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UK Research Clinical Collaboration – A New Initiative in Clinical Research

Professor Bob Stout, Director of Research and Development for the HPSS

Over the last few decades there have been enormous advances in the basic sciences in relation to medicine, particularly in the fields of genetics, molecular biology and imaging. Because of the excitement of working in these areas, many researchers have concentrated on this type of research and a great deal of funding has supported it. It is now realised that a gap has opened up between the advances in the basic sciences and their application to prevention, diagnosis and treatment of disease and the care of patients. It is also recognised that the NHS (HPSS in Northern Ireland) is a unique and potentially huge resource for clinical research, including clinical trials.

Cancer has led in rationalising clinical research in the NHS. When the Government introduced its Cancer Plan in 1999, it required cancer research funders to become more co-ordinated and strategic. The result was the formation of the National Cancer Research Institute (NCRI), consisting of the Health Departments, the Medical Research Council and the major cancer research charities. A strategic analysis of support for cancer research revealed that basic science was well supported but that research in prevention and palliative care were relatively under resourced. As a result new initiatives in these areas are under way. Associated with the NCRI is The National Cancer Research Network (NCRN), for clinical trials with which the Northern Ireland Cancer Clinical Trials Unit is closely associated; and there is also the National Translational Cancer Research Network (NTRAC), of which the Northern Ireland Cancer Centre is a member. The cancer research networks are a model for similar research networks in other disease areas. A question still to be answered is whether there is something unique in cancer, for example its leadership and the existing clinical networks, or whether the model can be applied successfully to other areas.

The UK Clinical Research Collaboration (UKCRC) was announced by the Chancellor of the Exchequer in the 2004 Budget along with an additional £25 million per year over four years reaching an additional £100 million per year by 2008 to Department of Health R&D funding to support it. The UKCRC is a partnership between Health Departments, the MRC, the voluntary sector, patients and industry to oversee clinical research in the UK. The Chair is the DH Director of Research and Development (Professor Sally Davies), with Dr Liam O'Toole as the acting Chief Executive. The UK Clinical Research Network will provide a world-class health service infrastructure to support clinical research. It will

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facilitate the conduct of randomised prospective trials of interventions (including prevention, diagnosis, treatment, and care) and other well-designed studies in the broad area of clinical research

The UK Clinical Research Network will consist of a managed set of Clinical Research Networks. The initial networks will cover cancer, mental health, medicines for children, diabetes, stroke, and Alzheimer's disease. Over time, it is intended that the UKCRN will enable research to be conducted across the full spectrum of disease and clinical need. Under the National Co-ordinating Centre for UKCRN there will be managed research networks each with a co-ordinating centre. In early October, advertisements were placed for co-ordinating centres for networks for medicines in children and diabetes. Networks for the other conditions will rapidly follow (a network for Mental Health Research already exists in England and this will be expanded and extended throughout the UK). The local Research Networks will support clinical research in all relevant settings including primary care.

This initiative is UK wide and all four Health Departments are participating. The R&D Office is doing so on behalf of the DHSSPS; the Director of R&D is a member of the Board of UKCRC, and of the joint MRC - Department of Health, Health Research Delivery Group which oversees the project.

In Northern Ireland we are well placed to participate in this initiative as we already have structures that map closely with UKCRC. The Clinical Research Support Centre supports clinical research and clinical trials and acts as a resource for clinical research and clinical trials in all disciplines in Northern Ireland. The subjects of the initial six networks are all supported by the R&D Office within the RRGs.

Discussions are already taking place with researchers in relevant areas to ensure that Northern Ireland participates fully in this important initiative which is designed to re-engineer clinical research in the UK over the next decade or more and to both improve the nation's health and increase national wealth.

Discussions on whether centres in Northern Ireland should bid for the co-ordinating centres either alone or in collaboration with others are also under way.

As well as the research networks, the UKCRC has a number of other objectives. Some years ago the Wellcome Trust funded six clinical research facilities attached to hospitals in Great Britain in which patients could be investigated as day patients or in some cases as inpatients. Northern Ireland was not successful in its bid for one of these. It seems likely that the Wellcome Trust will be allocating more funds and tendering for further bids for clinical research facilities. With support from the R&D Office both the Royal and City Hospitals Trusts are looking at the possibility of clinical research facilities.

Another objective of the UKCRC is to look at the workforce for clinical research and in particular the need for research training. The medical profession is being studied first and a joint working party between Modernising Medical Careers and UKCRC is looking at the need for post graduate medical training to be flexible enough to allow research training to occur. Other health and social care professions will be studied in future.

There is also a concern that the regulatory environment for research is becoming oppressive and perhaps a disincentive to clinical research. Research Governance, new regulations for ethical review, the Data Protection Act and the Human Tissues Act are important in protecting participants of research but together they provide a complex regulatory environment. The UKCRC will be studying this to see if some lightening the burden on researchers is possible while still providing protection for participants.

This is an exciting opportunity to take part in an important initiative supporting clinical research in areas where we are already active. The R&D Office will be participating fully in this initiative and we hope that both the Northern Ireland research community, and patients and clients will benefit.

Condition	RRG
Cancer	Cancer RRG
Medicines for Children	Child Health & Welfare RRG
Diabetes	Endocrinology & Diabetes RRG
Mental Health	Epidemiology and Neuroscience RRGs
Alzheimer's Disease	Neuroscience RRG
Stroke	Trauma & Rehabilitation and Neuroscience RRGs

Research and Development Office Research Sabbatical Training Scheme

University of Iowa – Center for Macular Degeneration Studies

Miss Giuliana Silvestri, Consultant Ophthalmic Surgeon at the Royal Victoria Hospital

Reason for Sabbatical leave

In 1994 I was appointed as a Senior Lecturer and Consultant Ophthalmic Surgeon. Since that time my primary focus has been on the development of my clinical practice, administration and teaching. After 10 very enjoyable years as a joint appointee, I found that I was having difficulty in achieving the required "Balanced Excellence". Last year I came to a crossroads in my career and felt that the time was right to make the decision as to whether I should completely focus my attention on clinical duties and apply for an NHS appointment or whether to pursue my research career with determination. I decided that if I could have the opportunity to undertake a research sabbatical, that this would allow me the perfect opportunity to make the correct decision for my future career development.

I had begun thinking about taking a research-orientated sabbatical approximately 1 year earlier and following enquiries I had received two offers for placements, one in Melbourne Australia with Dr David Mackey and one with Professor Gregory Hageman in the Centre for Macular Degeneration at the University of Iowa. In early 2003, I contacted Professor Hageman to firm up dates for the sabbatical, which would hopefully start in January 2004, therefore, allowing myself approximately 1 year to make arrangements for funding. Professor Hageman confirmed the possibility of the sabbatical, however, he indicated that he thought it advantageous that I start my sabbatical period in August 2003, so that my time in Iowa would overlap with Professor Dean Bok, who was also at the University of Iowa as Visiting Professor from the University of California. Professor Hageman felt that this would offer me an unparalleled opportunity to interact with a very eminent figure in ophthalmic science. Although an attractive opportunity, this put extreme pressure on me to come up with funding in a period of six months.

Planning for Sabbatical leave

My initial approach regarding sabbatical leave was to Professor Rod Hay, Dean of Faculty of Medicine and Health Sciences QUB, to request permission to undertake a sabbatical for a six-month period. It is within the University regulations that if a member of academic staff has served for a period of seven years or longer, that a period of sabbatical leave can be given at the discretion of the Dean. Professor Hay was extremely supportive and granted my request. I also applied to the Faculty of Medicine for the Charles Havelock Travelling Scholarship which would help fund 50% of my expenses. I was fortunate to become the beneficiary of this award for the year 2003-2004.

Having been granted leave from the University I then approached the Royal Hospitals Trust to seek approval for leave from my NHS duties. I approached Mr Patrick Johnston, Clinical Director of Ophthalmology and Mr David Adams, Divisional Director regarding the possibility of a period of six months sabbatical leave from my NHS duties. Both were extremely supportive and enthusiastic. However, it became clear that, if this were to become a reality, I would be responsible for bringing in enough funds to pay for a locum consultant for the specified period of time. At this point I began searching the national grant awarding bodies for a scheme that might be suitable for my application. It became clear that although such schemes were available, they would require an application perhaps a year in advance. It became evident that it would be difficult for me to obtain the funding required for the forthcoming 6-month period.

I was extremely fortunate that at this time the Northern Ireland R&D Office advertised a scheme for support for sabbatical leave, which met my needs. I made an application and I am pleased to say that I was successful and that the R&D Office funded the salary for my locum cover whilst I was out of the UK, 50% of my accommodation and travel costs and 50% of my laboratory consumable costs. This was a wonderful opportunity and without this scheme I feel that my sabbatical would not have come to fruition.

Objectives of Sabbatical leave

The main objectives for my sabbatical leave were as follows.

- To become conversant with a new area of research i.e.: the role of inflammation in the pathogenesis of Age-related Macular Degeneration (AMD).
- To increase my research standing internationally
- To work on some new material for publications
- To establish long-term international collaborations
- To spend a short time in N. Ireland free from clinical duties to revise and redirect ongoing research projects
- To reaffirm to myself that I wished to pursue research as a major part of my professional development.

Achievements during the Sabbatical period

During the 6-month period I was able to spend one month in Belfast coordinating and working on my local research projects. This was extremely helpful as it allowed me dedicated time to meet with my research team and to review progress and revise our strategy. During my time in Iowa I worked on the following 5 projects.

- Refractive correlations in 100 patients with AMD, 100 patients with vascular disease and 100 normal patients.
- Examination of 1-micron and 7-micron histological sections for the measurement of sclera thickness in patients with emmetropia, hyperopia and myopia.
- Typographical analysis of optic disc parameters in 300 patients who had normal fundi, AMD and vascular disease.
- Reviewing of clinical data associated with post infectious histological markers in AMD.
- The design of an AMD and vascular database for use by Professor Hageman's group

Problems for NHS Consultants planning Sabbatical leave

From my own point of view I had a wonderful time at the University of Iowa and found the whole experience of having a dedicated period of time for research has refuelled my enthusiasm. I would certainly recommend it to anyone whose interest is flagging perhaps due to extreme pressures from administrative and clinical duties.

However, planning a sabbatical for clinicians who have responsibilities for ongoing patient care is not easy. From my point of view, as a joint-appointee, the University side of the process was extremely simple because I was able to reallocate my duties to my colleagues who were extremely willing to help for the six-month period and I wish to take this opportunity to thank them for carrying out my administrative tasks during this time.

From the NHS side, however, initially the funding was an issue but this was resolved by the R&D Office Sabbatical Research Training Scheme. Having achieved the funding the next problem was to find a suitable consultant locum to step into the sessions. Whilst this might not be a problem for some of the larger specialties, in a small specialty such as Ophthalmology I needed to find someone who had experience in a specific discipline and who could take over a difficult and challenging case load of patients with inflammatory eye disease who are on heavy immunosuppressive therapy. In my case as a joint-appointee the situation was doubly complicated by the fact that I needed someone who was willing to work part-time. I found myself in a very fortuitous position in that Professor Desmond Archer, who had recently retired, was willing to work as a half time locum in this capacity. This suited my needs perfectly. Again I would like to thank Desmond Archer for his help. The arrangements for leave would be further complicated for those who have a private practice. Those with a significant private practice would incur a significant loss of earnings, which also needs to be allowed for when budgeting for the sabbatical.

Recommendations

In summary I would whole-heartedly recommend a period of sabbatical leave for someone who has the enthusiasm and energy to make all the arrangements required. It is certainly well worth the effort and I would like to commend the R&D Office for its foresight in setting up the scheme, which makes the funding of the NHS commitment much more possible. I would of course also recommend that sabbaticals be planned at least a year in advance. However, as in my case despite my best intentions, this did not work out. Regarding the benefits from the sabbatical I can

confirm that I have had enormous benefits both at a personal level and also on a research level.

My time in Iowa was short i.e. five months and most of my time there was spent gathering data. It is now obviously encumberant upon me to analyse these data and publish the work. Professor Hageman and I are confident that at least two to three publications will be forthcoming from my time spent in Iowa. Of course now that I have returned to reality and have resumed my clinical and administrative duties, I realise that it will be at least one year before these publications come to fruition. The other huge benefit from my time in Iowa is that it will now be possible for me to send postdoctoral students to Professor Hageman's laboratory for training and ongoing collaboration, which hopefully will result in continuing benefits for research in Ophthalmology in Northern Ireland for many years to come.

From a personal point of view I feel that the most likely long-term benefit is that this period of time has resulted in a significant strengthening of my desire to remain research active. I will therefore continue to strive for balanced excellence!

Miss Giuliana Silvestri MD FRCP FRCS FRSCOphth

Erratum Issue three, page 2

Please note that the 'byline quote' on page 2 was not related to the article on epilepsy by Dr Shane McKee. We apologise to Dr McKee for this editorial error and any confusion that this may have caused our readers.

Cancer RRG

Professor Stephanie McKeown, Professor of Cancer Biology at the University of Ulster

Introduction

The Cancer Recognised Research Group (RRG) is the largest RRG funded by the R&D Office with 16 Principal Investigators (PI) involved in 13 projects. Recently two new projects have been funded involving a further 6 PIs. The formation of the Cancer RRG has been a major force in developing a network of links among cancer researchers across Northern Ireland. In addition there are over 90 registered Associate Investigators. This wider group involves a range of professionals including specialists within the medical field, scientists, epidemiologists, nurses, medical physicists and many others.

The projects

There are 15 funded projects, covering several areas of investigation. These include:

Factors affecting tumour development and progression

This is the biggest interest group with 7 PIs involved. Two projects led by Prof. Helene McNulty and Prof. Sean Strain (UUC) and Prof. Charles Campbell (QUB) are designed to look at factors thought to promote tumour development. The UUC group is investigating the role of folate and other vitamins while the QUB group is interested in the role of inflammation in this process. Prof. Ian Rowland (UUC) is evaluating the use of faecal water as a potential screening device for predisposition to colon cancer. A new project involving Dr Tony Bjourson, Prof. Patrick Morrison and Prof. Yvonne Barnett (UUC) will investigate genetic factors involved in predisposition to breast cancer.

Tumour hypoxia

For tumours to grow to a size where we become aware of their presence, the growing mass must develop a new blood supply to provide oxygen and nutrients. Tumours do this rather badly and the supplying vasculature is often inadequate, leading to areas of low oxygen (hypoxia) in patches throughout the tumour. This leads to a number of biological problems/opportunities for targeting the tumour. At UUJ Prof. David Hirst and I have been investigating therapeutic opportunities afforded by specific differences in the tumour microenvironment as compared to normal tissue. Hypoxia also causes a range of signalling changes within tumour cells; the focus of the work of Prof. Terry Lappin's groups at QUB is to understand their importance in cellular responses to hypoxia.

Molecular targeting of tumour cells

Like all cells, tumour cells contain genes that are of importance to their growth. Often they behave aberrantly in tumours. There is potentially a large number of molecular targets within the tumour which offer therapeutic opportunities. Three groups at QUB are tackling aspects of this approach. Dr Hilary Russell previously identified a novel gene involved in tumour suppression in ovarian tissue. She is now working to characterise this gene with the aim to improve understanding of the development of ovarian cancer

and to identify ways to block ovarian tumour development. The work of Prof. Paddy Johnston's group is focused on characterising the central role of thymidylate synthase regulated signalling pathways in tumour cells. A better understanding of these pathways could lead to improved chemotherapeutic approaches to tumour control. Dr. Hendrik van den Berg is leading a group investigating natural products, with the aim of identifying novel anti-cancer drugs.

Control of the cancer cell

Cancer cells are essentially normal cells that have lost the ability to tightly control growth. Two projects at UUC involve investigation of these mechanisms in tumours. Dr Colum Walsh is interested in the mechanism that causes the silencing of genes and which may be aberrant in tumour cells allowing unregulated growth. All cells regulate growth using a cyclical system whereby they replicate at a characteristic rate. This cell cycle is subject to a series of checks and balances that are often defective in tumours. Prof. Stephen Downes and Dr Hugh McGlynn are studying tumour cells with a particular interest in the later stages of this cycle.

Stress responses in cancer

Cancer cells often respond differently in response to a range of endogenous and exogenous stresses. A greater understanding of these response pathways may lead to designing new ways to eradicate tumour cells. Dr Tracy Robson (UUJ), who discovered the stress response gene, DIR1, is involved in further characterisation of this gene. She is particularly interested in its potential in the radio - and chemo-sensitisation of tumours. BRCA1 is a gene that has an important role in cells. It is a central gene involved in stress responses and abnormalities in this gene can predispose to breast and ovarian cancer. Dr Paul Harkin (QUB) has a team working on the functional analysis of this gene.

Imaging and tumour evaluation

Prof. Peter Hamilton (Dept of Pathology, QUB) has developed a sophisticated computerised system to aid in the diagnosis and prognosis in cancer. He is evaluating its potential in a number of tumour model systems. A recent addition to the cancer RRG is the award of funding to Dr Alan Hounsell, Dr David Stewart and Prof. Peter Jarritt (Medical Physics Agency, NI). They are interested in the use of a new state of the art imager (PET-CT) which allows dynamic imaging of tumour tissue. They will be investigating the use of this imager in the treatment planning for non-small cell lung cancer.

Cohesion and collaboration

It is the aim of the RRG to develop strong links within and across disciplines. Through the cohesion fund allotted to the group we have run a range of research seminars, one day meetings and group retreats. The most recent was this September when over 100 people attended. We heard four excellent talks by researchers from the UK and the USA. In addition, we had several breakout sessions; these were designed around several of the interest groups within the RRG and were aimed to get investigators talking about further collaborations. They were generally deemed a success and a similar format is planned for next year's meeting.

Regular meetings of the PIs are held (3 per year) to make decisions about the running of the group, foster discussion on collaborative research and to plan events run by the RRG. A number of themed meetings have also been held and it is hoped to develop these further. Another feature of the Cancer RRG is the availability of small running cost grants awarded by the committee to promote cohesion and cross group collaborations.

It has been very gratifying that in the 3 years since the setting up of the RRG there has been a much greater interaction between all of those interested in cancer research in Northern Ireland. There is a growing camaraderie between staff in different groups, in the two Universities and many of the hospital departments.

The Northern Ireland cancer research community

This is a very exciting time for cancer research in NI with several major infrastructural developments that have been announced/implemented in the last 3 years. These include the building at the Belfast City Hospital (BCH) of a new Cancer Centre (due to open in 2006), the development of a Cancer Clinical Trials unit at BCH (under the directorship of Dr Richard Wilson), the announcement of the new Cancer Research Centre at QUB and the opening of the new Centre for Molecular Biosciences at the University of Ulster at Coleraine (UUC). In a novel initiative, promoted by the National Cancer Institute based in Bethesda, USA and the two Health Departments in the North and South of Ireland, there has been the establishment of a Cancer Consortium involving Cancer Researchers and Medical Staff throughout Ireland and in the

USA. This has provided a range of training and research opportunities for individuals involved in cancer research throughout Ireland. It has also fostered North-South links including the setting up of the All Ireland Co-operative Group for Cancer Clinical Trials.

The Cancer RRG has come some considerable way since it was first set up 3 years ago. With so many major new developments on the horizon Northern Ireland cancer researchers are well placed to be in the forefront of the fight to combat cancer; the existence of the Cancer RRG provides an added cohesion to our efforts.

Enabling older adults with impaired cognition to consent to take part in research

Mrs Jeannie Donnelly, R&D Office Special Nursing Fellow, Royal Hospitals/University of Ulster and Professor George Kernohan, Professor of Health Research, University of Ulster

Cognitively impaired people tend to be excluded from research due to difficulties in gaining consent. However, exclusion can lead to data, which does not represent the different needs and circumstances of the at-risk population. This issue arose in a study where patients 'at risk' of pressure ulcers were excluded due to their inability to provide informed consent.

Accordingly a literature review was undertaken to determine a means by which cognitively impaired people could be ethically recruited. The review showed that recruitment was possible because:

- The research aims to obtain knowledge for improved care within the vulnerable group.
- The research is designed to be responsive to patients' needs.
- No superior therapy is being withheld.
- The risks attached to the intervention do not exceed those associated with routine nursing care.
- It is unjust to deprive vulnerable people from research, which could directly benefit them[1].

Furthermore, it was established that an inclusionary consent process, which seeks to establish the unique identity of the person could be used to make the study meaningful to the participant[2]. This requires an exploration of the person in the context of their past and 'the here and now', an awareness of their usual level of well being or ill being (and how this is observed) and of how the person normally consents to care, i.e. verbal, non-verbal and behavioral indicators. The process is achieved through shared interactions, observation, a review of medical/nursing records and discourse with the patient, significant others/carers and staff.

Thus, the investigator is enabled to know when the person really means, "yes" or when they actually mean "no". This knowledge is vital to the consent process as true meaning may be implied rather than spoken in correct English. Clinicians, not involved in the research, must be made aware of these signs so that they can act as the patient's advocate at the first sign of distress.

The individual is given as much time as necessary to reach a measured decision. This includes time for consultation with others, or more time spent explaining the study and the subject's options in a way that suits their level of understanding, taking into consideration their maturity, intelligence, education, belief system and disabilities as well as the consequences of the early changes in cognition[3]. As consent is situation-specific, environmental cues and props, e.g. equipment or photographs can be extremely useful in describing the study. It is noteworthy that the patient's understanding of the study improves with their experience of being in the study.

Comprehension is assessed by exploring whether the person is able to:

- paraphrase what has been said (repeating and rewording explanations as necessary);
- compare alternatives, or to express any thoughts on possible consequences other than those disclosed;
- apply the information to his or her own case.

This information must be recorded so that the researcher can supply evidence about how permission was obtained.

Where prospective subjects are unable to consent, permission must be obtained from their legal guardian or an immediate family member/significant other who

by virtue of their relationship is suitable to act as their legal representative for the purposes of the trial, and is available and willing to act as a proxy.

The 'nearest relative' tends to be based on a hierarchy of family relationships, which is widely thought to reflect closeness e.g. spouse and then an adult child. If no one can be identified, the doctor primarily responsible for patient's medical treatment or a person nominated by the relevant health care provider can act as a proxy so long as they are not connected with the conduct of the clinical trial[4].

The proxy must:

- be provided with detailed information about the project
- be instructed to base their decision on the patient's previous wishes or
- if this information is not available, to make the decision on the basis of the person's best interests.

Although informed consent by proxy fulfils certain legal, moral and social responsibilities, it has limitations. For instance, a proxy could have personal interests and beliefs that may call their permission into question, e.g. protective caring may motivate the decision.

If a person's ability to make decisions is known to fluctuate, the researcher has a professional and moral duty to wait until the potential subject is in the best position to make an informed decision. If this is not practical, the investigator should at the very least review the decision whether to include or exclude the person. Maintaining consent will also become important and it may be necessary to repeat the process for each research encounter[2].

The inclusionary consent process has time implications and requires particular skills in relating with cognitively impaired older people and their carers. The process may only be suitable for certain research methodologies and may be affected by the extent to which a research intervention is intrusive or invasive.

For further information, see DONNELLY, J. (2004) Can adults with cognitive impairment consent to take part in research? Journal of Wound Care 13 (7) 257 - 262

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2. Dewing, J. From ritual to relationship: a personcentred approach to consent in qualitative research with older people who have a dementia. Dementia 2002; 1: 2, 157-171.
3. Department of Health, Social Services and Public Safety. Good practice in Consent: Consent for examination, treatment or care. DHSSPS, 2003.
4. The Medicines for Human Use (Clinical Trials) Regulations 2004

New developments with the Cochrane Library

The Cochrane Collaboration is an international organisation that aims to help people make well-informed decisions about health care, by preparing, maintaining and promoting accessible systematic reviews of the effects of health care interventions. Since 2002 users resident on the island of Ireland have enjoyed free access to the systematic reviews in the Cochrane Library.

The Cochrane Collaboration has appointed John Wiley & Sons Ltd as its new publishing partner for the Collaboration's publishing activities. Consequently, a new version of The Cochrane Library on Wiley InterScience is now available www.thecochranelibrary.com. Until the end of the year, the library will be available in both the Update Software and the Wiley InterScience versions. Then the library will revert to the Wiley InterScience version alone.

The agreement reached between the Cochrane Collaboration, which produces the library, John Wiley and Sons Ltd, the new publisher of the Cochrane Library (currently Update Software), the Health Research Board in Dublin and the R&D Office, will continue to make the Cochrane Library available, free of charge, to anyone on the island of Ireland.

The national license has been activated by Wiley and Island of Ireland resident users should be able to access the library via IP address recognition, without having to register. Should any resident users experience difficulty accessing the Library they should contact the customer service team at Wiley at cs-wis@wiley.co.uk.

Wiley have also created a transition page (www3.interscience.wiley.com/aboutus/sharedfiles/cochrane_transition) which contains a downloadable PDF library guide, promotional material, user hints, search tips, differences between the two interfaces, FAQ's and much, much more.

Centre for Clinical Raman Microscopy

A new cross-faculty development at Queen's University

Professor Stuart Elborn on behalf of the Centre for Clinical Raman Microscopy

What is Raman Microscopy?

Raman microscopy is a recently developed method for identifying compounds by using light emitted from samples, which is specific to the chemical nature of the sample molecules. This method has been widely used in physical sciences and more recently its potential to investigate biological systems has been recognized. As part of an innovative collaboration involving the Faculties of Medicine and Science and Agriculture at Queens University Belfast, the method is now being used to investigate complex biological systems. Our aim is to improve the diagnosis of serious diseases and provide a better understanding of their pathophysiology.

L-R: Dr René Beattie, Professor Stuart Elborn, Dr Vicky Kett, Professor Bob Stout and Professor John McGarvey

How does Raman microscopy work?

The Raman effect, which is the basis of Raman spectroscopy and microscopy, arises from the scattering of light by matter and was first reported as an experimental observation by C.V. Raman in 1928. When a beam of monochromatic light (nowadays from a laser) is directed onto a sample, most of the light which is scattered has the same colour as the incident beam (i.e. the scattering is elastic). However, a tiny fraction of the scattered light (1 thousandth part or less) will differ in colour from that of the incident beam, hence giving rise to inelastic scattering. It is the difference in colour between the incident and the inelastically scattered beams which is important. This colour difference is more conveniently expressed as a frequency difference which is equal to the frequency at which bonds of the molecules in the sample typically vibrate. The important implications of this is that each molecular species possesses its own group of bond vibrations and the collection of vibrational frequencies for a particular species constitutes a unique spectrum, which is in effect a 'fingerprint' of that species. In Raman microscopy, the analytical technique of Raman spectroscopy is combined with optical microscopy resulting in a method which functions not only as a highly specific probe of the molecular state and composition of a sample but does so with a high level of spatial resolution (~ 1µm), thus enabling studies in the case of biological species down to the cellular level. Although the initial idea of combining Raman spectroscopy with optical microscopy as Raman microscopy was put forward almost thirty years ago, it is only in the last 5-10 years that the value of the technique, especially in the biomedical field has been fully recognised. Analysing the intensity of the scattered light at the various shifted frequencies enables an understanding of the chemical and physical nature of the sample, giving rise to one of the main benefits of Raman in biomedical applications, its use as a 'chemical vision' technique. Furthermore, the native Raman vibrations of biochemical molecules can be probed, without need for any other type of labelling, e.g as often needed in confocal microscopy. One of the advantages of using the Raman effect in analysis is that it can be studied for any state of matter and is not adversely affected by aqueous environments, a point of particular importance for biological species. Thus, the analysis of fresh, unprocessed and even in-vivo tissue samples becomes possible. In Raman microscopy, by viewing the Raman scattering with a confocal optical microscope the technique effectively becomes a microprobe with spatial resolution of ca. 1µm, thereby enabling the acquisition of spectra for highly specific regions of a sample. This also means that the distribution of a particular molecular species can be mapped throughout a selected region of the sample, hence providing a very powerful means of species identification and characterisation as a function of location. It becomes possible for instance to map the distribution of proteins or drugs within a single cell.

Centre for Clinical Raman Microscopy

A number of researchers in the School of Chemistry with longstanding expertise in Raman Spectroscopy have combined with a number of groups from the Schools of Medicine and Pharmacy in Queens to investigate the use of this method for improving diagnosis of complex diseases. The group includes Prof John McGarvey, Dr Steve Bell and Dr Rene Beattie from Chemistry, Prof Alan Stitt from Ophthalmology, Prof Madeleine Ennis, Prof Stuart Elborn from Respiratory Medicine, Dr Vicky Kett from Pharmacy and Prof Peter Hamilton from Pathology as well as Prof Duncan Craig and Dr Susan Barker (both now School of Chemical Sciences and Pharmacy, University of East Anglia). The group is focusing on a number of areas related to the diagnosis and behaviours of cancers, factors affecting sight in diabetes and the formulation of new drug delivery systems.

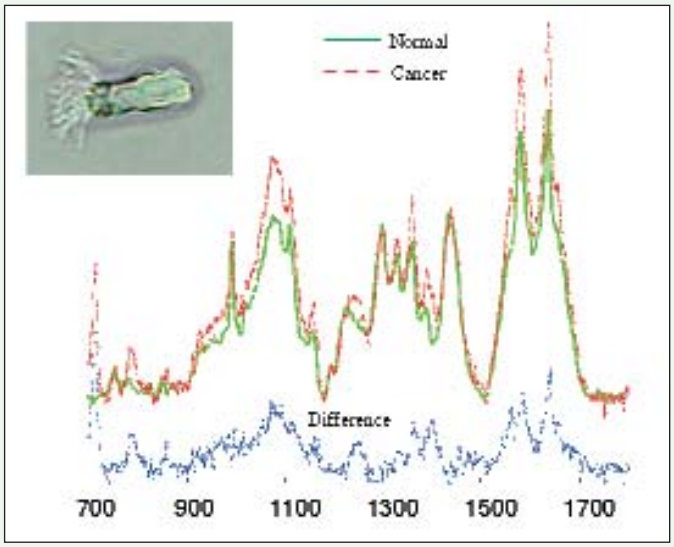
The BBSRC has provided a grant to purchase and install a Raman microscope and this funding has been matched by the R & D Office to support a post doctoral fellow and a technician.

Some Biomedical Applications of Raman

Cancer Research

Raman microscopy has interesting applications in cancer research. One of the groups, led by Peter Hamilton, is developing Raman microscopy for detecting and mapping chemical alterations in prostate cancer, from thin tissue slices and cell samples. By mapping the chemical signature of specific cancer cells, they are beginning to discover novel diagnostic and prognostic markers. They have already developed techniques to map Raman cell signatures in two-dimensions using computer visualisation and can distinguish benign and malignant prostate cells based on Raman chemometric analysis. Further work will explore the 3-D Raman characteristics of individual cells to help understand the spatial significance of cell biochemistry in cancer progression and response to cytotoxic therapy.

In a related project led by Professor Elborn, we will investigate the role of Raman as a method to enable the early diagnosis of lung cancer. This part of the work is also being supported by the R&D Office through a fellowship scheme (Dr Nick Magee will start his PhD in August). Lung cancer is the most common fatal cancer in Northern Ireland and the most effective way of improving the outcome is early diagnosis and treatment. Preliminary data have shown that we can differentiate between cancerous and non-cancerous cells taken from bronchial brushings. We plan to examine metaplastic, dysplastic, and neoplastic cells in lung cancer biopsy specimens. We will then develop the method to investigate the ability of Raman microscopy to differentiate between normal, dysplastic and malignant cells in sputum from patients with lung cancer. If these studies confirm the accuracy of Raman microscopy in the differentiation of malignant and non-malignant cells then further studies will be planned. Initially we will investigate the ability of the Raman microscopy to detect a second primary lung cancer in patients who have had primary lung cancer resections. Suitable samples will be available from the 5th Framework EU Lung Cancer Study. The technique could then be examined on an 'at risk' population. This population might include males over the age of 50 with a smoking history of at least 30 pack years. This could help target investigation or other screening methods such as low dose computed tomography or fluorescence bronchoscopy in these selected patients



Comparison of the Raman spectra of Normal and cancerous lung epithelial cells. Inset: lung epithelial cell (unstained)

Drug Development

Collaboration between Prof McGarvey, Dr Beattie and Dr Kett has let to some exciting developments in the quest to understand the interaction between protectant molecules and sensitive protein therapeutics. Recent biotechnological advances have resulted in large numbers of potential proteinaceous drugs that are too sensitive to be formulated in traditional dosage forms. Freeze-drying, in which the protein solution is frozen and the water removed under reduced pressure by sublimation, stabilises these

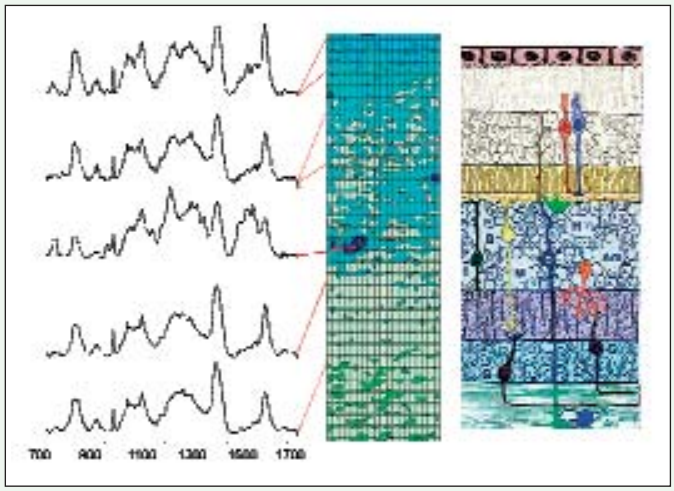
molecules as a solid that may then be reconstituted prior to injection. However, the process may result in degradation of the active molecule, warranting the inclusion of protectants such as mannitol. We have been studying the use of mannitol in freeze-dried formulations and have demonstrated that Raman microscopy may be used to analyse the effect of freezing rate and holding time on the structure formed and behaviour (ie polymorphic transformation) of this material in the frozen state. These highly encouraging initial studies indicate that we should be able to characterise incorporated protein therapeutics in the frozen state, leading to the exciting possibility of being able to directly monitor any degradation processes, a measurement that is not possible using existing techniques.

Vision Science

Within the Ophthalmology Research Centre two related projects are being studied using the Raman confocal microscope to address pathogenic issues in ophthalmic diseases.

The first project is investigating important issues in the understanding of retinitis pigmentosa (RP). Despite our increasing knowledge of the variant genetic mutations implicated in this blinding disease, there is still little evidence to indicate how these single mutations induce pathology in the complex stratified retina. We are presently employing Raman microscopy to study the spatiotemporal impact of neural degeneration in animal models of human RP and latterly in rare archival human RP tissues. This will generate a unique Raman fingerprint for retinal tissue in these animal models with disease progression and in human pathologies. This novel investigation will generate much-needed scientific data and aid in the development of new diagnostic and prognostic parameters.

A further study is employing Raman spectromicroscopy as a tool for identification and mapping of advanced glycated end products (AGEs) within Bruch's membrane-choriod complexes from donor eye cups retrieved post-mortem (in collaboration with University of Cardiff). It is envisaged that Raman spectra obtained in this study will complement and support other quantitative and qualitative methods of investigation (HPLC, ICC) to characterise AGE levels. Initial studies are encouraging and have identified collagen isoforms documented in Bruch's membrane and also significant levels of novel spectra, as yet unidentified. Further work in improving analysis and sampling are currently underway.



Micron spaced Raman map of retinal section compared with a diagram of the retinal layers

It is hoped that in both projects Raman can be used as a non-invasive method of analysis and that in the future the adaptation of current methods will enable a non-invasive *in vivo* analysis of the human eye to establish the levels of macular degeneration at an earlier stage than presently possible.

Conclusion

Raman microscopy clearly holds much promise for the investigation of complex biological tissues. The Clinical Raman Microscopy Centre is already investigating a number of key areas. However, further developments are already in the planning stage: e.g.

1. establishing the role of vitamin E (α-tocopherol) in the lung clarifying the presence of local α-tocopherol deficiency in human chronic lung inflammation
2. exploring 3-D confocal Raman microscopy for drug uptake in bladder tumour cells, developing a rapid assay of malignancy in urine samples from patients with bladder cancer
3. studying the distribution, form and interactions of drugs within polymeric films for biomedical and drug delivery applications to enhance understanding of how drug-polymer interactions affect clinical outcomes

We believe that there may be many more applications of this exciting technique and we will only need the money and other resources to explore them. We would like to thank the R & D Office for having the vision to help us fully exploit this unique opportunity to establish an internationally recognized centre for Clinical Raman Microscopy.

The new Health and Personal Social Services Research Ethics Committee (HPSS REC) system in Northern Ireland: an update

Dr Siobhan McGrath, ORECNI Manager

Background

The new Medicines for Human Use (Clinical Trials) UK Regulations 2004 require that an appointing authority (which in Northern Ireland is the Department for Health, Social Services and Public Safety (DHSSPS)) recognises an appropriate number of Research Ethics Committees capable of reviewing research proposals for clinical trials involving medicinal products for human use. In line with the rest of the UK, the DHSSPS has decided to adopt a common standard of ethical review for all forms of HPSS research, rather than introducing special arrangements for clinical trials. Therefore, the Health and Personal Social Services Research Ethics Committees (HPSS RECs) established by the DHSSPS in February 2004, can review all ethical applications within the field of health and social care, whether or not the research involves a medicinal product.

The DHSSPS decided to establish three ethics committees, funded by the DHSSPS and administered through the Office for Research Ethics Committees in Northern Ireland (ORECNI). Each has a remit covering the whole of Northern Ireland and meets monthly. The members of the REC are especially trained and possess experience in reviewing a wide spectrum of research proposals.

When should I apply to an HPSS REC?

Is your research in the field of health and/or social care? Does it involve hospital or non-hospital based HPSS services users or patients? Does it involve HPSS staff or use of HPSS premises? Do you need to access service user/patient/ staff data? Do you need to take tissue samples for your research from existing patients or the recently deceased? Is your proposal qualitatively based (e.g. questionnaire, focus groups) or a quantitative research project? If you have answered yes to one or more of the above questions, your project must be submitted for an ethical opinion from a HPSS Research Ethics Committee. (Contact the Office for Research Ethics Committees for Northern Ireland on Tel: 028 9055 3607, www.orecni.org.uk)

Transition Arrangements

Up until mid-April this year, the Queen's University of Belfast and the University of Ulster provided ethical opinion for research in Northern Ireland through their constituted committees. They have now handed over ethical review of research to the new HPSS Research Ethics Committees. Transition arrangements, agreed by the DHSSPS mean that the ethical opinion provided to researchers by the previous committees continues to have standing, and therefore there is no need for a researcher to re-submit to the HPSS RECs for a new opinion (provided the ethical opinion from a former committee is less than 5 years old). However, any researcher with an ethical opinion more than 5 years old should apply afresh to the HPSS RECs immediately.

The Office For Research Ethics Committees Northern Ireland (ORECNI)

The mission of ORECNI is to support Research Ethics Committee arrangements in Northern Ireland, and to ensure that HPSS RECs are able to comply with Governance Arrangements for Research Ethics Committees (GAfREC) and UK Regulations 2004. ORECNI is based within the CSA and works closely with the (DHSSPS) to ensure that the new arrangements for ethical review are implemented, and that the HPSS REC chairs, members, researchers, HPSS managers and the wider community all understand the new arrangements.

ORECNI's manager is Dr Siobhan McGrath, one of 13 regional OREC Managers throughout the UK, who works with the Central Office of Research Ethics Committees (COREC) to implement the new legalisation and promote consistent ethical review throughout the UK.

ORECNI provides a full range of support, training and administrative services for all HPSS RECs. It is responsible for ensuring that applications are allocated appropriately between HPSS RECs, and that time deadlines are met.

ORECNI has a website www.orecni.org.uk which has the rota for committee meetings, the ethics application, guidance for applicant leaflets and other advice, and is linked to the COREC website.

ORECNI develops and maintains effective working relationships with a wide range of bodies/individuals including, UKECA, COREC, DHSSPS, HPSS RECs, HPSS bodies, independent contractors, universities, research councils & research charities, commercial companies and researchers.

A brief explanation of the roles of some of these stakeholders is given opposite:

UKECA

The UKECA, established under the UK Regulations 2004, comprises the relevant Minister from the four UK Health Departments and has the authority to recognise HPSS RECs

COREC

Central Office for Research Ethics Committees (COREC) (www.corec.org.uk), works on behalf of the Department of Health in England:

- co-ordinates the development of operational systems for Research Ethics Committees, on behalf of the National Health Service in England
- maintains close contact with officials in the Department of Health with policy responsibility for wider issues of research ethics and with colleagues from Scotland, Wales and Northern Ireland
- develops, implements and maintains operating procedures and standards for RECs that will be consistent across the UK
- establishes and manages regional Offices of Research Ethics Committees (ORECs) to oversee the activity of RECs
- provides advice to the Department of Health on the implications and practicalities of transposing the EU Directive on Good Clinical Practice in Medicinal Trials in the UK

COREC works closely with colleagues with similar responsibilities in Scotland, Wales and Northern Ireland.

DHSSPS

In Northern Ireland, the appointing authority for an HPSS REC is the DHSSPS. The DHSSPS holds the authority for the appointment of new and replacement HPSS REC members, and is currently with the assistance of ORECNI, in the midst of appointing additional HPSS REC members to the current HPSS REC committees.

HPSS RECs

HPSS RECs form the core of the ethical review arrangements in Northern Ireland. They are convened to provide independent advice to participants, researchers, funders, sponsors, employers, care organisations and professionals on the extent to which proposals for research studies comply with recognised ethical standards. In reviewing a proposed research study, an HPSS REC aims to protect the dignity, rights, safety and well being of all actual or potential research participants. The operation of the HPSS RECs is prescribed in the UK Regulations 2004 and augmented by national sub-operating procedures provided by COREC.

Three HPSS RECs were established to which members were publicly appointed in March 2004. Each committee has up to 18 members, at least one third of whom must be lay.

HPSS REC 1: Chair Dr Marie Smyth
Administrator Mr Damian McHugh

HPSS REC 2: Chair Dr Theresa Donaldson
Administrator Ms Angelina O'Neill

HPSS REC 3: Chair Dr John Trinder
Administrator Ms Sandra Bell

Also, the DHSSPS has established a pilot NI Phase 1 Research Ethics Committee by limited public appointment for an initial period not beyond 30 April 2004, its remit is to review studies investigating medicinal product for the first time in healthy volunteers. Such studies have been made exempt from the UK Regulations 2004 until 1st May 2005. On 1st May 2005, however, ethical review of these studies will need to comply with the legislation.

The committees meet at various locations throughout Northern Ireland.

Latest News!

Review of full ethical applications
The HPSS RECs are receiving applications for review on a regular basis from researchers. The committees have been reviewing applications since May this year, each on a monthly basis. Applications are submitted to ORECNI (see the guidance for applicants leaflet on www.orecni.org.uk).

Other services
The HPSS RECs review Site-Specific Assessments (applications to deal with locality issues only, relating to single site or multi-site applications) safety reports, end of study reports and amendments to studies, which have been given a favourable opinion (including those safety reports, end of study reports and amendments related to previously approved studies from the former, university based committees)

New round of Public Appointments: See www.orecni.org.uk for the latest call for new applications to be a member of an HPSS REC the deadline for submissions was 29th October 2004. Tel: 028 9055 3607

Accreditation: In 2005, the committees will be undergoing an audit to support their working to national Standard Operating Procedures.

Please contact ORECNI for any information or advice on ethical review. The office, which is currently based at 12-22 Linenhall Street, Belfast, is fully staffed to give advice and answer queries related to ethical submissions. (Tel: 028 9055 3607 Fax: 028 9055 3609 www.orecni.gov.uk email: info@orec.n-i.nhs.uk)

Notice Board

Since the last issue of R&D Today a number of grants have been awarded across a range of schemes.

EDUCATION & TRAINING

Doctoral Fellowship

Yet again the Education and Training strand remains busy! The Doctoral Fellowship panel met in January 2004 and a total of 12 awards were made, 3 in the area of Health Services Research and 9 in the area of Clinical Research.

Health Services Research

Candidate	Title
Susan Patterson	An evaluation of an adapted United States model of pharmaceutical care to improve psychoactive prescribing for nursing home residents in Northern Ireland
Moyra Mills	A randomised controlled trial of a patient-held quality of life record (PHQLR) in patients diagnosed with oesophageal cancer
Carole McIlrath	Identification of appropriate benchmarks for an effective primary care based nursing service for adults with depression - an exploratory study

Clinical Research

Candidate	Title
Claire Benson	Genetics of familial hip osteoarthritis: identification of genetic susceptibility factors
Heather Ferguson	Antioxidant nutritional status in the development of reflux oesophagitis and Barrett's oesophagus
Clive Wolsley	The relationship between measurements of retinal thickness using optical coherence tomography and retinal function using multifocal electroretinography in patients with myopia and retinal disorders
Nicholas Magee	Early diagnosis of lung cancer by Raman Microscopy
Ishola Agbaje	Endocrine, cellular and molecular effects of diabetes on male fertility
Damian Finnegan	Acute Myeloid Leukaemia: Characterisation of response to chemotherapy by HOX gene expression profiling
Paula Scullin	The role of Interleukin-8 signalling as determinant of response to chemotherapy in Prostate Cancer
Alison Muir	A study of aspirin resistance in patients with cardiovascular disease
Martina Pirie	Periodontal disease and preterm, low birth weight - a biological link

MPhil Fellowship

In 2004 a new MPhil Fellowship scheme was introduced and the Evaluation Panel met in June. A total of 4 awards were made, all in the area of Clinical Research.

Candidate	Title
Karen Logan	Mediterranean diet and coronary heart disease
Jacqueline Gamble	Evaluation of the benefits of an individualised menu nurse led programme in difficult asthma
Claire McArdle	Energy requirements and severe brain injury
Damian McKay	Butyrate and HMG-CoA Reductase Inhibitors in Ulcerative Colitis

National Cancer Institute Summer Courses

The National Cancer Institute, USA runs two summer courses, Molecular Prevention and the Principles and Practice of Cancer Prevention and Control. The following is a list of course participants who were successful in obtaining funding from the R&D Office, to allow them to attend.

Molecular Prevention (2-6 August 2004)

Dr Angela Seaton
Dr Clodagh Finnegan
Mr Brendan Gilmore
Dr Mark Catherwood
Dr Sharon Doherty
Mr Stewart Church

Principles and Practice of Cancer Prevention and Control (6-30 July 2004) and Molecular Prevention (2-6 August 2004)

Dr Susan Rainey
Dr Patricia Heavey

GP Research Registrar Scheme (GPARTS)

The R&D Office provides joint funding, with the Northern Ireland Medical and Dental Training Agency, for two GPARTS per year. The successful applicants in 2004 were Dr Donagh MacDonagh and Dr Monica Hughes.

Health & Social Care Services Research (HSCSR) Studentships

This year also saw the introduction of the HSCSR Studentships with the aim of building capacity in this area. The award assists the successful individual to develop a career in HSCSR by undertaking one year of general research training and by following a three-year programme leading to a PhD. The Evaluation Panel met in May and a total of 4 awards were made.

Bursary Awards

A total of 16 bursary awards have been made since the beginning of 2004. A further 6 are currently being evaluated.

Successful Applicants	Title
Ms Ruth Alexander	Masters in Social Research Methods
Ms Ruth Alexander	Qualitative Research Workshop
Miss Joanne Mahon	Clinical Research Techniques Module
Miss Judith McCune	Master of Clinical Research
Ms Frances Dowds	Masters in Social Research Methods
Ms Gillian Leckey	Clinical Research Techniques Module
Mrs Christine Erskine	MSc Health Science
Miss Audrey Johnston	MSc Advanced Nursing
Ms Claire Kerr	Research and Statistics Summer School
Miss Catherine McAllister	Research and Statistics Summer School
Mr Paul Schofield	Masters in Social Research Methods
Mrs Susan Anne Ross	MSc Nursing
Mrs Janice Carlisle	MSc Advanced Nursing
Mrs Julie Morton	Master of Clinical Research
Mrs Katrina Hughes	Research and Statistics Summer School
Mrs Dorothy Patterson	MSc Nursing/Midwifery

Supervisor & Co-Supervisor	Title
Professor Frank Kee, Dr Adele Marshall	The cost effectiveness of surveillance for Barrett's oesophagus in Northern Ireland
Professor Ciaran O'Neill, Professor Usha Chakravarthy	The costs and consequences of visual impairment from age-related macular degeneration in older people
Professor David Marsh, Dr Karen Bailie	Red cell transfusion in Northern Ireland: epidemiology and determinants of practice
Dr Dermot O'Reilly, Dr Michael Donnelly	The admission of older people to nursing and residential homes in Northern Ireland - a prospective study of the variation and determinants

COMMISSIONED RESEARCH

The R&D Office recently commissioned research to support the Antimicrobial Resistance Action Plan.

Successful Applicants	Title
Dr Colin Goldsmith, Dr Wilson Coulter, Dr John Moore, Dr Peter McCarron, Dr Paul Leggett	An investigation into the true community levels of antibiotic resistance in S.pneumoniae and the relationship between pneumococcal and viridans streptococcal penicillin and quinolone resistance

Dr Michael Tunney, Dr Mary Kearney, Dr Michael Scott, Ms Dorothy Gardiner, Dr Sheila Patrick	Factors influencing the success or failure of MRSA decolonisation
Prof James McElnay, Dr Carmel Hughes, Dr Michael Tunney, Dr Grainne Crealey, Prof Frank Dobbs, Prof Phillip Reilly	A collaborative primary care-based approach to managing upper respiratory tract infections as a strategy to reduce antibiotic prescribing
Prof Rod Hay, Dr Ronan McMullan, Dr Hugh O'Neill, Dr Hugh Webb, Dr Sara Hedderwick, Dr Brian McCloskey	The impact of quantitative molecular diagnosis of invasive candida infection on antimicrobial drug prescribing in a regional intensive care unit

NIPEC Commissioned Research Programme

The Northern Ireland Practice and Education Council for Nursing and Midwifery (NIPEC) approached the R&D Office to assist in the commissioning of the two research projects to inform the Development Framework.

Successful Applicants	Title
Professor Vivien Coates, Mr William Kelly	An evaluation of approaches to assess nursing and midwifery performance
Professor Hugh McKenna, Miss Felicity Hasson, Mrs Sinead Keeney, Professor Brenda Poulton, Dr Marlene Sinclair	An exploration of innovative nursing and midwifery roles within Northern Ireland's HPSS

RESPONSIVE MODE RESEARCH

Ireland-Northern Ireland Co-operation Research Project Grants

Applications for the sixth round of this scheme were evaluated in June and July 2004. A total of three new grants were awarded.

Clinical & Health Related Basic Science

Northern Ireland Partner	Ireland Partner	Title
Williamson, Dr Kate	Dr Amanda McCann	The significance of S100A4 and other novel candidate EMT markers as key modulators of the metastatic phenotype of TCCB
Jordan, Dr Grant R	Dr G. Jane Farrar	Gene Therapy for Osteogenesis Imperfecta

Health Care Services Research

Northern Ireland Partner	Ireland Partner	Title
Murray, Dr Liam	Dr Harry Comber	Factors underlying differences and trends in PSA testing, biopsy and prostate cancer incidence in Ireland 1994-2003

DISSEMINATION & UPTAKE

Cochrane Systematic Review Courses 2004

The R&D Office continues to liase with the Health Research Board in Dublin and UK Cochrane Centre. A total of four courses on Cochrane Systematic Reviews were held in Ireland and Northern Ireland and the R&D Office funded 24 places in total during 2004.

Limerick Course
Mr Gavin Davidson
Ms Fenglin Guo
Mrs Fan-Ko Sun
Mrs Darian Shotton

Cork Course
Dr Barry Kelly
Ms Catherine Baird
Dr Lawrence Taggart
Mrs Suzanne Martin

Dublin Course
Mr William Robert Graham
Dr Sheila Lennon-Fraser
Miss Amanda Black
Ms Patricia McAllister

Belfast Course
Mr Jonathan Malloy
Miss Marian Traynor
Dr Emma Larkin
Ms Bernadette Lyons
Mr Martin McAnespie
Ms Lucia Jackman
Ms Eileen Dolan
Mr Seamus Dolan
Ms Iseult Wilson
Professor Deirdre Walsh
Mr Jeffery Campbell
Dr Greg Kelly