Joint Research Councils Research Complex (Diamond) and infrastructure programme: Science Case

THE CASE FOR BUILDING A RESEARCH COMPLEX AT THE RUTHERFORD APPLETON LABORATORY (RAL) TO SUPPORT DIAMOND

Executive Summary

A new synchrotron radiation source, Diamond, is being built at the Rutherford Appleton Laboratory (RAL). This paper puts the case for a new research building providing approximately 5000m^2 of laboratory and office space to be built alongside Diamond. The main purpose of this Research Complex will be to create a vibrant research culture on the site and allow the development of a leading multi-disciplinary centre of scientific excellence, maximising the opportunities for research provided by Diamond, ISIS and the Central Laser Facility. The building is intended to provide facilities for both life and physical sciences, to be used by research groups based there long-term and by short-term visitors working on site while using Diamond, ISIS or other shared facilities. On-site facilities will allow the development of a critical mass of life sciences research addressing technically challenging questions that will benefit from co-location with Diamond. Physical scientists will be able to use Diamond and the other facilities to undertake experiments of far greater technical complexity if they are not restricted by the need to prepare samples in their home laboratories and transport them to the shared facilities. The building will also provide facilities for beamline scientists to develop their own research programmes, and the connection thus promoted between technology and scientific discovery will drive technical innovation at Diamond and ensure that the technology is driven by the need to solve fundamental scientific questions. The proposed Research Complex will also promote interdisciplinary collaboration and the synergy between the neutron, laser, synchrotron and solid state nuclear magnetic resonance facilities on the RAL site.

1. Background

Diamond is a third generation synchrotron radiation (SR) source under construction at the Rutherford Appleton Laboratory (RAL) site in Oxfordshire. It is jointly funded by the Office of Science and Technology (via the Council for the Central Laboratory of the Research Councils (CCLRC)) and the Wellcome Trust. Diamond will provide world-leading SR beamlines for studies of the structure of matter, to be used by scientists in a wide variety of scientific fields including biology, environmental science, materials science, physics, chemistry and engineering. The very high brightness of the insertion devices will allow UK users to probe the structure of materials at new levels of spatial and time resolution, and at extremes of pressure and temperature, and to gain new insights into the structure and function of biological macromolecules. The RAL site is also home to other facilities used in different ways to study structure at the molecular level, namely ISIS (the UK neutron spallation source), the Central Laser Facility and the National Solid State Nuclear Magnetic Resonance Facility. In many fields, for instance engineering and materials science, studies of matter under extreme conditions, pharmaceutical and energy research, and hard condensed matter physics, scientists already use both X-rays and neutrons, and one important reason for deciding to build Diamond at RAL was to promote synergy between Diamond and other facilities on the site. The building of Diamond and the second target station at ISIS offers an important opportunity for the UK to develop a flagship centre supporting leading-edge research in structural science at the RAL site. Together these two projects will represent the biggest investment ever (>£500m) in new large scale facilities in the UK, and it is imperative that the necessary infrastructure is in place to ensure that UK science can make the best possible use of them.

2. Objective and outline of the Case

The core objective of this programme is to deliver a multidisciplinary centre of international scientific excellence to maximise the research capability and scientific opportunities afforded by Diamond and the other facilities at the Rutherford Appleton Laboratory site. To achieve this end the proposal is to build a new research complex on the RAL site adjacent to Diamond and to provide essential infrastructure such as hostel accommodation and improved catering facilities for visiting and resident scientists. This document sets out the case for the Research Complex – the case for other essential infrastructure will be put in a separate document.

This document first describes the needs for the life sciences (section 3) and the physical sciences (section 4). Following consultation with potential users, it is clear that the two branches of science require slightly different usage from the Research Complex. In the life sciences there is a need for long-term research groups based on the RAL site that can establish a research area and provide a lead for others. These groups will form a focus for shorter-term researchers and visitors and for the research of the beamline scientists. In the physical sciences there is a need to provide medium-term support for visiting groups in order to establish robust facilities for sample preparation and experimentation and also to allow for beamline scientist research. Options considered to meet these needs are outlined in section 5. The vision for the Research Complex is to provide an interdisciplinary centre housing both the life sciences and the physical sciences, promoting interaction between the two. This is described in more detail in section 6. Subsequent sections deal with infrastructure, timing and funding.

3. The requirements for the life sciences

3.1 Experience at other synchrotrons

Experience at other synchrotrons around the world has shown that research facilities close to the source have allowed visiting and resident research teams to achieve remarkable advances, benefiting from close collaboration with the beamline scientists and other technical experts at the facility. Life sciences research centres have been established at many synchrotron sources including for example ESRF, Grenoble; DESY, Hamburg; SSRL, Stanford; CHESS, Cornell; NSLS, Brookhaven; APS, Argonne; Photon Factory, Japan; Spring8, Japan. At SSRL there has been a 25 year association between the synchrotron and structural biology which has led to a co-ordinated and integrated programme between research scientists and beamline scientists to the benefit of both. At Grenoble four laboratories - the European Synchrotron Radiation Facility (ESRF), the European Molecular Biology Laboratory (EMBL) Outstation, Institut Laue-Langevin (ILL) and the Institute for Structural Biology (ISB) - have recently come together to create a Partnership for Structural Biology (PSB) with a new building and research programme. CHESS, Cornell has founded MacCHESS with a remit to promote high throughput structural biology and with a core research programme on important biological topics supported by NIH. In Japan groups of about 30 scientists have been established at the Photon Factory. At Spring8 the Riken Harima Institute houses some 200 scientists, including a dedicated structural biology institute and a high throughput protein crystallography factory.

The presence on site of leading edge research teams tackling demanding research problems and interacting closely with the beamline scientists has driven technical innovation. Key advances have come from such teams. For example in structural biology, researchers at the EMBL Outstations at ESRF, Grenoble and DESY, Hamburg contributed to work which led to the image plate detector, microcrystal data collection and the microdiffractometer, high resolution high precision protein crystallography, automatic methods for electron density map interpretation and the development of small angle X-ray scattering software. An early highlight was the use of the microfocus beamline at ESRF by the group at ISB, Grenoble to determine the first X-ray crystal structure of the membrane protein bacteriorhodopsin with very small crystals.

3.2 The benefits for the life sciences of a Research Complex at RAL

For the life sciences, a Research Complex would complement the significant investment at the Diamond synchrotron. Diamond will provide three macromolecular crystallography beamlines in year 1 (January 2007). Macromolecular crystallography will be further strengthened in Phase 2 with the addition of a micro-focus beamline for examination of very small crystals and a fixed wavelength side station. A sixth beamline for long wavelength (~2 Å) anomalous scattering, which will allow almost automatic structure determination, is under consideration. Also in Phase 2 there will be a non-crystalline diffraction beamline allowing studies on biological fibrous proteins and solution scattering, a circular dichroism beamline for analysis of protein folding, and an infrared spectroscopy beamline for characterisation and diagnostics. There is currently very little life sciences research on the RAL site, with the notable exceptions of the National Solid State Nuclear Magnetic Resonance Facility and, at the adjacent Harwell site, the MRC Radiation and Genome Stability Unit and the MRC Mammalian Genetics Unit. In order to exploit the maximum potential of Diamond and the other RAL facilities for life sciences research, it is important to develop a critical mass of life sciences research programmes at RAL.

The aim of the Research Complex will be to promote the connection between technology and scientific discovery and to provide the research space for cutting-edge biology research programmes together with the beamline scientists and other Diamond scientific staff. The synchrotron is not simply a tool, albeit an important one, for others to exploit but should also be leading in new discoveries. Facility staff, who deliver in an effective and efficient manner the required beam conditions and ancillary devices to enable experiments to be performed by an external academic community, are also in a unique position to understand the ultimate capabilities of their tools. The user community benefits if beamline scientists spend a proportion of their time on their own research programmes (which also promote technical innovation at the facility). Diamond wishes to offer its beamline scientists access to space and facilities for research in order to attract the highest quality staff. The small laboratories around the ring will not provide the space, high quality specialised equipment and facilities needed to sustain a research programme.

External users of synchrotrons in the life sciences are interested in the fundamental questions of biology. Macromolecular crystallography has been enormously productive in providing structural solutions that give insights into basic biological phenomena and which have been exploited for medicine. Productivity has been primarily the result of technical advances at synchrotron sources combined with protein expression, purification, crystallisation and software development. Macromolecular crystallographers for the most part see themselves and are seen by their peers as immunologists, cancer researchers, virologists, cell biologists, enzymologists, chemists and so on. The field has moved from a technique driven field to one that is asking fundamental biological questions. In the age of high-throughput structure determination, it is even more important that the right biological questions are asked. Many technical advances have come from laboratories trying to solve a particular biological problem. In the future much more data collection for macromolecular crystallography will be carried out remotely with users sending crystals. This will remove from Diamond a source of wider scientific interaction that comes from visiting research groups. Given this, it is even more vital that there are local life scientists. The Research Complex will ensure that the science is not driven by technology; rather, the technology is driven by the need to answer fundamental scientific questions.

3.3 Organisation in the Research Complex for the life sciences

We envisage a significant number (5-8) of long-term research teams based in the Research Complex, the major research endeavours of which will be in the exploitation of synchrotron radiation and the other facilities hosted by CCLRC at the RAL site. Scientists of international standing will lead these teams, and the work will focus on technically challenging problems. Some of the research team leaders will have joint appointments between Diamond or RAL and a University. Their research programmes will be funded by programme grants or other medium- or long-term funding mechanisms, gained in the normal competitive process. Some of the groups in the Research Complex may be part of larger teams based in University departments.

Alongside the larger, long-term groups will be younger scientists, seeking to establish their independent research careers with a period of time focused exclusively on research. These will be supported largely by fellowships from the Research Councils, the Royal Society and charitable research funders. The Research Complex will also provide an exciting environment for PhD students, working under the supervision of those with joint appointments with Universities.

Members of the Diamond scientific staff, whose research may be either internally or externally funded, will be provided with appropriate space in the Research Complex to develop their research programmes. By working alongside or in collaboration with the long-term groups maximum benefit can be obtained both for future development of the beamlines and for scientific advances.

The core capabilities available on the site will influence the teams of scientists visiting it for the new, ground-breaking studies. Some of the most exciting beamtime applications usually rely on the ‘local flavour’, i.e. research focus developed at a particular site. Such developments will be encouraged and supported systematically within Research Complex. Some visiting life scientists coming to use Diamond or the RAL facilities are likely to require more extensive laboratories than can be provided around to the synchrotron ring. In macromolecular crystallography, there is likely to be increasing use of frozen crystals shipped to the synchrotron and mounted there on the robot sample changer, screened and data collected mostly automatically, with users interacting in real time with staff to assist data collection and analysis. The user will then wish to ask functional questions such as: Has phase determination been successful? Has the ligand bound? If not, why not? Has the protein been damaged by radiation? Does the state of the protein in the crystal need to be characterised by mass spectrometry or visible spectrometry? Should cryo-conditions be improved? Are new additives or detergents required to improve crystallisation? Does controlled dehydration improve crystallinity? Should a new crystallisation strategy be devised? The user can address these questions on-site if access to appropriate facilities is available in the Research Complex. The ability to answer these questions will greatly speed up the time between design of an experiment and the delivery of biologically significant results.

Discussions are in progress with Professor D. I. Stuart and the MRC with a view to moving part of the MRC funded Oxford Protein Production Facility (OPPF) to the Research Complex. The synergistic partnership between a dedicated protein production and crystallisation facility and the Diamond Light Source would enhance the capacity for high-throughput protein structure determination and underpin biological science at Diamond. The facility, once functioning, would offer an expert service or technical advice to groups wishing to undertake protein structure determination using Diamond, engage with beamline scientists and provide a pipeline of suitable crystals.

Advanced data-processing facilities for interpretation of results will be provided at the beamlines but there is also a requirement for high-performance computing facilities available on site that would enhance the computational experimental capability and encourage software development. There would be a considerable advantage in locating the BBSRC funded Collaborative Computational Project in Protein Crystallography No 4 (CCP4), currently located at Daresbury, in the Research Complex. CCP4 has played a crucial role in the development and distribution of software for macromolecular crystallography. Relocation of CCP4 to the RAL site, should that be the wish of those concerned, would facilitate interactions between those involved in program developments and the end-users, both scientists working at the Research Complex and visitors, to the benefit of both. This has the potential to create a world-class nexus of technology and science in structural biology. The automation of computational tasks sited alongside the high throughput biological work would be a unique feature of Diamond. However, as with OPPF, the case for moving CCP4 to Diamond is dependent upon a strong research culture being established at the Research Complex. Similarly it is already intended that part of the Collaborative Computational Project No 13 in Fibre Diffraction and Solution Scattering (CCP13) will be based at RAL in time for the operation of Diamond. Beamline staff at the non-crystalline diffraction beamline on Diamond and staff at the Large Scale Structures Group at ISIS will interact closely with CCP13 staff for developing software.

The Research Complex should be well equipped and well supported with technical infrastructure for the life sciences, including facilities for bacterial and cell culture, ultracentrifuges, UV spectrometers, bench-top centrifuges and extensive chromatography. In non-crystalline diffraction or in small-angle scattering, wet laboratory facilities are required to prepare fresh samples. At least one 4^0 cold room is required for protein purification, and dedicated rooms with accurate temperature control are needed for protein crystallisation. Crystallisation robots and automatic microscope scanning of crystal trials are required for crystallisation. Mass spectrometry, fluorescence spectrometry and infrared spectrometry are required for characterisation and assays. Such equipment will need technical support to ensure it is kept in optimum working order and to assist inexperienced external users.

3.4 Life sciences research

It is intended that the life sciences research programme within the research complex will focus on major and challenging areas that can best be addressed by proximity to the Diamond synchrotron source. It is not possible to define now exactly what programmes will be developed within the Research Complex. There will need to be flexibility and scope for change as the science develops and as new opportunities open up, and in order to maintain responsiveness to the priorities of funding organisations. Possible programmes to be developed within the Research Complex include:

- Structural studies on membrane proteins.

- The study of large macromolecular complexes
- The study of intracellular signalling proteins
- High throughput functional structural genomics related to disease and enzyme mechanisms
- The development of macromolecular crystallographic technologies, especially addressing the problems of radiation damage and new phasing methods
- Biological imaging.

Research programmes within these areas are described in more detail in Appendix 1. Each of them addresses problems that require innovation and which will provide challenges for beamline development that will benefit the user community. They are all areas of current key interest that focus principally, but not exclusively, on macromolecular crystallography. However, the expectation is that the exploitation of other technologies, such as non-crystalline diffraction, CD, X-ray spectroscopies and neutron scattering and diffraction will also be relevant.

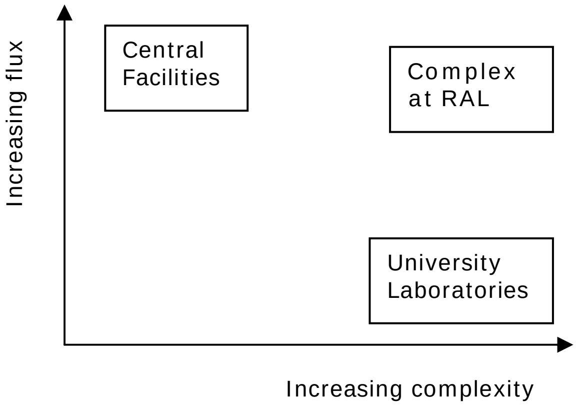
4. The requirement for the physical sciences

4.1 Experience of existing central facilities

Around the world, the principal modus operandi of the front-rank central facilities is one of short-term visits by university researchers that last from a day to a week. Most physical scientists have long become used to limiting their central facility experimentation to what can be done at a distance from, and travelling from, their home institutions. There are countless ways in which this limits the effectiveness, complexity and scope of research. The requirements of complex sample loading, for example, may prevent any modification of an experiment, or a restart should the sample fail, if the necessary loading facilities are based two hundred miles away in a university laboratory. Sample characterisation can commonly only be done before setting off from, or after returning to, the home laboratory thus making it impossible to derive new information that might influence the central facility experiment during its progress. It is also clearly difficult to construct the best and most appropriate complex, experiment-specific facilities for control, manipulation and probing of a sample on a beamline where a series of different experiments, each lasting only a few days at most, are carried out by a sequence of different users.

Thus it is often not possible to carry out at central facilities complete, authentic experiments – in the sense of successfully making complete, definitive measurements where the data required to answer the question addressed are not known, or not completely known, in advance; this is because of these limitations on the options, information and time available to the experimenters. Nonetheless, extraordinarily exciting, effective and novel research is performed on front-rank central facilities around the world, opening up areas of science that are not accessible with laboratory facilities. This largely flows from the very high flux of central facility sources. Indeed, many high-profile results are achieved with relatively simple experimental set-ups that rely on data-rates and data quality that are simply not achievable with laboratory sources. There are, of course, a few examples of some very complex experimental apparatus based at central facilities but, broadly speaking, the best internationally competitive research depends mostly on advanced instrumentation utilising high source flux at central facilities, and mostly on refined experiment-specific sophistication in university laboratories (Figure 1).

Figure 1: Areas of research activity in terms of source flux and experimental complexity



4.2 The benefits for physical sciences of a Research Complex at RAL

There is now a unique opportunity at RAL to take the lead internationally across a wide spectrum of the physical sciences by developing an enhanced exploitation of central facilities to make possible a new generation of experiments that combine high source flux with greater experimental complexity to a far greater extent than has been done hitherto. Visitors using Diamond, ISIS or the CLF will increasingly want to do more complicated experiments, including those that need access to beamtime at several different stages in an experiment, with periods of laboratory work in between, or time to analyse and feed back results from one aspect of an experiment into the preparation of the next stage. A large majority of potential Diamond users in the physical sciences who responded to the consultation exercise envisaged a need to use facilities in the Research Complex, most of them as short-term users while conducting experiments on site. Also, as for the life sciences, Diamond wishes to offer space and facilities for research in order to attract the highest quality physical sciences beamline scientists. Access to space, high quality specialised equipment and facilities in the Research Complex will be needed for them to develop and sustain their own research programmes.

Many users' programmes would be completely transformed by access to high-grade facilities for sample preparation and characterisation, both before and after insertion in the beam. The Research Complex will provide well-found laboratories (equipped to the standard of an excellent university laboratory) for the various areas of science represented amongst the Diamond users and access to the e-science grid. Establishing part of the footprint of university research alongside the central facilities at RAL will create a partnership between the excellence of problem-driven university research and the provision of leading edge central facility instruments. This partnership will benefit a broad range of fundamental and applied physical sciences research from catalysis and chemical processing, to nanoscience engineering, the study of matter under extreme conditions and condensed matter physics, materials synthesis, pharmaceuticals and energy materials. The proposed Research Complex would underpin this far-reaching enhancement in the use of central facilities, and also make it possible for groups to benefit by utilising more flexible scheduling and exploiting multi-central facility opportunities in research.

4.3 The requirements for physical sciences research

It is neither desirable nor affordable to reproduce the whole range of relevant University-based equipment in the RAL Research Complex. But major advances could clearly be very beneficially made in two broad categories:

- Equipment and facilities that would give highly cost-effective benefits to a wide range of central facility science
- Equipment and facilities that would make it possible to carry out substantially more advanced and complex research in selected key areas that would particularly benefit.

In Phase 1 Diamond is hosting physical sciences beamlines for nanoscience, extreme conditions, materials and magnetism and microfocus spectroscopy. In Phase 2 there will be beamlines for non-crystalline diffraction, surface and interface diffraction, surface and interface structural analysis, small molecule crystallography, high resolution powder diffraction, infrared spectroscopy, X-ray spectroscopy and core XAS, and a joint engineering, environment and processing beamline.

Examples of physical sciences research that will exploit these beamlines and the other facilities at RAL, and that will benefit from provision of facilities in the Research Complex, include research in:

- Catalysis
- Chemical processing (synthesis, formulation and polymers)
- Surface and nanoscience
- Engineering
- Matter under extreme conditions
- Hard condensed matter physics
- Drug development and delivery
- Energy research.

Potential approaches and requirements for research programmes in these areas, and the potential impact of high grade on-site facilities, are listed in Appendix 2.

The range of equipment required for the physical sciences covers sample preparation (e.g. chemical preparation, glove-boxes, electro-machining), sample characterisation (e.g. chemical analysis, single-crystal and powder X-ray diffraction, FT-IR and Raman spectroscopy, NMR, calorimetry and rheometry, optical and fluorescence microscopy, nanoparticle characterisation, microhardness) and other complementary measurements (e.g. conductivity, superconductivity and magnetic property measurements). More specialised equipment such as electron and atomic-force microscopes, and diffuse X-ray scattering diffractometers would also be desirable but may have to come at a later stage. In addition the Research Complex will require an infrastructure to support advanced data-processing facilities for interpretation of results, grid-based applications, and software development.

It is envisaged that the equipment listed above will mostly be obtained through responsive mode grant applications to Research Councils, often involving collaborations between University groups, and that effective use of the facilities will lead to a significant number of research-group members being based long-term in the Research Complex. The presence on site of a multi-disciplinary range of leading research teams will create an exciting environment, and create numerous opportunities to tackle challenging complex problems. As the facilities develop, an increasing number of research leaders are likely to be attracted to spend extended periods working on site, and some may be supported through joint appointments between Diamond or RAL and a University. Research programmes linked to the provision and maintenance of Research Complex equipment may be funded by programme grants or other medium- or long-term funding mechanisms, gained in the normal competitive process. The Research Complex would be an attractive base for holders of research fellowships to pursue research programmes that rely on the use of central facilities, and provide an exciting environment for PhD students.

5. Options

5.1 The do-nothing option

The current budget allocation for Diamond includes funding for some laboratory space around the storage-ring to house activities immediately relevant to beamline operation and development. There is no laboratory space currently available on the RAL campus that could accommodate new research teams, allow development of life sciences research capacity or provide space or specialist equipment for visiting users of Diamond to carry out experiments on site. There are also no existing buildings available for refurbishment.

The advantages of providing research facilities alongside Diamond on the RAL site have been set out in sections 3 and 4. Without new research facilities the exploitation of Diamond and the new target station at ISIS will be sub-optimal, and the UK scientific community will not be able to obtain maximum benefit from the very large investment in these facilities.
Specifically, the implications of <u>not</u> building new research facilities at RAL are:

- Lack of life sciences research on the RAL site, leading to an inability to exploit the maximum potential of Diamond and the other facilities at RAL achieve major advances in life sciences research.
- Limitations on the nature of experiments that can be done at Diamond and ISIS to those which can be prepared in a home laboratory and transported to RAL. This would significantly reduce the scope of work that could be done using the facilities.
- Limitations on the level of complexity of experiments achievable at RAL compared with University lab-based science. This would be a critical limitation preventing Diamond achieving its maximum potential in the physical sciences.
- Limitations on the scope for conducting open-ended experiments as against data collection.
- Inability to establish an on-site facility for high-throughput protein production and crystallization, leading to less efficient usage of the beamlines for protein structure determination.
- A lack of space for beamline scientists to do their own research, leading to difficulties in recruitment and retention of high-calibre staff for Diamond and ISIS.
- A limited capacity for activities to promote synergy between different facilities at RAL, leading to an inability to realise the potential afforded by co-location of the facilities.
- The danger that Diamond would develop a “service-only-facility” culture, making it more difficult to remain at the forefront internationally.
- Difficulty for Diamond and ISIS staff to develop close working activities with users.
- Lack of the science capacity on site needed to provide the high level technical support for a remote operation/Fedex service for more routine data collection in the future.

- Less efficient use of beamtime. On-site research teams can use "spare" time arising from cancellation or rescheduling of experiments at short notice.

5.2 The proposed solution

In developing the proposed solution, the Programme Board consulted widely with members of the Synchrotron and ISIS user communities, via a workshop, questionnaires and discussion at the Synchrotron users meeting (see Appendix 3).

The unanimously favoured model is to build a single Research Complex, housing teams (including those led by Diamond staff) funded from multiple external sources through competitive mechanisms, alongside shared facilities for short-term users.

The advantages of this approach are:

- Co-location of research teams in different disciplines in a single building would promote interaction and inter-disciplinary collaborations. Shared facilities would promote interaction between short-term visitors, and between visitors and resident research teams.
- A shared building would promote a problem-focused (rather than a technique-focused) culture.
- Funding via competitive mechanisms ensures research in the building stays at the leading edge and that some turnover can take place where appropriate to accommodate exciting new research areas. It also provides considerable flexibility to funding bodies to vary their funding commitment up or down in line with demand from their research communities.
- This model provides opportunities for University-based researchers to expand their teams into space in the Research Complex and benefit from co-location of members of their research teams alongside the facilities.
- The Complex would provide opportunities to foster close collaboration between the facilities and HEIs via joint appointments.

Possible disadvantages with this approach include:

- Uncertain funding streams could lead to inefficient use of space.
- Possible difficulties in providing stable technical support for shared facilities and equipment and a suitable career structure for technical staff.

5.3 Other possible options considered

Two other possible models were considered for provision of research facilities on the RAL site.

5.3.1 A large joint Research Council funded research institute.

The key feature of this option would be concentration of UK research using neutron and SR beams on the RAL site.

<u>Advantages of this approach would be:</u>

- Concentration achieves critical mass and a high level of interaction between scientists using the different facilities at RAL.
- Scientific leadership and vision would best come from a single director.
- An institute would provide stable funding and clear career structures for in-house research teams and support staff.
- An institute could have a budget for resourcing technical support for shared facilities for short-term visitors.

<u>Disadvantages</u>:

- For the supporting Research Councils this would represent a long-term high-level funding commitment, with a lack of flexibility to re-focus

- research programmes to take advantage of new opportunities in emerging research areas.
- Concentration of research at RAL would challenge universities' role in leading creative thinking.
- Concentration would be perceived as a threat by university-based scientists as it would reduce responsive mode research funding available
- Universities are likely to be opposed because of implications for Research Assessment Exercise (RAE) ratings of a shift from indirect to direct support.
- Managing a jointly funded Institute to cater adequately for all the sponsoring Research Councils' needs would be difficult. The breadth of the research portfolio would be enormous, from planetary sciences to biology.

5.3.2 Two or more smaller research institutes

These could either be associated with different facilities or focus on different scientific areas, and could be separately funded by different Research Councils.
Advantages of this approach:

- Stable funding and career structures as for a single institute.
- Possible savings in construction costs by having the different facilities required for physical and biological sciences in different buildings.
- Buildings could be physically located close to the separate facilities.

Disadvantages:

- Actively discourages synergy between the different facilities and promotes an inward-looking culture.
- Even greater lack of flexibility to refocus funding over time than for a single institute.
- Greater perceived threat to university-based research.

Neither of these models was favoured in the consultation with the scientific community and the Programme Board considered that the disadvantages outweighed the potential advantages.

6. The vision for the Research Complex

6.1 Research culture and scientific staff

The proposed Research Complex will generate the culture of research at Diamond and the other RAL facilities. A Research Complex, housing a critical mass of research programmes with their international competitiveness assured by their dependence primarily on grant income, will ensure that Diamond produces the greatest scientific impact over its whole life period, and that maximum benefit is derived from co-siting with the other leading facilities at RAL. It will ensure that these large-scale facilities will not only be service providers but also be leading centres for new discoveries. The scientific agenda of the Diamond staff is closely related to the properties and applications of the Phase 1 and Phase 2 beamlines. Because of the input of the Research Councils to the assessment of beamline priorities, this science profile will map on to EPSRC, BBSRC, MRC and NERC programmes and priorities. The Research Complex will provide members of the Diamond scientific staff, whose research may be either internally or externally funded, with appropriate space to develop their own research programmes. In addition to the benefits for the science, the presence on site of leading beamline scientists' research teams, tackling technically demanding research problems, will drive technical innovation at Diamond itself.

The success of the Research Complex will also depend on the quality of research scientists it attracts. A significant number of the major research appointments must be long-term and at senior level in order to create a substantial scientific programme and to give continuity. This is most important for the Life Sciences. There are a number of possible mechanisms suitable for funding salaries for senior staff, including MRC Professorships, BBSRC Special Diamond Fellowships or Senior Fellowships, and Wellcome Trust Senior or Principal Fellowships. Many of these could be joint appointments with or secondments from Universities. This would allow post-graduate students to pass through the facility creating a strong research culture. The notion that staff could return eventually to their home University would create flexibility and allow for change.

The management structure will be key to delivering the vision for the Research Complex and the synergy between the different facilities on the RAL site. This will have to include a mechanism to ensure the needs of all the stakeholders (OST, the Research Councils, Diamond Light Source, users of the facilities and the UK research community in the universities) are taken into account. A management model is being developed by the stakeholders and will be presented as part of the business case for the Gateway 1 review.

6.2 Promoting synergy and interdisciplinary working

One of the most potent reasons for deciding to site Diamond at RAL was the potential for synergy between neutron, laser and X-ray science. The RAL site will be unique: at no other research centre will there be three such world-leading facilities (Diamond, ISIS and the Central Laser Facility) within easy walking distance. The synergy between X-rays and neutrons is well-recognised in parts of the physical sciences programme. In engineering and condensed matter research, some of the best research groups use both techniques. At present the synergy between X-rays, neutrons and lasers in life sciences has not been fully explored. Most X-ray users in the life sciences exploit the phenomenal progress made in crystallography. A major trend in structural biology is the study of larger and more complex systems where the structures of the individual components may already be known. Wide-angle and solution X-ray scattering beamlines are being built at Diamond early in Phase 2. Neutron scattering studies in solution, using contrast matching to identify the contributions from individual components, can give rise to shape determination, which, together with modelling studies, can produce indications of overall topology, relationships between macromolecules and their conformational changes in responses to signals. Such studies will become possible at ISIS when the second target station is completed. In addition the Research Complex will facilitate active links with the space optics, laser optics and microstructure/nanofabrication facilities at the RAL site. The proximity of groups with expertise in a number of disciplines will result in a larger vision for macromolecular assemblies than can be achieved by one technique.

The Research Complex will bring together those working on problems in the Life Sciences and in the Physical Sciences outlined in Sections 3 and 4 and in Appendices 1 & 2. Some of the best and most exciting science is done at interdisciplinary boundaries – areas where physics and engineering, life sciences and materials, chemistry and biology come together. Once Diamond becomes operational, the RAL site will provide a unique staging ground for innovative multi-disciplinary research. The Research Complex will create the scientific culture of multi-facility working where the right people will be placed alongside each other in well-equipped spaces for appropriate periods of time. We envisage that this vision will be realised by drawing together a blend of people prepared to work across the traditional boundaries of science, possibly promoted by joint appointments. Long- and medium-term fellowships jointly funded by the stakeholders (Research Councils and HEIs) will provide the stimulus necessary for this to take place

The Research Complex could also take a wider role in encouraging interdisciplinary science in the UK, by hosting workshops and seminar series in which the aim is to foster discussion between groups that would not normally meet together. These workshop meetings could follow the format of the Isaac Newton Institute in Cambridge in which topics are identified and groups of experts are drawn together for extended periods of time to address and solve difficult problems.

6.3 Interactions with industry

The Research Complex will also provide opportunities for increasing the level of industrial exploitation of Diamond and other facilities at RAL. Researchers working in industry will be using Diamond, and will have access to the Research Complex facilities for short-term visitors in a similar way to academic researchers, thus promoting interaction with other users of Diamond and ISIS. In addition industry could establish collaborations with teams based in the Research Complex or sponsor projects based there, taking advantage of the specialised research expertise that will be developed.

6.4 Contribution to research training

The Research Complex will provide an excellent environment for research training for PhD students in internationally competitive research teams, with exposure to multi-disciplinary working, good access to shared facilities and the opportunity to interact with and learn from the wide range of visitors using the shared facilities. It will also be able to provide facilities for specialised training in new techniques for structure determination or sample preparation developed by researchers using the facilities.

6.5 The building, facilities and equipment

The Research Complex building should be attractively designed, comfortable and spacious and of good quality, rather than merely functional, in order to help attract the best scientists to work there. The new Research Complex will operate over several decades to come and it is important at this stage to make provision for flexibility. Tomorrow's science will evolve according to its own logic, and it is not easy to foresee future requirements in detail. To allow flexibility of use the building must be constructed in a way that allows a range of different uses of lab spaces over time, and the structure of internal walls should allow for re-configuration of space as usage changes. The building should also be designed to encourage multi-disciplinary science. This will require careful planning of offices and meeting spaces in order to provide opportunities for users of the Research Complex to mix and talk.

The building will be equipped to a good laboratory standard for the various areas of science it is intended to support. Some of the equipment highlighted in sections 3 and 4 for shared use could be provided as part of the initial fit-out, but other more specialised equipment will be provided via grant funding as the building is occupied. It will be essential that advanced experimental facilities in the Research Complex are provided with high-level technical support, robustly managed, to ensure that the facilities are kept in optimum working order when being used by a number of different users of varying skills. One way to achieve this would be to place equipment under the care and management of an on-site team that needs the equipment and uses it regularly, this team also having the responsibility of providing access to external users for a certain proportion of the time. In some cases, equipment may in any case be provided for, and reserved to, particular research programmes.

7. Supporting infrastructure

In addition to the scientific facilities, development of appropriate infrastructure on the RAL site is essential to accommodate the increased numbers of visitors and longer term staff that will use the site once Diamond opens. The programme for developing such infrastructure includes plans for good-quality hostel accommodation within walking distance of Diamond and ISIS, improved catering and meeting facilities on the site and upgrades to the basic infrastructure at the RAL site including power supplies, security and access infrastructure. The plans for developing this improved infrastructure are being taken forward in parallel as a separate project.

A housing development is planned on land belonging to UKAEA near to the RAL site. This development is expected to include a proportion of affordable [low cost] housing, some of which could potentially be used for key-worker housing. The UKAEA is undertaking a survey of the residential needs of employers at the campus, including CCLRC and Diamond Light Source Ltd, to inform a planning application for the housing and its subsequent development. Thus, the housing development might contribute to meeting the housing needs of people employed at RAL, Diamond and the Research Complex (and, possibly, the provision of rental accommodation for longer-term visitors). The bulk of the housing is expected to be developed by the private sector.

8. Time constraints

Commissioning of the Phase 1 beamlines is scheduled to start early in 2006, and the first seven beamlines will be available to users at the beginning of 2007. Thereafter commissioning of the Phase 2 beamlines will begin, with new beamlines being added at the rate of four per year, until a total of 22 beamlines are available in 2011. To promote the optimum development of a research culture on the RAL site the Research Complex ideally should be available when Diamond becomes operational or as early as possible thereafter; the window of opportunity is short. If the building is not available within 1-2 years of the start of operation then there is a risk that many of the objectives of Diamond will not be met. In particular, the opportunity to influence recruitment of scientific staff to Diamond and the nature of the research culture that develops at the facility will be lost.

The operational needs of Diamond itself also affect the time window for construction of the Research Complex. During commissioning, and once Diamond is operating, it will be important to avoid vibration in the vicinity of the ring. Therefore, if the Research Complex is to be built close to Diamond, piling and heavy excavation work to dig foundations should ideally take place before commissioning. Otherwise this work might have to be fitted into machine downtime. There are also time constraints on the construction of the Research Complex imposed by other construction activity on the RAL site. As well as the construction of Diamond itself, construction of second target station for ISIS has also started. The construction activity for the Research Complex will have to be scheduled to ensure that the overall operation of the RAL site is not adversely affected.

9. Funds available and estimated costs

The RCUK strategy group has provisionally agreed to allocate a total of £26m from the Large Facilities Capital Fund for essential infrastructure at RAL and the building of a Research Complex. This funding is distributed across financial years as follows:

2004-05	2005-06	2006-07	2007-08	2008-09
£2.0m	£3.0m	£2.0m	£7.0m	£12.0m

Unfortunately the funding presently available does not allow for delivery of a research building until early in 2009, some two years after the start of operation of Diamond. Six million pounds will be devoted to the infrastructure projects and design and planning costs for the research complex in the early financial years, leaving a total of £20m available for the Research Complex building itself.

Consultation with potential users of the complex and the Research Councils indicates that the optimal size of building required will be approximately 5000 m^2 usable space, of which 4000 m^2 would be for laboratories and the rest for offices, meeting rooms etc. This estimate is made up as follows:

User	Lab space (m^2)	Office/Other space (m^2)	Notes
EPSRC	300	90	Long term groups: physics, chemistry, materials science
NERC	400		Shared inorganic geochemistry, microbiology/geochemistry equipment and space
BBSRC	500	200	3 long-term groups
MRC	700	200	Protein production facility and life sciences groups
Diamond staff	300, rising to 600 by 2010	40, rising to 70 by 2010	Increases with Diamond scientific staff complement
CCLRC	1000	60	All scientific areas
Shared use for visitors	500		Shared equipment and general lab space for short term users (physical & life sciences)
CCP4 & CCP13		80	Small number of collaborative computing project staff.
General		300	Library, meeting & seminar rooms, coffee rooms, washing up & media prep

Based on the cost of current research building construction projects and advice from quantity surveyors the estimated budget for a building of this size is £23m at January 2004 prices. This estimate includes construction cost, design management and planning fees for a good quality building with some flexibility, and basic laboratory equipment. However, it does not allow for inflation and VAT. Inflation in building costs is running at approximately 4% per annum, so for completion in the first quarter of 2009 an additional £2.7m should be allowed for inflation. VAT at 17.5% would add a further £4m to the cost. Advice is currently being sought on how to minimise non-recoverable VAT. Provision of fully flexible space that can be used for either physical or life sciences during the building lifetime would be desirable to allow usage of the Research Complex to adapt to scientific demand, but the likely cost per square metre would be higher.

Thus a fully fitted out building of the optimum size and specification is clearly not achievable within the funding presently available. £30m would be a more realistic budget if VAT is payable and cannot be recovered. Options for filling the funding gap are to seek capital contributions to the cost of the building from the Research Councils involved, or to seek funds from a private source (a company or a foundation). The Research Councils are not likely to wish to put substantial amounts of capital into this building, as they see their major contribution to the overall enterprise being the funding of research programmes and specialised equipment within the building. An alternative option would be to reduce the size of the building and build to a lower specification, but if the building were too small the objectives of encouraging interdisciplinary working and building up a critical mass of research activity would not be met. A third option would be to build the shell of the building and only partly fit it out to start with. The remainder of the building could then be fitted out in the 2009/10 financial year, when additional money might be available from the Large Facilities Capital Fund. If not, research councils or other organisations sponsoring the research might be willing to contribute to fit out costs, but this option carries with it a risk that the building will be unattractive to users and research sponsors would be unwilling to pay the fit-out costs. These options will be explored in more detail in the business plan.

Appendix 1: Life sciences research programmes that could benefit from location in the proposed Research Complex.

1. Structural studies on membrane proteins.

Membrane proteins are a supreme example where more effort is needed for structure biology. The results of various genomic projects have shown that approximately 30% of proteins (about 10,000 proteins) encoded by the genes in eukaryotic cells are membrane proteins. Of the 23,000 structures in the Protein Data Bank, about 80 are unique membrane proteins. In order to understand the basic cellular phenomena of signal transduction, the generation of electrical signals, molecular transport and energy conservation (respiration and photosynthesis) more structural research is necessary. A survey some years ago indicated that of the validated targets for therapies, some 50% were membrane proteins. A very large number of these are G protein-coupled receptors. Membrane proteins are therefore of key interest to the pharmaceutical industry. Membrane proteins are notoriously difficult to work with. Expression, solubility, and crystallisation pose problems but these are beginning to be addressed. Groups promoting membrane protein research on site would be able to lead the UK in methods for preparation of membrane protein crystals sharing their expertise with the community. A particular problem with membrane protein crystallography is the poor diffracting quality of the crystals due to the large solvent content. This requires ready access to a synchrotron. Diamond could foster and promote this important area by providing excellent X-ray facilities adjacent to the biological laboratories. Many conditions must be explored requiring innovations with solubilising detergents, lipid micelles and cryoprotectants. Ready access to Diamond would allow rapid turnaround between design and execution of experiment and interaction with beamline scientists for optimal design of optics and diffractometer for weakly diffracting crystals. The UK has a good critical mass of scientists in this field, and research in this area would build on current initiatives both within the UK and within Europe.

2. The study of large macromolecular complexes.

In recent years structural studies on large complexes (e.g. the nucleosome, the proteasome, the ribosome, RNA polymerase and viruses) have been enormously informative on how macromolecular assemblies can result in complexes whose functionality is greater than the sum of the parts. Now that it is possible to reconstruct many biological processes in cell-free systems in the laboratory, it is clear that the central processes in a cell are driven by highly co-ordinated, linked sets of protein machines and assemblies. Knowledge of these is needed in order to obtain a more complete understanding of cellular processes (e.g. the anaphase promoting complex for recognition of proteins for destruction, the pre-replication complex for initiation of DNA replication, the complete assembly of transcription factors such as TFIIH for regulation of transcription). Such work requires skill and dedication for production and purification of complexes, which may be only transiently stable, and a combination of methods in addition to crystallography such as neutron and X-ray scattering and electron microscopy. The crystallography is challenging. In the study on the 30S ribosome complex approximately 500 crystals were tested in order to provide about 30 crystals that were suitable for high-resolution data collection. Scientists in the Research Complex working with such challenging problems would be able to achieve a quicker turnaround to scan suitable crystals, and also be able to lead the community in developing automatic methods for scanning, evaluation of diffraction quality and approaches to improve success rate. This field leads naturally to synergies with neutron and X-ray solution scattering methods. Sometimes the whole complex proves intractable to crystallisation but knowledge of the structures of the individual components can inform significantly the results from solution scattering data. Solution scattering can show the overall shape of the complex. Selective deuterium labelling combined with solvent contrast matching methods can allow information of the locality of individual proteins in the complex. Further in solution the response of the complex to ligands, activators and inhibitors can be monitored in ways that are not always possible in the crystal lattice.

3. The study of intracellular signalling proteins.

Proteins and protein machines interact with other sets of macromolecules, creating a large network of protein/protein and protein/nucleic acid interactions throughout the cell. To understand the cell, one will also need to analyse these interactions. Large-scale screening efforts are underway to map these interactions and these suggest that an average protein in a human cell may interact with between five and 15 different partners and some with as many as 100 other proteins. In recent years there has been considerable progress in understanding the structures of the key players in intracellular signalling mechanisms. Structures of GDP/GTP exchange proteins, adaptor proteins, protein kinases and protein phosphatases have illuminated mechanism of molecular recognition and regulation. The structures of transcription factors and their DNA complexes show how the signal can be conveyed to the nucleus for regulation of DNA. For some pathways, representative structures of the individual consecutive proteins are known such as the Ras, Raf, Mek1, Erk2 pathway, the pathway that regulates cell growth and which is perturbed in many cancers, especially colon cancers. The question now is how do these proteins recognise each other? What role does sub-cellular localisation and scaffolding play? The problems for the future address the specificity of these pathways and how cross-talk can in some circumstances be prevented and in others exploited. In cascade signalling we need to understand the complexities of how one enzyme recognises another, in many instances through surfaces outside the catalytic site, and how scaffolds can both provide localisation and specificity. As with the study of large macromolecular complexes, we see advances in this area coming not only from macromolecular crystallography but also other X-ray methods such as non-crystalline diffraction and other physical techniques available on the RAL site.

4. High throughput functional structural genomics related to disease and enzyme mechanisms.

Enzymology is one of the areas where life sciences meet chemistry and falls under the broad banner of chemical biology. Enzyme mechanism driven by structural biology has long been one of the UK's great strengths in chemistry (Whitesides Report). The UK pioneered studies of enzymes such as lysozyme and chymotrypsin. The fascination to the chemist is the way in which nature has evolved strategies to make and break bonds that have served as a guide to new chemical strategies. For the biologists enzyme mechanism not only provides insight into a particular biological problem but it is also part of rational drug design. The convergence between chemistry and biology has been driven by several factors. Improvements in expression technology have meant that targeted proteins are no longer unattainable in the quantities needed for structural studies. This has opened up complex biosynthetic pathways to detailed analysis by chemists. As resolution has improved with synchrotron data, much more detailed chemical questions about enzyme mechanism can be asked and answered. The ability accurately to place atoms of substrate and atoms of the enzyme has led to a much deeper understanding of chemical processes. Notable examples are the high-resolution studies of chitinase, glycosyl transferases, cellulases and isopenicillin synthase. As tunable sources have become widely available, and the computational effort has simplified, biological scientists can now solve an entire pathway of enzymes rather than single enzymes. Recent examples of complete pathways undertaken in the UK are the pantothenate biosynthetic pathway and rhamnose. Underway at the moment in the UK is a structural characterisation of the non mevalonate biosynthetic pathway, a new and exciting antibacterial and anti-parasite target. Structural enzymology has seen the description of DNA replication and repair machinery and identified the mode of action of the front-line anti-tuberculosis drug isozionid. Natural product chemists have turned to studying how biology makes molecules in an effort to harness this biosynthetic power; again, the UK has made important contribution in this area including penicillin and clavulonic acid. The advent of higher throughput expression technologies, continuous improvement of computational technologies, a new high intensity synchrotron source and increasing interest in chemical biology should herald a golden opportunity for Diamond to lead in this field. This work will be strengthened by facilities such as circular dichroism and solution scattering, which provide complementary information to that of X-rays. Whilst each has its own strength as a field of study, both techniques can operate in a service mode, and are very useful for identifying mis-folded proteins and in designing of constructs for crystallisation. Bringing together technologies in the Research Complex promises significant scientific advances; it is also an area where physical sciences and life sciences interact.

5. The development of macromolecular crystallographic technologies especially addressing the problems of radiation damage and new phasing methods.

Radiation damage has become a key factor in limiting the precision of macromolecular data-collection at third generation synchrotron sources. Cooling crystals to liquid nitrogen temperatures can significantly alleviate radiation damage, but advantages in reducing temperatures below that of liquid nitrogen have still to be evaluated. Improvement in data-collection efficiency through use of optimal geometry and absorption corrections and with a focus on detector development is likely to yield considerable benefits. There are exciting possibilities with new solid-state pixel detectors that are under development. The use of free radical scavengers has had success for certain individual proteins and this chemical approach needs to be developed further. There is likely to be a need to update data-processing software following detector development and different recording geometries. Modelling, using molecular dynamics simulations, appears to be a useful way forward in understanding the local and longer-range effects of radiation damage. Advances in this field will come from those working in close proximity to the synchrotron and from those with computational and theoretical skills in radiation physics. The proximity to the MRC Radiation and Genome Stability Unit should allow productive collaborations.

6. Biological imaging.

This area addresses long-term developments in the field of structural biology and future beamline constructions at Diamond. New methods of imaging are under development, which complement the existing powerful optical confocal microscopy and electron microscopy methods. Structural biology will soon seek to understand larger macromolecular aggregates, such as components involved in cell division (e.g. the kinetochores, centrosomes, the mitotic spindle) or those involved in DNA replication and translation (e.g. the spliceosome) and the imaging of sub-cellular components in greater detail. Macromolecular crystallography can define the structures at atomic resolution but the larger complexes are unlikely to be crystallisable. Currently X-ray imaging using tomography can achieve 60 nm resolution and electron tomography (in the hands of the most skilled exponents) can achieve 5 nm resolution. Exploitation of the coherent X-radiation produced by undulators on low-emittance sources (such as will be available at Diamond) has allowed direct imaging of single particles (e.g. an E. coli bacterium) using over-sampling methods for direct phasing. Radiation damage is a critical feature in all methods. As the field progresses, imaging sub-cellular structures would provide a vision for the future where scientists in the Research Complex would have a unique opportunity to develop methods.

Appendix 2: How physical sciences research programmes could benefit from access to the proposed Research Complex.

1. Catalysis

Researchers in the UK have pioneered the use of 'in situ combined techniques' in the search for understanding of existing catalysts and in the pursuit of novel catalysts. They are forced to do this because many important catalysts are complex heterogeneous materials, the behaviour of which is greatly affected by subtle details of the method of sample preparation. Success rests upon a strategy whereby data from many techniques are combined, and this strategy depends upon ensuring that the results are gained from samples in the same state. In almost all current experiments there is a temporal and spatial gap between sample preparation and characterisation. The Research Complex will make it possible to bridge this gap, via the development of 'experiment modules'. These would permit offline pre-preparation, characterisation and alignment followed by transport directly to the beamline under active conditions, in a state for immediate structural analysis. It will also be possible to develop high-throughput X-ray characterisation techniques for catalysis. This work is of strategic importance for the UK catalyst community, and it makes sense to develop this in the only place where it can be exploited. One goal of catalysis is to shorten the development cycle. There is a challenge and also opportunity to increase the throughput of catalysis research by an order of magnitude. This research will be greatly promoted by the three X-ray spectroscopy beamlines scheduled to be built at Diamond.

2. Chemical processing

There are two aspects of chemical processing that have a large potential to benefit from on-site facilities for preparation and characterisation of samples – synthesis and formulation. Polymer research is a third area, which would also benefit. The provision of spectroscopy (FT-IR, Raman and perhaps even split-coil NMR) and thermal analysis (differential scanning calorimetry and rheometry) in an on-site laboratory, with the option to port these techniques onto beamlines, would allow a much wider range of chemical processing research to be done. The very process of chemical reactions in solution, such as the production of minerals or drugs, can be studied by combined spectroscopy and diffraction with the important caveat of the need for other characterisation techniques either in situ or ex situ. The problem of polymorphism is critical in a wide range of industry, including food and agrochemicals as well as pharmaceuticals, and cannot currently be properly tackled. A facility to prepare reactors for transfer to a beamline, or to further characterise materials produced on a beamline, would allow a more exciting range of problems to be studied without the problem of transporting metastable systems back to a university laboratory. Formulation of consumer goods (for example, personal-care products) requires screening of a wide range of variables, and high-throughput capabilities are important. The polymer science community has a strong interest in nano-scale characterisation of materials during processing and a much wider range of nascent morphology development would be enabled through the provision of on-site facilities for ex-situ measurement. The chemical state analysis in the Research Complex would be complemented by analysis on beamlines for powder diffraction, non-crystalline diffraction and X-ray spectroscopy.

3. Surface and nanoscience

The matrix of structural detail and chemical speciation against spatial analysis can be extended greatly with third generation synchrotron sources like Diamond, with some degree of structural detail becoming attainable in the 10 nm – 1µm regime. This is of great importance for studies with surfaces and nanoscience. The ability to manufacture and probe systems at the nanometre length scale will address fundamental questions such as behaviour at the quantum/classical boundary and macroscopic quantum effects. These are important for long-term applications such as quantum computing and data storage. Many existing limits on the performance of industrial materials can be overcome by using nano-structured assemblies, for example, thin films made from pre-formed mass-selected nano-clusters that can be deposited in conjunction with a matrix. The field is developing rapidly and encompassing emerging technologies such as heterogeneous chiral catalysis and sensors for genomics and proteomics research. New facilities are needed to support the UK research programme and encourage future technological advance. The Research Complex would contribute as a focus for research in this area, in parallel with beamline developments which will provide the UK with access to high-resolution X-ray photoelectron microscopy and those for diffraction studies on surfaces and interfaces.

4. Engineering

High-energy synchrotron radiation is a unique tool capable of real-time, high-spatial resolution mapping of the performance of real components and assemblies in complex environments over timescales ranging from months to milliseconds. To obtain information of true engineering value, it is essential that appropriate experimental conditions be delivered in situ. This requires a collaborative effort between instrument scientists, materials scientists, engineers and industrial teams and involves a great deal of planning, investment and cooperation. The Research Complex would provide the infrastructure to support the development of new and exciting experiments. In particular, it would provide facilities for additional characterisation by conventional methods required before or during experiments for fully effective research, e.g. microhardness, off-line X-ray diffraction, optical microscopy, coordinate measurement, electro-discharge machining. Also, advances in X-ray imaging are attracting a whole new community of engineers with no experience or expertise in synchrotron radiation and, at present, our inability to process quickly the mass of data being collected means that it is impossible to perform fully controlled experiments where the engineer can determine the path of the experiment and interpret the data in real time. Advanced data-processing and visualisation facilities on site would transform the community's ability to exploit synchrotron beamtime fully and optimally. Also, academic and industrial staff could be seconded to the Research Complex for 3-12 months to work on particular projects or to develop particular environments. Facilities at the ESRF have been rapidly expanding the horizons of what engineers can do. The Research Complex at Diamond will enable researchers to go even further and undertake complex experiments under realistic conditions that are difficult to achieve on a fast turnaround facility such as the ESRF.

5. Matter under extreme conditions.

Samples subjected to extremes of pressure and temperature, up to megabars and thousands of degrees Kelvin, often behave in unexpected ways. There may be unexpected reactions with containment materials, a sample may become affected by unintended non-hydrostatic stresses, or the containment might fail. For these and other reasons, it is commonly essential to repeat loading and characterisation of samples to obtain definitive results, and provision for this at central facilities is generally quite limited. Advances in the effectiveness of central facilities programmes have been achieved over the past decade through the Edinburgh University Group's development of on-site specialist facilities at both ISIS and SRS. But these have been limited principally to basic sample-loading, pressure measurement and the capacity to operate with multiple samples. A whole new range of possibilities for richer science would flow from on-site access to facilities for handling reactive and otherwise 'difficult' samples, and facilities for characterisation of samples before and during experiments with (off-line) X-ray diffraction, optical spectroscopy and measurements of physical properties like conductivity. Some of the most adventurous and difficult experiments, such as studying the relationship between pressure and the melting temperature of iron for understanding of the Earth's core, and other extreme geoplanetary studies, will particularly benefit from high-grade on-site research facilities. These and other demanding areas of high P-T research would also be enhanced by facilities for advanced engineering of diamond anvils for pressure cells, in addition to crystal-cutting and -polishing facilities. Another exciting dimension would be opened up by on-site facilities for high P-T growth of novel materials in large-scale presses. This research will be promoted by the Extreme Conditions beamline to be built in Phase 1 at Diamond, but needs these complementary facilities for full exploitation.

6. Hard condensed matter physics.

The co-location of Diamond and ISIS, with their growing portfolio of cutting-edge instrumentation, will make the RAL site one of the premier centres world-wide for scattering from hard condensed matter. However, all the most powerful and state-of-the-art experimental techniques such as X-ray photoelectron microscopy depend on high-quality samples to be effective. This is particularly true for techniques requiring highly specialised samples, such as single-crystal neutron spectroscopy and magnetic X-ray scattering, where the growth of larger and better crystals almost invariably results in major research breakthroughs. Given the crucial importance of crystal growth for this and other fields of research, there is a marked lack of provision for single-crystal samples within the UK, in striking contrast to research institutes in Japan and laboratories such as Ames in the USA - a fact that limits exploitation of the superb scattering facilities available in this country. Increasing competition from overseas X-ray and neutron centres for a limited supply of the highest-quality samples places current and future investments at a significant risk. The availability of on-site facilities for the growth and characterisation of samples specifically designed for X-ray- and neutron-scattering experiments, operating as user facilities and supported by in-house expertise, would address this crucial issue and provide an exciting range of new opportunities for cutting-edge physics research at Diamond and ISIS. Even more advantage would flow from complementary on-site facilities for the characterisation of sample structure, microstructure and properties.

7. Drug Development and Delivery

The process of drug discovery is the mainstay of pharmaceutical industry, delivering new chemical entities with both novel and targeted properties. The 'high-throughput' macromolecular crystallography and the small molecule crystallography beamlines at Diamond will greatly assist optimisation of lead compounds against validated targets. Use of these beamlines is eagerly awaited by pharmaceutical industries in the UK. Our ability to complement the pharmaceutical industries R&D effort on problems of drug development (i.e. physicochemical and analytical problems) would be greatly assisted by the creation of a 'pre-formulation' laboratory on-site for the preparation and characterisation of solid-state samples prior to measurements at Diamond or ISIS. Innovation in this area is often not led by industry; for example, the revolution in the use of powder diffraction for complete structural characterisation within the pharmaceutical industry has its origins in research carried out at universities and facilities. Likewise, fundamental studies of the phenomenon of polymorphism have been carried out mainly by academics such as the Basic Technology ‘Control and Prediction of the Solid State’ initiative in which CCLRC scientists have a prominent role. The results have industrial benefits in application areas such as crystallisation, tableting and stability testing. On-site preparative facilities allow us to innovate in problems of drug delivery, such as characterisation of drug-loaded nanoparticles and microspheres. These ‘pre-formulation’ and ‘formulation’ laboratories will generate new materials, data and results in fundamental research areas that go well beyond the focused scope of pharmaceutical industry.

8. Energy research.

One of the key socio-economic challenges that will dominate the first half of the 21st century is the development of a low-carbon economy. Hydrogen storage and production, fuel cells and batteries will all play a crucial role in our decreasing dependence on fossil fuels as an energy source. Central facilities such as Diamond and ISIS can play a crucial role in energy research - from the discovery of new materials through the characterisation of materials processing and device development to the monitoring of pilot plant and devices, using the techniques cited above. This requires an integrated approach that involves chemists, materials scientists and chemical engineers working together with the scientists and engineers at Diamond and ISIS to provide a broad range of in situ and ex situ fabrication and characterisation facilities. Diamond and ISIS together can provide a detailed atomic and molecular understanding of the material processes that in turn, by rational design, can determine the next generation of fuel cells, batteries and hydrogen storage devices. The Research Complex will provide a natural focus for drawing together the diverse expertise of chemists, materials scientists and engineers. Energy materials research infrastructure will have significant benefits ranging from an increased efficiency in the discovery of new materials through to the optimisation of chemical processing and device performance.

Appendix 3:

Consultations with the potential user community: A summary of the consultation process and outcomes

A consultation workshop was held in July 2003, attended by 48 scientists and representatives of funding organisations likely to be involved in research using Diamond. After introductory presentations, breakout groups considered questions related to the type of research that would benefit from co-location with Diamond, how to promote a productive research culture, facilities and equipment required for different potential user groups, and social and residential facilities required. Those present at the workshop were agreed on the need for a research complex at RAL to support Diamond, and this was seen as an important opportunity to create a world-leading facility in the UK. It was agreed that a research centre was required, rather than simply provision of facilities. The recommendations from the workshop that relate to the requirements for scientific infrastructure were as follows:

1. Research based in the building must be that which will benefit from proximity to Diamond and other facilities on the RAL site. Examples in biology would be work on membrane proteins, and large complexes. Examples in physics would be research on extreme conditions, in-situ research and dynamic structural chemistry.
2. Research on site should be technically challenging, to ensure that the beamlines are pushed to operate at their best.
3. There would be benefit in relocating CCP4 and CCP13 within the research complex, in order to bring in computational modelling expertise
4. There should be a single building to accommodate both physical and biological sciences.
5. The laboratory accommodation should be flexible to allow groups to expand and contract, and the building itself should be capable of expansion.
6. There should be shared facilities such as seminar rooms, coffee rooms and library facilities to encourage interaction between scientists from different disciplines.
7. There must be enough research groups on site to provide a critical mass of research activity e.g. a minimum of four groups in biology.
8. All scientists associated with or using Diamond should be able to apply for space in the building.
9. The research complex should be available for industry sponsored research.
10. Scientists in the research complex should be able to apply for external funding
11. There should be a core staff, including a good laboratory manager, to ensure shared equipment and facilities are kept working optimally.
12. The complex should cater for the research needs of beamline scientists employed by Diamond and the Diamond scientific directors.
13. Synergy between the central facilities on the RAL site cannot be promoted artificially. It will flow from having the right scientists appointed to work in the research complex. A shared hostel and catering facilities will promote interaction between scientists on site.
14. Only a small amount of space in the research complex will be needed for short-term visitors.
15. The majority of research within the research complex should be medium- and long-term, with scientific staff on 5 year renewable contracts. Joint appointments should be explored as a means of ensuring attractive career prospects.
16. Facilities for short-term visitors should include well found laboratories for materials preparation and synthesis.
17. Scientists in the complex will need access to large shared equipment and facilities, but decisions on exactly what is needed should wait until after the teams working there have been appointed, and justified on the basis of their research needs.
18. There is a demand for a protein production and crystallisation facility on the RAL site
19. Shared facilities for extreme conditions (pressure and temperature) research should be set up at RAL.
20. There should be improved library facilities (possibly electronic).
21. There should be video conferencing facilities.
22. There should be access to the e-science Grid for visitors as well as longer-term staff.
23. Meeting rooms and seminar rooms are needed in the research complex.

Issues on which agreement was not reached included the best way of managing the complex (though it was agreed that good management would be crucial) and how research should be funded.

The workshop report and questionnaire were circulated widely to Synchrotron and ISIS users and posted on the Diamond website: people were asked to rate their agreement with, or level of priority they afforded to, the workshop conclusions and recommendations. They were also asked to comment on their own requirements for space and facilities at RAL and how the Complex should be managed and work in it should be funded.

The questionnaire results were as follows:

- Ninety-three responses were received, 71% from physical scientists and 29% from life scientists. Almost all the respondents (99%) were potential Diamond users and 80% were also existing or possible ISIS users.
- There was strong support for the vision of a research complex housing sufficient long- and medium-term research programmes to provide critical mass. Respondents felt the complex should also provide shared facilities for short term visitors using Diamond and ISIS. Most agreed that both physical and life sciences research should be together in a single building and that there should be shared facilities to encourage interaction between disciplines. Eighty-eight percent of respondents envisaged themselves as possible users of the Research Complex.
- There was strong support for the need to develop a critical mass of long-term research teams on site, and a large majority agreed that longer-term research in the Complex should be technically challenging and be in areas where there was a clear benefit from co-location with Diamond and other RAL facilities.
- However, respondents did not agree that only a small amount of space was required for short-term users, and many envisaged themselves using the complex while visiting RAL to use Diamond or ISIS. A large majority felt that all scientists using Diamond should have access to the building.
- Respondents felt that longer-term research programmes should be funded in open competition, and were concerned that a research complex should not reduce funding available to university-based researchers.
- Respondents envisaged short-term visitors needing facilities for preparation, manipulation and characterisation of samples before and after insertion in the beams. Facilities mentioned included well-found laboratories for various disciplines and specialised equipment for sample characterisation (e.g. various types of spectroscopy and microscopy). There was strong support for the need for core staff to keep such facilities functioning optimally.
- A majority agreed access to the e-science grid was needed and there was support for location of computational expertise within the complex.

Following the workshop 3 additional representatives of the user community (both life scientists and physical scientists) were appointed to the Joint Research Councils Programme Board and contributed extensively to the development of the science case.
Representatives of key stakeholders in the project (including Diamond, ISIS and the user communities) attended a value management workshop, at which success criteria for the project were agreed.