Strong**)

2) **Changes made in response to feedback from the Department of Health**

2B

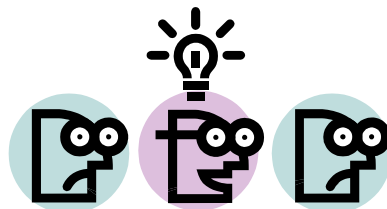
Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	10	10
4) Number of peer-reviewed publications (financial year 2005/06)	15	15
5) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	1	1
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.	
7) Examples of impact on health services or policy	<p>Limited inappropriate off-label use of triamcinolone by findings of randomised controlled trial. This negative finding of research benefits patients by reducing the side effects experienced.</p> <p>Development of novel functional assessments to better understand the progression of macular ischaemia, a main cause of visual loss in diabetic retinopathy.</p> <p>Refined current screening with optical coherence tomography</p>	

measurement for greater efficiency. This has had an impact on meeting the standards within the NSF for diabetes in diabetic retinopathy screening.

Programme 5

Gene Therapy



Gene Therapy

The field of ocular gene therapy continues to enjoy rapid progress. Gene-based therapies present the means to correct gene defects in inherited ocular disorders by gene replacement or silencing, and offer broad potential applications as a sophisticated system for the targeted, sustained and regulated delivery of therapeutic proteins in a range of acquired ocular disorders.

1. We have demonstrated that lentiviral vectors are able to mediate therapeutic effects in RPE-based inherited retinal degenerations. Recombinant adeno-associate virus (rAAV)-mediated gene replacement of retinitis pigmentosa GTPase regulator interacting protein (RPGRIP) preserves photoreceptor cells and retinal function in a model of Leber's congenital amaurosis (LCA). This has implications as a future therapeutic option for this group of conditions.

Generic gene therapy strategies that aim not to correct the gene defect but to ameliorate its consequences offer the possibility of therapies that are widely applicable across a range of conditions.

2. We have demonstrated that expression of GDNF in combination with gene replacement therapy augments the morphological and functional improvement mediated by gene replacement alone. This illustrates the potential of gene therapy strategies to modulate immune responses in the eye without unwanted systemic effects. For example, in the corneal endothelium we can increase corneal endothelial cell density.

Recent advances in ocular gene therapy have led to a number of proposals in the United States for clinical trials of gene therapies for both inherited and acquired ocular disease.

3. We have developed a protocol for a clinical trial of rAAV-mediated gene therapy for patients with severe early-onset inherited retinal degeneration due to defects in RPE65. This flagship trial is funded by a £1 million grant from the Department of Health and has received a favourable opinion from the UK Gene Therapy Advisory Committee (GTAC). Moorfields Pharmaceuticals are developing the facilities to import and store clinical grade gene therapy vectors for this trial. The first batch of vector has been manufactured for us by Targeted Genetics in the United States. We expect to import vector for our trial in September 2006 and aim to enrol the first patients by the end of the year. This will be the first ocular gene therapy trial in Europe and one of the first in the world.

In anticipation of an expanded gene therapy programme that will require manufacture of a variety of vectors, we are working with both UCL and Moorfields Pharmaceuticals to develop local GMP vector production capacity. We are now exploring whether we might be able to utilise Moorfields Pharmaceuticals GMP infrastructure for this purpose. As part of a feasibility study, in August 2006, Alan Kroll, Nick Precious and Robin Ali visited an academic GMP vector manufacturing facility in Galway.

1) **Summary of programme area and objectives**

The development of gene therapy has become a major initiative in many areas of biomedical research. Until recently however, translation of this technology to clinical effect has been limited primarily because of deficiencies in vector systems. Vector systems have now been developed, that mediate efficient, long-term gene expression in a wide variety of cells and tissues.

The eye offers many unique advantages as a target organ for the development of gene therapy. It is easily accessible and allows localised exposure of the target tissue to therapeutic agents with limited risk of systemic effects. Furthermore, the outcome of treatment can be monitored by a variety of non-invasive examinations.

The joint site facilitates the identification of clinical problems, research into mechanisms of disease, an environment for the trial of new therapies and their introduction into clinical practice. The focus for gene therapy is thus on:

- *Genomics* - understanding the relation between the various genetic mutations leading to inherited retinal degeneration and gene therapy for neovascular disease
- *Genetic epidemiological studies* - links between genotype and environmental factors.
- *Improvements in vector technology* - pre-clinical development in animal models across a whole spectrum of eye conditions and production of a clinical grade vector.
- Pre-clinical toxicity and safety testing.
- *Pre-clinical development of therapy* - the most appropriate initial clinical trial of gene therapy for inherited retinal degeneration will involve patients with childhood onset severe retinal dystrophy due to mutations in the gene encoding RPE65 - Initial clinical trial of patients with childhood onset severe retinal dystrophy due to mutations of the gene encoding RPE65. Patient recruitment commenced 2004. Trial anticipated to begin in early 2006.
- Clinical trial of gene therapy - treatment of choroidal neovascularisation associated with AMD. A trial will be facilitated by pre-clinical toxicity and safety testing for the RPE65 trial and would benefit from economies of scale for clinical grade vector production. It is intended to initiate a pilot clinical study of gene-based delivery of an anti-angiogenic protein (such as the VEGF inhibitor sFlt-1) in a small group of patients with advanced neovascular AMD.
- Development of therapies that combine gene transfer with cell transplantation, including autologous adult cell transplantation and stem cell transplantation

There are current research projects developing both autologous RPE cell transplantation and immortalised cell transplantation that can be combined with ex-vivo gene therapy. In the 5-yr period to 2010 it is intended to develop clear clinical strategies to use this combined mode of treatment to enhance the outcomes resulting from cell transplantation alone. This will be especially relevant to the problem of neovascular recurrence following surgical transplantation techniques.

(The Department of Health rated this programme in 2005 as **Strong**)

2) **Changes made in response to feedback from the Department of Health**

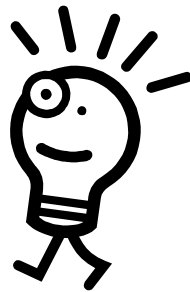
2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	11	11
4) Number of peer-reviewed publications (financial year 2005/06)	16	16
5) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	2	2
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	<p>In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.</p>	
7) Examples of impact on health services or policy	<p>None BUT a proposed trial of gene therapy for patients with severe early- onset retinal dystrophy due to mutations in the gene encoding RPE65 has received a favourable opinion from the Gene Therapy Advisory Committee. This trial represents the culmination of 10 years of preclinical research with the Institute of Ophthalmology and is funded by a £1 million grant from the Department of Health. The trial is due to commence in the autumn and if successful will save the sight of children who would otherwise be blind by the age of 20.</p>	

Programme 6

Glaucoma



Glaucoma

1. The patented visual field analysis software, PROGRESSOR, has been licensed to Medisoft and is available for clinical use
2. The copyrighted Moorfields Motion Detection Test (MDT) which measures the psychophysical level of visual function, obtained MHRA approval and CE mark. A normative database is under development
3. New optic nerve imaging progression software developed for HRT; Heidelberg Engineering is funding a PhD student to continue development
4. Research on a new non-contact tonometer that measures a corneal biomechanical response have shown a likely impact on future IOP assessment in clinical practice
5. Incorporation of new techniques for glaucoma surgery developed by the glaucoma service (large surface area of treatment) into international consensus book on surgery.
6. Results of 8 year Medical Research Council/ Moorfields 5-Fluorouracil study "More Flow Study" shows an improvement in intraocular pressure control in patients treated with the 5 minute 5-fluorouracil sponge treatment developed at Moorfields Eye Hospital and the Institute of Ophthalmology. This improvement continues for 8 years of follow up and the treatment appears safe and easily implemented in the UK and many other countries. There is a marked racial difference in the response to surgery – the first time this has been properly shown in a prospective study. This has very significant implications for the implementation of surgery in different racial groups in the UK and around the world.
7. Results from sister Singapore 5-fluorouracil glaucoma surgery study showing improved control of intraocular pressure with intraoperative 5-fu and a trend towards better disc and field survival
8. Collaborative study from Birmingham and Moorfields showing that advances in trabeculectomy surgery pioneered at Moorfields can result in good outcomes and low complications of surgery in high risk patients even with mitomycin-c
9. As part of establishing a programme in Genetic Epidemiology we have collaborated with the University of Sydney (Paul Mitchell) and conducted a statistical analysis of IOP data from the Blue Mountains Study. We have identified evidence for a major genetic component determining IOP

1) **Summary of programme area and objectives**

- Improve the detection rate of glaucoma in the community
Approximately 50% of individuals with glaucoma have not been detected and diagnosed. This area of research focuses on barriers to diagnosis, including access to and utilisation of the health care system, the efficiency of primary care services and the role of new technologies in improving diagnosis rates.
- Optimise health care delivery for patients with glaucoma
This priority focuses on the efficiency and effectiveness of health care delivery to patients with glaucoma. The hospital eye service copes with patients at low risk of reduced quality of life as a result of glaucoma, many of whom could be managed in the primary care setting by appropriately skilled and equipped optometrists as part of an integrated eye care service with the hospital. The research includes access to diagnostic services and to disease management and treatment services.
- To establish the impact of vision loss on patients' quality of life and everyday function in the real world, and develop strategies for rehabilitation

Glaucoma accounts for 13% of those on the blind register in England and Wales. Little is known of the impact of glaucomatous visual impairment on the function of individuals in their environment. Tests used in the clinic to document the visual function of the eye in glaucoma have little relevance to visual function needs of individuals in the real world. This research will focus on impairment in everyday tasks such as reading, shopping, using stairs and driving.

Rehabilitation strategies form a separate programme.

- Improve the description and classification of the features of glaucoma (phenotyping)
- Current classification methods for Primary Open Angle Glaucoma (POAG) and Primary Angle Closure (PAC) do not reflect the subtle description of ocular features that is required for genotyping studies and studies of environmental risk factors.
- Develop measurement techniques to improve diagnosis and detection of disease progression.
- New measurement techniques enable more refined measurements of the eye structures relevant to POAG and PAC. Research is required to establish the role of new technology and to further our understanding of glaucoma through application of new measurement techniques. This will elucidate disease-causing mechanisms, risk factors and will enable more accurate and precise measures of disease progression.
- Discover the genetic and environmental causes for glaucoma
In a collaborative venture with the University of Cambridge, we intend to collect detailed ophthalmic phenotypic data on several thousand individuals living in urban and rural communities in Norfolk. This will provide an invaluable measure of disease in the community, as well as control data.
- Develop and investigate improved treatments for glaucoma
This research priority centres on the continued development of novel treatments, optimal treatment strategies and the evaluation of newly-available therapies. Much of this priority will be achieved through the Ocular Repair and Regeneration Biology programme.

2)

(The Department of Health rated this programme in 2005 as Strong)

2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	27	27
4) Number of peer-reviewed publications (financial year 2005/06)	20	20
5) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	2	2
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	<p>In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.</p>	
7) Examples of impact on health services or policy	<p>The 'Moorfields Analysis' software, that is incorporated into the Heidelberg scanning laser ophthalmoscope, has been demonstrated to have good predictive value, identifying ocular appearance in glaucoma suspect patients who subsequently go on to develop glaucoma. This enables earlier and therefore more effective treatment.</p> <p>The PROGRESSOR software developed at Moorfields (which uses trend analysis to identify rate of change in visual sensitivity in glaucoma) has been demonstrated to be both an indicator of therapeutic effect but also (by integrating the visual fields of the two eyes) to be related to ability or lack of ability to maintain visual standards for driving a motor vehicle.</p> <p>Following the introduction of anti-scarring (anti-proliferative) agents into routine glaucoma surgery there has been an increase in adverse events (complications). The development, at Moorfields, of modifications to the standard operation have led to a significant reduction in the number of adverse events improving patient safety.</p> <p>The development of a training scheme for glaucoma care by optometrists has shown how this can be carried out in a community setting in London.</p> <p>Ethnic specific glaucoma awareness advertisements have greatly improved the ability to find hitherto undiagnosed cases of glaucoma in immigrant communities.</p>	

Programme 7

Ocular Immunology



Ocular Immunology

This year has been very successful in the introduction of new therapies into the clinic as well as considerable progress achieved in identifying the patients at risk of severe visual loss.

1. Intraocular triamcinolone has been assessed in a large number of patients with uveitis and its effectiveness demonstrated as well as showing that the safety profile is acceptable. We have introduced intraocular triamcinolone at the end of cataract surgery for uveitis patients instead of the requirement for 2 weeks of high dose corticosteroid therapy and found it to be very acceptable to the patients and more effective at control of surgical induced inflammation. In addition infliximab has been used in the management of acute and chronic disease and found to be beneficial.
2. Patients at high risk of visual loss have been found to have certain cytokine gene polymorphisms and this work continues to determine a cytokine/chemokine DNA profile in patients most likely to respond badly to current treatments and lose vision. This work will be further consolidated over the next year as new treatments come into clinical trials.

1) Summary of programme area and objectives

Inflammatory processes are orchestrated by the immune system whose role is to seek out and destroy invading organisms. White blood cells patrol the body in search of foreign bodies to destroy. In autoimmune disease, the immune system reacts against the host causing damage to normal healthy tissue. This problem can occur in various parts of the body including the eye (uveitis). When an autoimmune response is triggered in the eye the light sensitive retina can be damaged with consequent visual loss.

The research programme is aimed at investigating the role that retinal blood vessels play in recruiting white blood cells to the eye. Once activated, the white blood cells migrate into the eye where they are responsible for causing the damage that results in visual loss. The research focuses on the need to understand the intricate sequence of biological events that lead to the development of immune-mediated disease. By identifying these factors new treatments can be designed to interfere with the disease process and prevent its progression.

Priorities

- To develop research into inflammatory eye disease, guided by both relevance to the National Plan and our research strengths. The disorders studied include uveitis (a severe inflammatory disorder of the posterior segment responsible for 10% of all registered blind patients under the age of 65 years) and inflammatory diseases of the external eye, including allergic eye disease and mucous membrane pemphigoid, which are either common or severe and blinding. It is also important that research into an immune pathogenesis of age-related macular degeneration be developed.
- The appointment of another consultant ophthalmologist with 50:50 clinical and research contract to develop the research into anterior segment inflammatory disease.
- Provision of studentships for clinicians undertaking research programmes at the Trust and Institute leading to a PhD or MD to further support the interaction between the Trust and the outstanding researchers in immunology at the Institute.
- To develop and expand the use of Trust's clinical research infrastructure to increase the volume and quality of clinical trials and collaborative research in this field which is a focus for development by the pharmaceutical industry.
- Participate in multicentre studies testing new forms of therapy for non-infective posterior uveitis.
- To secure our position as one of the outstanding international centres in this field.
- Establish a line of research to phenotype retinal conditions associated with ocular inflammation. This activity is ongoing for the past 2 years with Professor Ono's laboratory but is need of funding for a fellow so as to facilitate future research grant submissions in this area.
- Study of steroid-induced glaucoma by phenotyping patients who develop high intra-ocular pressure on topical steroid therapy and also by animal research.
- Establish a programme for the identification of immunologic factors associated with chronic posterior uveitis.

(The Department of Health rated this programme in 2005 as *Moderate*)

2) Changes made in response to feedback from the Department of Health

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	11	11
4) Number of peer-reviewed publications (financial year 2005/06)	9	9
5) Number of higher degrees directly funded by NHS R&D Support Funding (unspecified year type)	0	0
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	<p>In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.</p>	
7) Examples of impact on health services or policy	<p>The projects undertaken on the use of intraocular triamcinolone in patients with uveitis and during cataract surgery, have greatly changed the way these patients are managed. They now require much less in the way of systemic corticosteroids and other immunosuppressive agents such as cyclosporin and mycophenolate. The visual improvement is better and the quality of life vastly improved with this improved vision and the reduced side effects from the systemic drugs.</p> <p>The Trust has is one of the largest treatment centres in the world for the management of ocular mucous membrane pemphigoid. Previous studies have identified a new use for sulphapyridine in the management of this disease and we have recently found mycophenolate to be effective. Changes in UK practice have disseminated out to other centres from the effect of both publication and tertiary referrals, to the benefit of patients. A new multicentre randomised treatment trial has been coordinated by Moorfields and is currently underway and is integrated with laboratory studies at the Institute.</p> <p>A randomised treatment trial at Moorfields indicated treatment of corneal transplant rejection is successful in reversing the episode in the great majority of patients. This has been followed up with our studies into the immunobiology of rejection to provide better insights into prevention of rejection in transplant recipients. Our first study of intraocular samples from corneal graft recipient eyes at the time of presentation with rejection has commenced.</p> <p>Age related macular degeneration, one of the leading causes of blindness, may have an immunological component. Evaluation of the potential immune pathogenesis of age related macular degeneration has shown that approximately 80% of sera from patients with AMD and, currently, no sera from age sex matched controls are positive for anti-retinal antibodies. This is an important area of study that could lead rapidly to new therapies with existing drugs.</p>	

Programme 8

Ocular Repair and Regeneration Biology



Wound healing research within ORRB generated clinical trials in glaucoma, vitreoretinal surgery and paediatrics.

1) **Summary of programme area and objectives**

Until recently treatment for diseased tissues within the eye was dependent on their removal and/or bypass. With the advent of stem cell surgery, gene therapy targeted tissue modulators. Using this approach it is possible to develop new concepts of treatment, be it for diseases of the outer eye, the glaucomatous eye or the damaged retina. These approaches have been gathered together in the division of ocular repair and regeneration. The general principles involved mean that specific remedies may be applicable to different parts of the eye and offer the promise of spectacular healing as a result.

Priorities

General

- To further investigate the mechanisms and develop new treatments for repair and regenerative processes in the eye which play a part in either causing or the failure of treatment of every major blinding disease in the world today.
- To continue to work with a develop the translational research mechanisms to facilitate the development of new treatments both within and outside the group.
- To continue to develop research and treatments that benefit patients coming to the new ICEC and build on past successes.
- To establish Moorfields and the Institute as the worlds leading centre for research into and the development of new treatments to modulate repair and regeneration that leads to the prevention of blindness and restoration of vision of patients in the UK and around the world.

Specific

- To develop the MMPI patent to prevent scarring after glaucoma surgery, vitreoretinal surgery, retinopathy of prematurity and oculoplastic surgery.
- To develop anti-inflammatory dendrimers for use in ocular surgery and disease.
- To continue to refine existing antiscarring treatments for clinical use nationally and internationally.
- To establish corneal stem cell therapy.
- To improve methods of delivering corneal stem cell therapy.
- To develop Moorfields institute progenitor cells for human transplantation in conditions such as macular degeneration and glaucoma.
- To develop new anti-inflammatory and matrix modulating strategies to facilitate cell transplantation.
- To develop improved pharmaceutical techniques and methods for delivering these therapies.
- To develop further improved surgical techniques for use in conjunction with these new generation therapies.
- To continue collaborative clinical trials both in the UK and abroad to deliver these new treatments

All surveys show that the sense people fear losing the most is their vision. With the ageing population around the world the common causes of blindness continue to increase. The longer term strategy is to develop a translational bioincubator into disorders affecting vision, with the specific aim to develop more new innovative treatments to restore sight and prevent blindness within 5 - 10 years. The planned groups will have a strong track record in developing new treatments and have several new

innovative treatments in development for sight restoration in the short and long term. We will fill niches not currently filled by pharmaceutical companies to benefit people with sight loss.

(The Department of Health rated this programme in 2005 as **Strong**)

- 2) **Changes made in response to feedback from the Department of Health**

2B Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	5	5
4) Number of peer-reviewed publications (financial year 2005/06)	8	8
5) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	2	2

- 6) **Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating**

In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.

- 7) **Examples of impact on health services or policy**

Having established that progression of glaucoma can be arrested if wound healing is adequately controlled guidelines for glaucoma management have been developed in the UK and around the world. The focus since this finding has been on a continual improvement in anti-scarring regimens to update the guidelines.

We have developed the techniques and laboratory systems to deliver stem cells to the cornea and the retina for therapy in the NHS. This has had a major impact on the treatment options for corneal opacity from loss of the epithelial stem cells which is a major cause of chronic eye discomfort and sight loss. Many have been given a permanent cure.

Programme 9

Ocular Surface Disease



Ocular Surface Disease

1. Techniques for surface reconstruction: in vitro amplification of corneal epithelial stem cells has been established between the Institute of Ophthalmology and Moorfields and is the first lab in the UK to be accredited for ocular tissue engineering. This technique is critical to the development of ocular surface reconstruction techniques. It is subject to review by NICE and complementary to the use of hydrogel keratoprosthesis, now approved by NICE, and for which Moorfields is one of the few centres in the UK. (see Stem Cell programme)
2. Contact lenses are used by about 5 million Britons and are associated with a small risk of severe ocular infection. Epidemiological studies at Moorfields and the Institute were used in the 1990's to prove that extended wear soft contact lenses are a major risk factor for infectious keratitis, and that Acanthamoeba keratitis is a disease caused by avoidable high risk contact lens practice.
 - Both of these findings have been incorporated into the advice given to the public by contact lens practitioners.
 - A new, externally funded, 2 year study of the more recent lens wearing modalities has just been completed and can be expected to have the same impact. This is now being prepared for publication.
3. Study of susceptibility of microbial isolates from keratitis. This is a multicentre study co-ordinated by Mr Tuft with Birmingham, Manchester and Liverpool.
 - This study is essential for providing guidance on the choice of antimicrobial as antimicrobial resistance has been rapidly developing to the most widely used antibiotics for this condition in the USA and India for example.

1) **Summary of programme area and objectives**

Priorities in the national ophthalmology research plan are determined by gaps in the current knowledge base, including disease prevalence, the evidence base for clinical practice and feasibility in the light of scientific developments. Research on interventions needs to be directed at both the primary care level, in order to impact on the majority of patients with minor problems, and at the tertiary level to improve treatment strategies for those with blinding disease. The latter requires collaboration with a range of other disciplines to investigate pathogenesis and develop more effective treatments.

Priorities

Healthcare Delivery

- Piloting the integration of hospital based, and community optometry based, primary eye care for common surface diseases such as blepharitis and conjunctivitis together with the devolution, from the hospital to the community, of the long term follow up for more complex but stable disorders such as herpetic eye diseases and rosacea.

Epidemiology (risk factors, prevalence and surveillance of disease)

- National study of the prevalence and management of ocular mucous membrane pemphigoid.
- Identification of risk factors in contact lens related disease.
- Antibiotic resistance in keratitis and endophthalmitis

Pathogenesis, treatment & management strategies.

- Clinical trials on the management of ocular surface diseases and evaluation of new treatment strategies as they are introduced including in vitro amplification of corneal stem cells (see Stem Cell Programme) amniotic membrane and lamellar keratoplasty techniques, artificial corneas.
- Randomised controlled trial of anterior deep lamellar keratoplasty in keratoconus grant in application.
- Rapid diagnosis of ocular infections and antimicrobial resistance.
- Enhancing survival rates in corneal graft material using gene based techniques and bioengineering techniques.
- Molecular genetics of the stromal corneal dystrophies (monogenic) and keratoconus (polygenic).
- Gene-based therapy for aniridia (see Gene Therapy Programme)
- Microbiology initiatives dependent on expanded laboratory facilities.
- Studies in molecular diagnosis, descriptive epidemiology (resistance patterns and risk factors) and analytical epidemiology (risk factors, incidence and prevalence studies) are already ongoing and described above. A new laboratory staffed by a post doctoral researcher, microbiology technician and research student will be needed for:
- Enhanced development of new treatments including the evaluation of disinfectants, new antimicrobials and novel strategies such as the use for defensins.
- Ecological microbiology: Biofilm related infections: J Dart, PhD Student, collaborators in other institutions.
- The cell biology resources in the investigation of the control mechanisms of bacterial phenotype plasticity.
- Integration with wound healing research for the control of corneal ulceration in infection.
- Integration with Immunology for investigation of the host response in conditions as diverse as amoebic keratitis and endophthalmitis

2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
2) Number of projects ongoing on 31 March 2006	17	17
3) Number of peer-reviewed publications (financial year 2005/06)	11	11
4) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	1	1

(The Department of Health rated this programme in 2005 as **Strong**)

- 5) **Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating**
- In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.
- 6) **Examples of impact on health services or policy**
- The projects in this area have identified that the addition of oral ciprofloxacin had no significant effect on visual outcome in patients with bacterial endophthalmitis and that nearly one quarter of the isolates were resistant to it. All isolates were found to be sensitive to moxyfloxacin and it is known that this antibiotic achieves significant levels in the eye to kill the common bacteria involved. This has led to a change of practice in that the standard initial therapy now has swapped moxyfloxacin for ciprofloxacin and the initial patient outcomes are very encouraging.
- For rare but devastating causes of corneal infections the development of topical biguanides at Moorfields, and other modalities, for the treatment of Acanthamoeba keratitis has been taken up internationally. Our new studies have identified management strategies for the 5% of resistant cases. The UK outcomes for fungal keratitis have also recently been reviewed by a Moorfields study which is informing UK practice.
- Our large patient base and our close collaboration with the Institute of Ophthalmology have been used to study inflammatory eye diseases including mucous membrane pemphigoid (MMP) and chronic allergic eye disease. These have resulted in the introduction of new therapies such as sulphapyridine, and now mycophenolate, for MMP and topical ciclosporin for allergic eye disease. These practices have been disseminated into UK ophthalmology via our publications and effect of advice given to tertiary referral centres.
- In vitro amplification of corneal epithelial stem cells has been established at Moorfields and is the first lab in the UK to be accredited for ocular tissue engineering. Corneal stem cell

transplantation has been done for a year and is critical to the development of ocular surface reconstruction techniques. It is subject to review by NICE. The technique will facilitate the introduction of gene-based therapies for the treatment of corneal disease being developed here. It is complementary to the use of hydrogel keratoprosthesis, now approved by NICE, and MEH is one of the few centres in the UK.

Contact lenses are used by about 5 million Britons and are associated with a small risk of severe ocular infection. We demonstrated in the 1990's that extended wear soft contact lenses are a major risk factor for infectious keratitis, and that Acanthamoeba keratitis is a disease caused by avoidable high risk contact lens practice. Both of these findings have been incorporated into the advice given to the public by contact lens practitioners. A new 2 year study of the more recent lens wearing modalities has just been completed and can be expected to have the same impact.

In 2002, with City University and Camden and Islington, we piloted the integration of hospital based, and community optometry based, primary eye care for common surface diseases such as blepharitis and conjunctivitis. We intend to continue to pursue this to include the devolution, from the hospital to the community, of the long term follow up for more complex but stable disorders such as herpetic eye diseases and rosacea.

Programme 10

Paediatric Ophthalmology and Ocular Motility



Paediatric Ophthalmology and Ocular Motility

Clinical research in paediatric ophthalmology has been undertaken across a broad front within the service but the major research efforts are concentrated in three areas; inherited retinal disease, congenital abnormalities of the eye, assessment of visual function and amblyopia.

1. Inherited retinal disease.

Over the last two years we have recruited nearly 200 subjects into a study of Leber's amaurosis and early onset severe childhood retinal dystrophies. We have phenotyped all participants and undertaken molecular genetic studies to identify the underlying genetic mutations. The aim is to identify patients that have sufficient residual visual function to benefit from novel therapies such as gene therapy (currently there are no effective therapies for this group of disorders). Specifically we have identified 21 subjects with mutations in the gene RPE65; we hope that the gene therapy trial (funded by the Department of Health) for subjects with retinal disease due to mutations in RPE65 will start within the next 6 months. If successful this will completely transform the management of children with retinal dystrophies.

2. Congenital abnormalities of the eye

Over the last 20-25 years Richard Collin has built up a large cohort of anophthalmia patients the study of which has led to advances in our understanding the epidemiology of anophthalmia and microphthalmia. This has led to improvements in knowledge of prevalence and risk factors that we can pass on to our patients. Before the identification of any genes for anophthalmia or microphthalmia was made we gave an empiric recurrence risk to parents of single cases of anophthalmia-microphthalmia of around 5-10% if there were no other factors to be taken into account (e.g. consanguinity). Dr Ragge and her team have been at the forefront of an international collaboration to identify the genes causing microphthalmos and anophthalmia and have identified two genes SOX2 and OTX2 as major causes of these severe eye malformations. This has greatly improved the accuracy of genetic counselling for families with affected children and has allowed prenatal diagnosis to be considered for the first time.

Professor Khaw and his colleagues have continued their groundbreaking research on modulating the scarring response after surgery for congenital glaucoma using anti-scarring agents. This has had a major impact on the success rates of surgery and the long term prognosis of children with congenital glaucoma. In this field, new PITX2 mutation identified in Axenfeld Rieger syndrome in Moorfields congenital glaucoma patients and new classification system for anterior segment dysgeneses with ICH and Newcastle

3. Investigation of visual function in children

Many of the visual acuity tests we use in young children are not as robust as those used in adults and have not been validated across a wide range of age groups. Dr Salt and her colleagues have developed a new LogMar test for children and have established age norms across a wide range of age groups. This clinical research will feed immediately into the clinic with more reliable testing of visual acuity in both the clinical and research setting.

John Sloper and his colleagues have been investigating the functional deficit in the visual system in amblyopia, using detailed electrophysiological and psychophysical testing. There are differences in patients with early and late onset strabismic amblyopia which may help explain why some patients respond poorly to occlusion. This research will ultimately help improve treatment protocols for amblyopia.

National Survey of childhood Glaucoma completed. This has provided evidence of prevalence and causation allowing better targeted therapeutic approaches.

1) Summary of programme area and objectives

The reorganisation of ophthalmology services for children at Moorfields Eye Hospital (MEH) and the building of the International Children's Eye Centre (ICEC) will increase the profile of MEH and the Institute of Ophthalmology (IO) as a centre for research in, and treatment of, paediatric eye disorders. Our research priorities are based on those diseases which cause childhood blindness, such as genetic retinal dystrophies and childhood glaucoma and those conditions such as squint and amblyopia which are common, cause substantial visual disability and which consume extensive NHS resources. The ultimate aim of these research programmes is to improve the care and visual outcomes of children with eye disorders. Such improvements are of lifelong benefit to the children.

The main aims over the next 5 years are:

- To identify the genetic mutations causing disease in a large cohort of children with early onset retinal dystrophies. This will involve identifying mutations in known genes and the identification of novel genes. To carry out careful genotype phenotype correlations in order to identify those genetic disorders that may benefit from gene therapy.
- To develop methods of phenotyping which are appropriate to infants and young children (see also amblyopia section below).
- To identify children with RPE65 mutations who will be suitable for the gene therapy trial and to carefully document retinal structure and function and natural history of disease.
- To have started the gene therapy trial in 6 children with mutations in RPE65.
- To have completed a national survey of childhood retinal dystrophies.
- To plan the next gene therapy trial.
- To identify the remaining genes causing childhood cataract and to improve understanding of the mechanism of cataract formation.
- To have identified the first genetic variation to predispose to childhood myopia.

In ocular motility the focus is to understand why binocular function breaks down in some children and what changes occur in the brain in different types of amblyopia and at different ages of onset. Our main aims are:

- Completion of studies of binocular function in different types of intermittent squint.
- Development of electrophysiological methods for evaluating binocular function.
- Completion of multi-centre study of the natural history of intermittent exotropia in children.
- Multicentre randomised controlled trial of squint surgery to identify predictive factors for children who will benefit from surgery.
- Development and evaluation of colour and motion VEPs in children.
- Studies of magnocellular (motion) and parvocellular (colour) function in amblyopic children using electrophysiology and psychophysics.
- Evaluation of outcomes following surgery for congenital cataract. The aim is to improve visual outcomes particularly in children with cataracts in both eyes who often have poor vision for life.

- Recruitment of cohort of children with squint and high refractive errors for gene mapping.
- Evaluation of the part played by amblyopia in congenital glaucoma and genetic retinal dystrophies.

(The Department of Health rated this programme in 2005 as *Strong*)

2) Changes made in response to feedback from the Department of Health

The feedback from the Department of Health last year was that the "programme 'Electrophysiology' was small in scale and the rationale for creating a stand-alone programme was not entirely convincing and it is not clear whether the programme comprised a coherent body of work". Since the majority of the programme related to ocular motility we have merged this small programme into the Paediatric Ophthalmology and Ocular Motility programme.

2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	15	15
4) Number of peer-reviewed publications (financial year 2005/06)	20	20
5) Number of higher degrees directly funded by NHS R&D Support Funding (unspecified year type)	0	0
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	<p>In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.</p>	
7) Examples of impact on health services or policy	<p>A study focusing on the different screening methods in use for diagnosing retinopathy of prematurity identified the best method in terms of minimising stress to tiny babies.</p> <p>A large programme of work in genetic analysis looking for mutations that cause severe ocular malformations or visual impairment has provided a greater understanding of the genetic conditions and enabled a high quality family counselling service to be developed.</p> <p>The study of blepharoconjunctivitis in children has enabled the documentation of this condition for the first time and leading to the development of guidelines for improved diagnosis and treatment of this condition.</p>	

Programme 11

Stem Cell Research



Stem Cells

In ophthalmology stem cells have the potential to treat a number of chronic ocular surface diseases and retinal degenerations, for which there is at present no effective therapy. The aim of the Cells for Sight Transplantation and Research Programme, led by Dr Julie Daniels, is to understand the biology and therapeutic potential of stem cells.

1. Production of stem cell therapy is tightly regulated. In 2005 the Cells for Sight Tissue Bank attained accreditation with the MHRA and this year has been granted a full licence with the new Human Tissue Authority. These measures are in place to ensure patient safety and quality of treatment.

This year we have achieved the commencement of treatment of Moorfields' patients with stem cell therapy. To date 9 patients suffering from difficult to manage ocular surface diseases involving the loss of corneal stem cells have been treated. Of these 9 patients, 5 have experienced good clinical progress including improved vision and comfort. Our longest and continuing successful follow-up time is 8 months.

Research is going on into optimising techniques and preparing other epithelial tissues as alternatives to corneal tissue (in donors who have lost both corneas) such as buccal mucosa.

The completion of an additional state-of-the-art tissue culture cleanroom within the new Moorfields Eye Hospital Eye Bank later this year will facilitate the expansion of the Cells for Sight Programme, allowing patients outside of Moorfields to also benefit from this new treatment.

2. Collaboration with Prof Robin Ali on work to establish the development of stem cell gene therapy for children suffering from aniridia.
3. Work has been undertaken to understand how the niche environment supports and regulates limbal epithelial stem cells. The clinical aspect of this work involves assimilating clinical data before and after patients have received cultured limbal epithelial stem cell therapy. These investigations utilised state-of-the-art corneal imaging techniques at Moorfields.

1) Summary of programme area and objectives

Priorities

- To deliver stem cell-based therapies for the treatment of debilitating and blinding eye conditions.
- To target key areas of research including, developmental biology, cell biology, immunology, molecular genetics, gene therapy and transplantation that will underpin the future translation and delivery of novel stem cell therapies.
- To maintain the initiative we have achieved by obtaining accreditation for the first clinical stem cell transplantation program in the UK.
- To maximise the clinical potential of the International Children's Eye Centre. A proportion of the potentially treatable patients with ocular surface failure will be children.

Accreditation for the 'Cells for Sight Transplantation Programme' is approaching completion. This will provide the mandatory facilities and quality system (operating good manufacturing practice) required to deliver cell-based therapies to patients.

The research programme involves understanding the basic biology and further therapeutic potential of limbal epithelial stem cells in order to provide effective stem cell therapy for greater numbers of patients suffering from blinding ocular surface conditions.

By combining our limbal stem cell research effort with that of gene therapy, we are working together to try to correct the genetic defect associated with aniridia, which at present can only be treated conservatively. Many more patients suffering from retinal degenerations could in the future benefit from stem cell therapy.

Another avenue of investigation is the Muller stem cell research programme. Early work has shown promising data for restoration of visual function in an animal model. In addition we are also exploring the potential of Muller stem cells to restore neural function in patients suffering from glaucoma.

The programme also focuses on the potential of limbal epithelial stem cells to 'transdifferentiate' into cells of the retina. Limbal epithelial stem cells are derived from the neural ectoderm, which also gives rise to the retina during development. It may be possible in the future to manipulate this very accessible source of stem cells from the limbus for the autologous treatment of retinal degenerations.

New research using embryonic and retinal stem cells should also increase our understanding of the mechanisms controlling stem cell and progenitor regulation and differentiation. In the longer term these findings may allow us to manipulate embryonic and / or retinal stem cells in vitro and in vivo for the development of new therapies to treat blinding eye disease.

Using just a few examples of our stem cell research activities above, it is clear that the IOO/MEH site can deliver stem cell-based therapies now and has the potential to deliver more in the future. Our research and development programme is tackling problems from the front to the back of the eye, providing hope for patients with currently untreatable blindness.

(The Department of Health rated this programme in 2005 as *Moderate*)

2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
2) Number of projects ongoing on 31 March 2006	14	14
3) Number of peer-reviewed publications (financial year 2005/06)	3	3
4) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	1	1
5) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	<p>In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.</p> <p>The Cells for Sight state-of-the-art class 100 clean room facility was accredited in accordance with pharmaceutical standard GMP last year. This process was labour and time intensive and so the publication rate decreased temporarily.</p>	
6) Examples of impact on health services or policy	<p>Corneal opacity from loss of the epithelial stem cells is a major cause of chronic eye discomfort and sight loss. Transplantation of new epithelial stem cells is the definitive treatment. The 'Cells for Sight' class 100 laboratory has now been accredited. We can provide cultured epithelial stem cells derived from either the unaffected contra-lateral eye of the patient or from donor tissue. This has opened a new treatment option for these patients and initial results suggest a permanent cure in some eyes. To date this treatment has been provided for 10 patients and a further 17 are waiting.</p>	

Programme 12

Vision Impairment and Rehabilitation



Visual Impairment and Rehabilitation

1. In a study funded by North Central London Research Consortium, Dr. Crossland has evaluated the expectations of low vision patients with AMD before and after their low vision evaluation. One particularly interesting finding from the study is that more than 1/3 of patients have misconceptions about the causes of AMD, attributing it to prior medical treatment, trauma, or overuse of the eyes earlier in life.
2. We have reported results from a comprehensive epidemiological study supported by the National Institutes of Health in the USA on the role of vision in motor vehicles accidents among the elderly. This study of 1800 drivers over the age of 65 reveals that glare sensitivity, visual field defects, and impaired visual attention are significant risk factors, but that most older drivers modify their driving behaviour to maintain their crash risk at a level that is comparable to those without any visual impairment.
3. Dr Bex has developed new screening techniques for the early detection of visual field defects in glaucoma and diabetic retinopathy. One technique identifies irregularities in the afterimage of a campimetry-type stimulus. A different screening technique targets glaucoma and exploits the contribution of newly-identified melanopsin-expressing retinal ganglion cells to the pupil response to light.
4. Visual acuity is the most widely used measures of visual function and the primary outcome for most clinical trials in ophthalmology. For decades, visual acuity has been measured with poorly standardized and inaccurate visual acuity charts. Research has demonstrated that visual acuity can be more accurately measured with the new style of logMAR chart first introduced in the 1980's but still not widely used in the UK. We have recently shown that logMAR charts can be successfully integrated into a busy clinic and we are now using logMAR charts for all optometry and low vision examinations at the Trust. This will ensure that accurate, standardized data are recorded for all patients and will improve our ability to detect changes in visual function during treatment and rehabilitation.

1) Summary of programme area and objectives

Priorities

- To quantify ocular, cortical and behavioural effects of visual impairment using contemporary research methods.
- To develop a solid evidence base for low vision rehabilitation programs, by applying rigorous scientific methods, including randomised controlled trials, to the evaluation of low vision intervention.
- To maximise the research potential of the ICEC and to develop paediatric low vision research projects.
- To maintain the Department's reputation as a world-leading centre for clinical low vision rehabilitation research, building on the Hospital's global reputation and the Institute of Ophthalmology's double 5*A RAE rating.

Progress towards knowledge of cortical adaptations in visual impairment;

with particular reference to reorganisation of the central nervous system after visual processing is disrupted or drastically impaired, and how this plasticity could be exploited to enhance the use of residual vision or other sensory/cognitive systems in the visually impaired.

A strategy to identify optimal models for low vision care.

At present, considerable variation exists in the provision of low vision care in terms of location (community, hospital, resource centre), staff (optometrists, multidisciplinary teams, rehabilitation workers) and approach (optical aids, rehabilitative training etc). No clear evidence points to a particular model as being "optimal." Rigorous outcome measures are required to quantify the relative merits of these approaches. The first stage in identifying the optimal model for low vision care is to quantify what patients expect to gain from low vision assessment; a project is in progress which uses qualitative research methods to determine patient expectations in the low vision clinic.

An improved understanding of the efficacy of low vision rehabilitation;

with emphasis on the quantifiable benefits of low vision rehabilitation (for example reading speed improvement, quality of life improvement or ability to maintain independence). Other considerations will be the efficacy of programs developed to train the use of eccentric viewing in patients with central field loss, such as those used in Scandinavia and by the Visibility charity in Glasgow.

Validation of the utility of electronic test charts.

Current opinion is that the Trust will move from Snellen charts to electronic test charts for visual assessment in the future. Prior to the Trust implementing electronic test charts in all clinical areas, validation of these charts (in terms of test-retest variability and comparison to established gold standards) is required. The optometry department will perform detailed analyses of these charts' applicability and utility.

Development of a paediatric low vision research strategy

A research lead in paediatric low vision will maximise the visual rehabilitation research potential of the International Childrens Eye Centre.

In conjunction with the MEH paediatric strategy group under Prof Tony Moore, a strategy for research into visual impairment in

children will be developed.

(The Department of Health rated this programme in 2005 as *Strong*)

2) Changes made in response to feedback from the Department of Health

2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	12	12
4) Number of peer-reviewed publications (financial year 2005/06)	7	7
5) Number of higher degrees directly funded by NHS R&D Support Funding (financial year 2005/06)	1	1

6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating

In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.

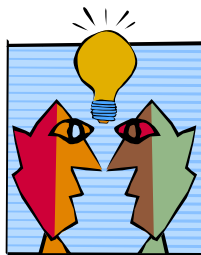
7) Examples of impact on health services or policy

High tech low vision devices and extensive training in reading rehabilitation appears to have little benefit over conventional low vision rehabilitation. This has a significant cost implication since extended training is labour intensive and costly. The high tech devices are of benefit only in very special circumstances. This also has cost implications as patients can be targeted according to potential benefit.

Visual acuity is the most widely used measure of visual function and the primary outcome for most clinical trials in ophthalmology but is often measured with poorly standardized and inaccurate charts. We have demonstrated that visual acuity is more accurately measured with the logMAR chart first introduced in the 1980's but still not widely used in the UK. LogMAR charts can be successfully integrated into a busy clinic and ensures accurate, standardized data is recorded for all patients. This improves our ability to detect changes in visual function during treatment and rehabilitation.

Programme 13

Vitreoretinal Surgery



Vitreoretinal Surgery

1. Proliferative vitreoretinopathy

Completion of the third in a series of clinical trials to investigate the effect of the adjunctive medications 5 fluorouracil and low molecular weight heparin to prevent PVR. The most recent study is one of the largest randomised controlled trials ever completed in vitreoretinal surgery and in addition helps define the role of vitrectomy in the primary management of retinal detachment.

The use of adjunctive combination drugs including 5 fluorouracil to prevent PVR in high risk cases has now been adopted by vitreoretinal surgeons worldwide. The safety of such an approach was borne out by experimental study demonstrating the process of cellular and subcellular pathology in human PVR and in experimental models.

2. Quality of life after vitreoretinal surgery

Analysis of the outcome and patient satisfaction following vitreoretinal surgery has been carried out. No difference was found in the functional outcome between retinectomy and encirclement allowing either to be used in clinical practice.

The visual function and subjective perception of visual ability following macular hole surgery was considered to be improved by the patient.

3. The demonstration of early adverse responses to intravitreal silicone oil will alert clinicians to these consequences and should alter clinical practice.

1) Summary of programme area and objectives

Vitreoretinal disease remains a major cause of visual impairment and blindness worldwide. Complex and often multiple vitreoretinal interventions are commonly required for complicated retinal detachment and penetrating ocular trauma which frequently result in a process of intraocular fibrocellular scarring termed proliferative vitreoretinopathy (PVR). PVR is the most common cause of blindness following severe ocular trauma - globally it has been estimated that 1.6 million people are blind as a result of ocular trauma with 2.3 million suffering bilateral low vision and up to 19 million with unilateral blindness or low vision. Currently it is estimated that almost one million people in the United States live with trauma-related visual impairment, and 40,000 to 60,000 individuals are diagnosed as new cases of trauma-related blindness each year. Vitreoretinal disease also has a significant economic impact. For example Prevent Blindness America estimated that in 1988 approximately 90,000 disabling eye injuries occurred at the workplace, resulting in a total direct cost of \$354,870,000; with indirect cost (lost wages, medical expenses, and insurance administration cost), the sum reached \$709,740,000. When the cost of all non-disabling eye injuries is included, the total easily exceeds \$1 billion.

Priorities

- To investigate clinical applications of adjunctive medications to prevent proliferative vitreoretinopathy (PVR) and to improve outcomes in established disease.
- To further analyse the cellular and molecular processes which result in PVR and the relationship of these changes to visual outcome.
- To investigate surgical treatments for retinal vascular occlusion.
- To undertake a national retinal detachment epidemiological study in Scotland and through this collaboration to establish a group of vitreoretinal surgeons able to undertake prospective clinical studies of retinal detachment prevention and outcome.
- To extend current studies of the assessment of quality of life outcomes following retinal surgery

Vitreoretinal surgery deals with complex and blinding ophthalmic disease. The role of vitreoretinal intervention has increased in the management of many retinal diseases in recent years. Significant challenges, however, remain in particular the control of intraocular proliferation and the refinement of techniques to deal with retinal vascular disease.

(The Department of Health rated this programme in 2005 as *Strong*)

2) Changes made in response to feedback from the Department of Health

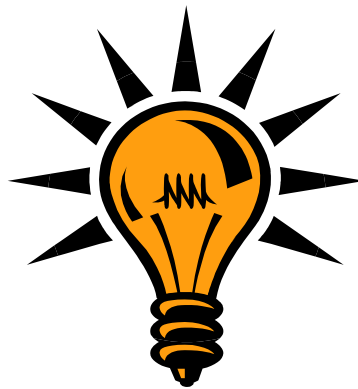
2B

Research deliverables

	Total for reporting organisation	Total for programme across all organisations
3) Number of projects ongoing on 31 March 2006	8	8
4) Number of peer-reviewed publications (financial year 2005/06)	20	20
5) Number of higher degrees directly funded by NHS R&D Support Funding (unspecified year type)	0	0
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	<p>In previous years the number of projects given throughout the form related to all those that had been live at any time during the financial year. These figures therefore related directly to the external grant income and the budget/spend for support funding. On more careful reading of the guidance we realise that the project number should have been a snapshot figure of projects ongoing on 31st March 2006. Apologies for the misinterpretation in previous reports.</p>	
7) Examples of impact on health services or policy	<p>In response to the recent promotion of day-case surgery at Moorfields, research studies are ongoing to identify those patients having vitreoretinal surgery who are likely to benefit from routine review on the first postoperative day. By identifying those patients for whom first day postoperative review is not indicated, the patients will be able to avoid an unnecessary journey back to hospital after discharge, and available hospital resources can be directed to the management of patients who are likely to benefit.</p> <p>Pilot prospective randomised controlled trials are ongoing to investigate the importance of prolonged postoperative posturing following vitrectomy and gas for both retinal detachment and macular hole. Prolonged posturing, advocated largely on historical grounds, presents a formidable challenge to many patients and its effect on</p> <p>surgical outcome is unproven. The results of the ongoing studies will help form an evidence-base with which patients can be informed of the likely value of posturing.</p>	

Programme 14

Predictive Oncology:
Individualising Cancer Therapy
through a Programme of
Translational Oncology Research



2A

Aims and objectives

1) Contribution of organisation to the programme

Oncology is currently an empirical discipline in which all patients with a particular type of cancer are treated as though they were the same. The weight of evidence (and paper) suggests that this is incorrect: patients' tumours differ from each other as much as they do - perhaps more so. Patients with the same form of cancer often show variable responses to treatment. This variation is the result of the complex biology of cancer cells, understanding of which will lead to increasingly individualised therapy for patients. As new drugs come onto the market, so oncologists and patients are faced with a bewildering array of choices. Which patients need treatment? How long do they need it for, and at what dose?

Predictive testing has much to offer: advances in the molecular understanding of cancer allow the design of specific tests for some drugs (e.g. ER, HER2, EGFR), while for cytotoxic drugs, cellular assays or DNA arrays assays may be useful. Improved and earlier assessments of patient response are also critical. The next 10 years are set to be an exciting time in oncology, but as drugs improve, tests must improve too. This programme focuses on the development and practical application of predictive methods to patient care. It aims to bridge the gap between basic cancer research and clinical practice to improve the prevention, diagnosis and treatment of cancer.

Aims of The Programme

The primary objectives of the programme are to conduct multidisciplinary, multiprofessional translational research, which investigates:

- The relationship between individualised cancer treatment and survival gains for patients.
- The development of predictive methods to guide cancer treatment.
- The use of predictive methods for the development of new cancer regimens and the evaluation of new drugs during their development.
- Investigation of the molecular mechanisms involved in sensitivity and resistance to anti-cancer drugs.
- The development of a national cancer tissue bank suitable for use by programme members

The contribution Moorfields makes to this programme relates to all the projects focusing on uveal melanoma.

2) Changes made in response to feedback from the Department of Health

Changed the title in line with the Portsmouth Consortium

2B

Research deliverables

Total for reporting organisation

3) Number of projects ongoing on 31 March 2006	1
4) Number of peer-reviewed publications (financial year 2005/06)	11
5) Number of higher degrees directly funded by NHS R&D Support Funding (unspecified year type)	0
6) Explanation by administrative organisation for any significant fall in deliverables since 2005 that may adversely affect the programme's rating	<i>Not applicable</i>
7) Examples of impact on health services or policy	The use of human tissue for scientific research is a highly sensitive issue. A lack of confidence in patient recruitment is an important issue so recruitment procedures need to be as effective and sympathetic as possible. The authors recruited patients with uveal melanoma into a postmortem study investigating tumour latency in this cancer. The researchers more than doubled (88.5%) the average rate of 40% quoted by the National Institute for Clinical Excellence (NICE). Key features are a sympathetic personal approach by experienced oncology nurses, the provision of clear information, and the in

Section 2F: Research activity that does not form part of programmes

Projects ending after 31st March 2005 ordered by title:

1) Project title	2) Externally funded?	3) Primary external funder	4) Ongoing in 2006/07?	5) Main base?
A serial study using non-invasive imaging markers of axonal loss and remyelination following acute optic neuritis	No		Yes	No
A study of mechanisms of recovery and persistent disability following optic neuritis	No		Yes	Yes
CIRTED Trial: Radiotherapy for thyroid eye disease	Yes	Special Trustees	Yes	No
Diagnosis and outcomes of patients presenting with diplopia to Moorfields Casualty Department	No		Yes	Yes
Does OCT appearance predict the response to treatment for cystoid macular oedema in uveitis?	No		Yes	Yes
The contribution of brain reorganisation to recovery in patients with optic neuritis	No		Yes	Yes

Summary

This is calculated automatically from the records shown above. It should match the numbers in the first row of Table 2 columns I and J

Ongoing externally funded projects 1
Ongoing projects without external funding 5

Section 3: Financial information and tables

Table 1: R&D support funding resources and associated spend in 2005/06

1A: Resources

	Amount (£)
a) Balance brought forward from 2004/05 (overspend is negative; underspend is positive)	0
b) Allocation in 2005/06 (including RM&G and EU Directive funding)	5,164,812
c) Ad hoc funding in 2005/06 (ie invoiced and received in year, <u>not</u> total approved)	0
d) RM&G funding in 2005/06 (accounted for in Section 4 if applicable)	0
e) Total NHS R&D support funding available in 2005/06	5,164,812

1B: Expenditure

	A. Total Spend (£)	B. Percentage of 1.k	C. Total number of ongoing projects
1.a) Research Council Work	692,756	13 %	14
1.b) University Work	197,727	4 %	5
1.c) Charity Work	1,660,392	32 %	38
1.d) DH/NHS R&D Programme work	269,272	5 %	4
1.e) Other work	328,437	6 %	3
1.f) (Sum 1a - 1e)	3,148,584	61 %	64
1.g i) R&D outside of HSG (97) 32-commercial partner	251,324	5 %	5
1.g ii) R&D outside of HSG (97) 32-other	695,612	13 %	24
1.h) R&D that has no external funder	660,467	13 %	71

1.i) Training	245,663	5 %	
1.j) Management costs	163,162	3 %	
1.k) Total spend using NHS R&D support funding (Sum 1f - 1j)	5,164,812	100 %	164

1C: Balance

	Amount (£)	Percentage of 2005/06 resources (1A row e)
Balance carried forward to 2006/07 <i>(overspend is negative; underspend is positive)</i>	0	0 %

1D: External funding

	Amount (£)
2) External funding for spend shown in 1a - 1h above	6,035,303
3) External income to organisation from externally funded R&D	2,412,522

Table 2: Spend on programmes and by national priority

Columns A-G

A) Programme identifier	B) SFS Funding allocated 2005/06 (£)	C) PNF Funding allocated 2005/06 (£)	D) Actual SFS spend (£)	E) Actual PNF spend (£)	F) Variance	G) Explanation of variance
Non-programme activity:						
	32,827	50,111	35,240	51,188	SFS: £2,413 (7%) PNF: £1,077 (2%) Total: £3,490 (4%)	
Programmes declared in Section 2A-2E:						
RHU Predictive Oncology: Individualising Cancer Therapy through a Programme of Translational Oncology Research	37,604	9,475	32,465	18,562	SFS: £-5,139 (-14%) PNF: £9,087 (96%) Total: £3,948 (8%)	Increased costs of genetic nurse counsellors over and above anticipated costs.
RP6 Age-Related Macular Degeneration	646,310	361,073	486,931	442,199	SFS: £-159,379 (-25%) PNF: £81,126 (22%) Total: £-78,253 (-8%)	The transfer between SfS and P&N funding is due to the re-incorporation of the Retinal Degeneration - Surgical Strategies programme which did not attract so much SfS funding and the severe competition for prestigious external charitable funding.
RP6 Cataract and Refractive Surgery	87,222	58,481	72,440	66,287	SFS: £-14,782 (-17%) PNF: £7,806 (13%) Total: £-6,976 (-5%)	Decrease in research activity in the clinical areas and an increase in translational research which consumes less R&D Support Funding.
RP6 Community Eye Health	156,554	69,932	205,637	95,220	SFS: £49,083 (31%) PNF: £25,288 (36%) Total: £74,371 (33%)	Response to an increased emphasis on delivery of eye services in the community and the focus on optometrists in the National Eye Care Plan. (Optometrists are our primary care focus before GPs)
RP6 Diabetic Retinopathy and Retinal Angiogenesis	201,832	123,106	195,862	130,430	SFS: £-5,970 (-3%) PNF: £7,324 (6%) Total: £1,354 (0%)	
RP6 Electrophysiology	0	0	0	0	SFS: £0 (0%) PNF: £0 (0%) Total: £0 (0%)	

RP6 Gene Therapy	225,646	97,351	232,010	70,355	SFS: £6,364 (3%) PNF: £-26,996 (-28%) Total: £-20,632 (-6%)	Clinical trial of gene therapy slightly delayed and will fall in this current year.
RP6 Glaucoma	446,150	302,010	412,605	310,840	SFS: £-33,545 (-8%) PNF: £8,830 (3%) Total: £-24,715 (-3%)	
RP6 Ocular Immunology	219,802	128,769	202,635	135,840	SFS: £-17,167 (-8%) PNF: £7,071 (5%) Total: £-10,096 (-3%)	
RP6 Ocular Repair and Regeneration Biology	319,222	103,987	310,110	105,460	SFS: £-9,112 (-3%) PNF: £1,473 (1%) Total: £-7,639 (-2%)	
RP6 Ocular Surface Disease	300,737	191,137	290,245	192,483	SFS: £-10,492 (-3%) PNF: £1,346 (1%) Total: £-9,146 (-2%)	
RP6 Paediatric Ophthalmology and Ocular Motility	183,369	122,227	204,620	128,555	SFS: £21,251 (12%) PNF: £6,328 (5%) Total: £27,579 (9%)	
RP6 Retinal Degeneration - Surgical Strategies	0	0	0	0	SFS: £0 (0%) PNF: £0 (0%) Total: £0 (0%)	
RP6 Stem Cell Research	137,738	73,200	185,220	74,225	SFS: £47,482 (34%) PNF: £1,025 (1%) Total: £48,507 (23%)	Significant increase in research activity following formal accreditation of the 'Cells for Sight' laboratory. The accreditation process took up a great deal of time and effort last year.
RP6 Vision Impairment and Rehabilitation	232,699	119,945	225,900	129,460	SFS: £-6,799 (-3%) PNF: £9,515 (8%) Total: £2,716 (1%)	
RP6 Vitreoretinal Surgery	77,331	48,965	80,508	41,280	SFS: £3,177 (4%) PNF: £-7,685 (-16%) Total: £-4,508 (-4%)	Successful application for Sfs funding in year.
Table 2 Total	3,305,043	1,859,769	3,172,428	1,992,384	SFS: £-132,615 (-4%) PNF: £132,615 (7%) Total: £0 (0%)	

Table 2: Spend on programmes and by national priority

Columns H-J

	A) Programme identifier	H) Total external funding 2005/06 (£)	I) Ongoing externally funded projects	J) Ongoing projects without external funding
Non-programme activity:				
		13,735	1	5
Programmes declared in Section 2A-2E:				
RHU Predictive Oncology: Individualising Cancer Therapy through a Programme of Translational Oncology Research		42,306	1	0
RP6 Age-Related Macular Degeneration		553,862	7	5
RP6 Cataract and Refractive Surgery		161,231	2	6
RP6 Community Eye Health		483,102	3	4
RP6 Diabetic Retinopathy and Retinal Angiogenesis		557,681	5	5
RP6 Electrophysiology		0	0	0
RP6 Gene Therapy		1,005,022	10	1
RP6 Glaucoma		544,722	12	15
RP6 Ocular Immunology		292,424	5	6
RP6 Ocular Repair and Regeneration Biology		412,620	4	1
RP6 Ocular Surface Disease		280,318	10	7
RP6 Paediatric Ophthalmology and Ocular Motility		486,284	11	4
RP6 Retinal Degeneration - Surgical Strategies		0	0	0
RP6 Stem Cell Research		686,742	12	2
RP6 Vision Impairment and Rehabilitation		420,074	6	6
RP6 Vitreoretinal Surgery		95,180	4	4
Table 2 Total		6,035,303	93	71

FORWARD LOOK: The National Institute of Health Research (NIHR)

In 2006 the Department of Health announced its proposals for a radical reshaping of R&D funding for the NHS. It created a virtual institute for health research (NIHR) and restructured the way R&D funding was allocated in the NHS.

Currently R&D funding has been allocated as a core (support) grant based on the old Culyer allocation which in turn was based on an assessment of the resources required to fund the infrastructure that supported research programmes. We are presently in a transition phase which will involve a rapid reduction in the R&D core funding received by the Trust and its replacement by competitively acquired funding for research. The routes by which we can obtain funding in the future will be partly by achieving status as a Biomedical Research Centre (and we are currently shortlisted with an application for this to be completed in the autumn), by acquiring funds for programmes of applied research (the initial call for proposals was for five targeted areas, none of which were ideal for ophthalmology. The next call for programme grant applications will be announced in April 2007), and for lesser amounts of funds for academic salaries, health technology, patient support etc.

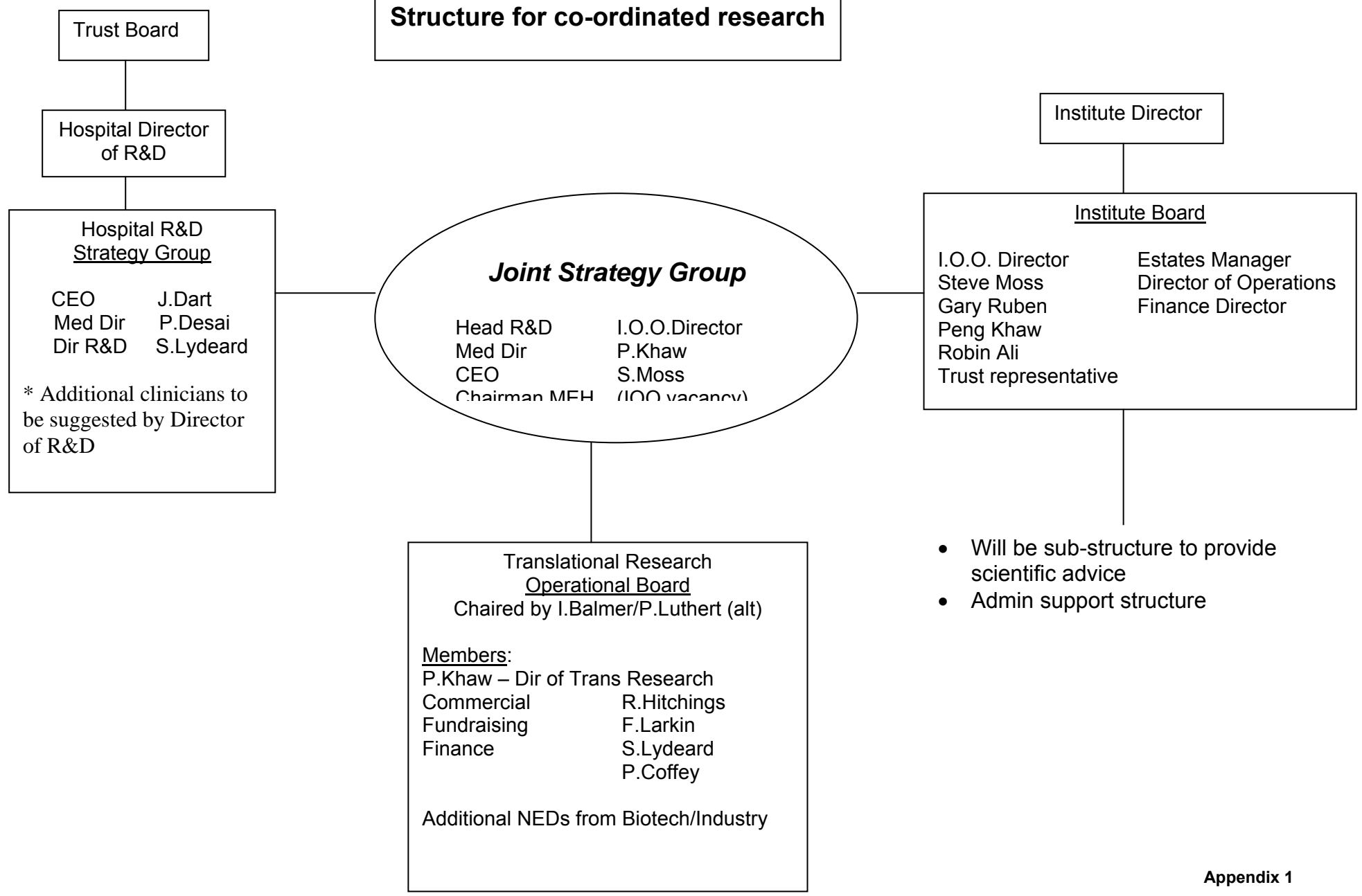
The government has announced the availability of £1 billion in R&D funds annually. It would appear that one third of this will come from the Medical Research Council and the other two thirds from funds directly available from the NHS. Of this £1 billion approximately £250 million has been accounted for. Of the remaining £750 million approximately £400 million will be allocated through comprehensive research networks (CRN's), run through strategic health authorities and allocated on a per capita basis. At the time of writing details of the process by which this will be undertaken remain sketchy, the remainder will probably be allocated by the MRC.

There are some grounds for optimism as well as grounds for uncertainty in this new system of R&D funding. The optimism stems from the fact that money for the Biomedical Research Centre (BRC) will be allocated for research that can be shown to have a clearly defined clinical end point and be translational in nature. Secondly (as has been shown in Appendix 3) although ophthalmology accounts for 8% of NHS expenditure a recent analysis shows that it only receives 4% of the research funding from the major charities and only approximately 2% from the NHS R&D Support budget so that we can make a strong case for an overall increase in R&D funds. Thirdly, as has been detailed earlier in this report, the Ophthalmic Research Network should allow Moorfields to act as a co-ordinating centre for NHS R&D in ophthalmology.

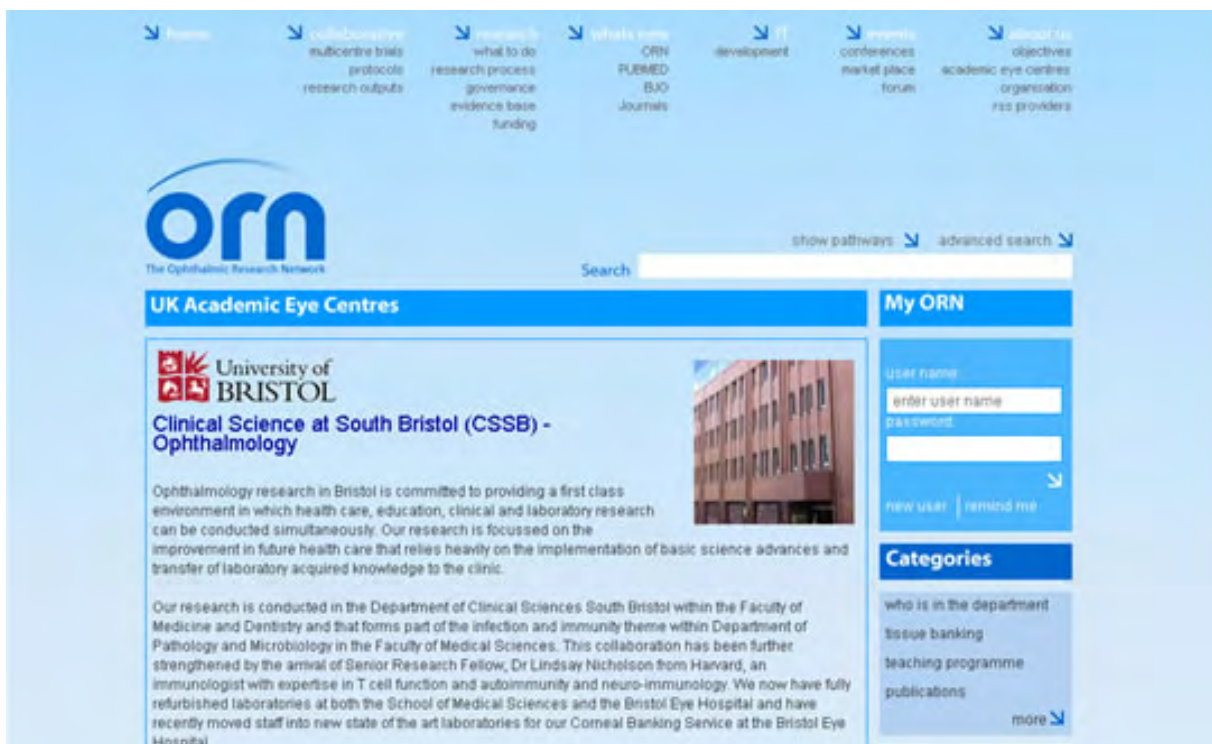
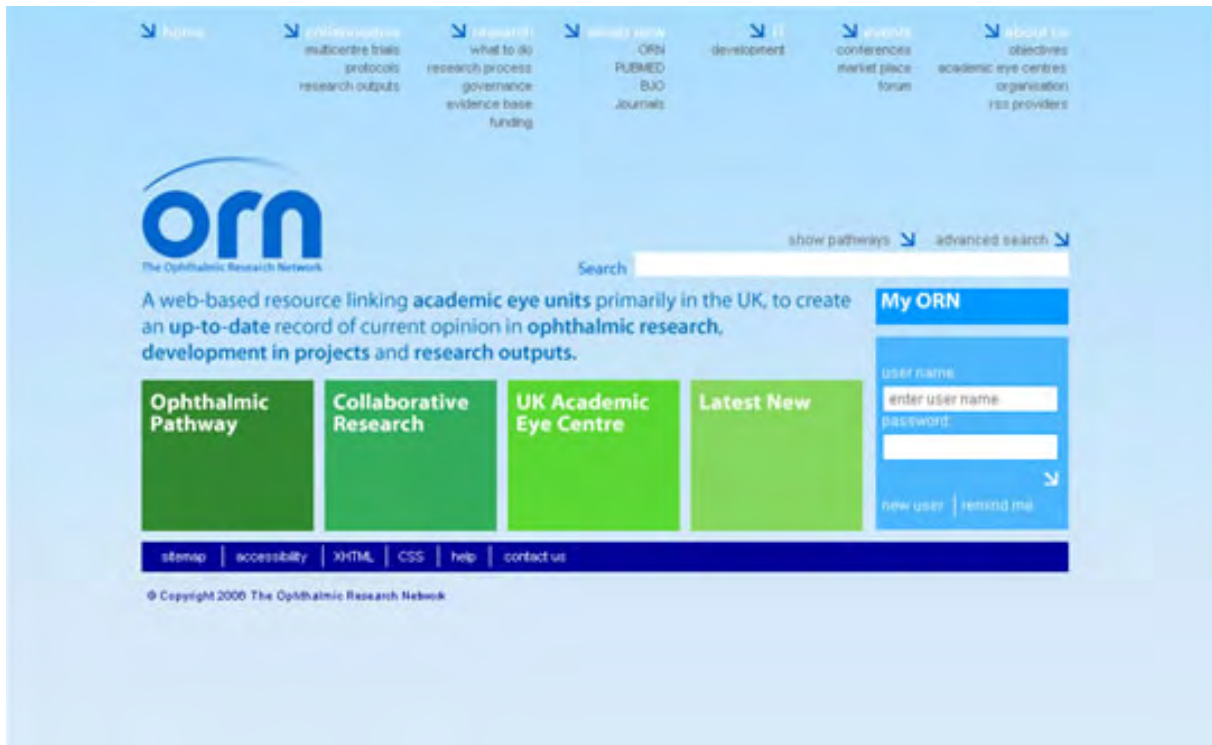
The grounds for concern arise principally from the uncertainty of the routes and mechanisms by which R&D funds will be apportioned. Secondly, even if we are successful and achieve BRC status this year we will still suffer from a considerable financial shortfall with a 50% drop in core R&D funding in April 2007 and a further reduction cumulating to a 90% drop from the current levels by April 2008. Although some of this shortfall may be compensated for by successful bidding for programmes, as the next round is only going to be announced in April 2007 there will be an interval of at least 7 to 12 months before money from successful bids will be realised.

In addition, to date R&D support funding has been focused on infrastructural support (i.e. indirect costs) for research programmes and portfolios. It is becoming clear that the new funding streams are directed much more towards the direct costs of research raising uncertainties about the way in which infrastructural support will be resourced.

Structure for co-ordinated research



- Will be sub-structure to provide scientific advice
- Admin support structure



Relative Spend - a comparison of research & service budgets

Source: UKCRC - UK Health Research Analysis, Department of Health Annual Report & WHO Global Burden of Disease Project

