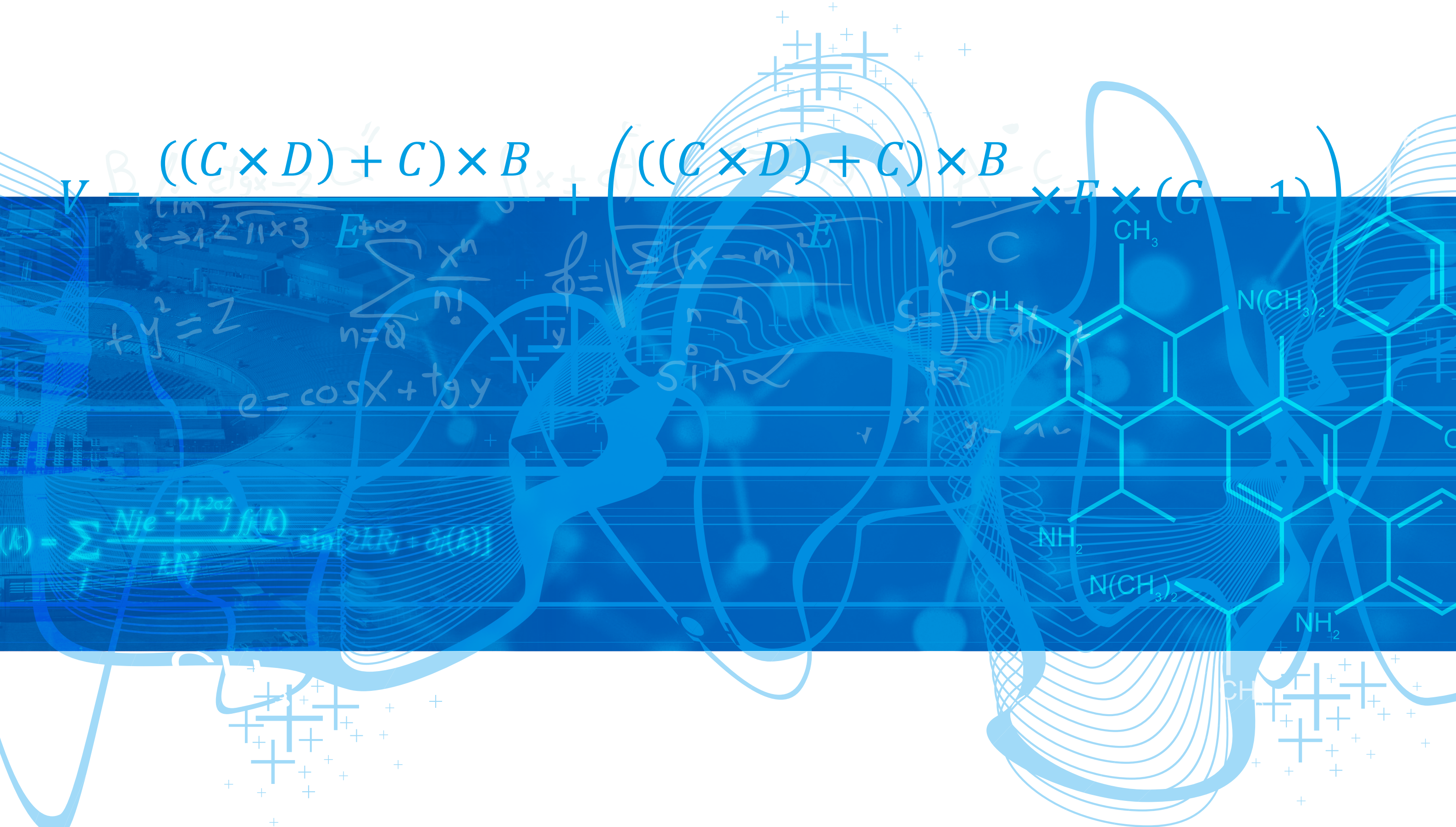
technopolis group

Socio-Economic Impact Study

Appendices

May 2021



diamond

Contents

A.1 Industry case studies

A.1.1. Rolls-Royce – Understanding materials for power and propulsion systems

Summary: Rolls-Royce is a major international engineering company that designs and manufactures a range of different power and propulsion systems including jet engines, nuclear reactors (for the UK submarine fleet), and diesel systems for power generation. Advanced manufacturing is central to the company's success (from advanced robotics to additive layer manufacturing). Not only does it enable quicker and more cost-effective production, but more importantly for Rolls-Royce, it can enable new manufacturing methods that allow more freedom in product design (e.g. developing new engine architectures). Diamond has played an important role in helping Rolls-Royce in these areas. The company has been a regular user of Diamond – both directly, and in collaboration with academic institutions. Its activities have centred around understanding the residual stress profile of the materials used in components, which has then helped the company to demonstrate product capability when bidding for new contracts, and provided a better understanding the service life of products currently in use – helping to reduce repair bills.

Rolls-Royce has conducted a range of different research at Diamond. This has included:

- An examination of different metal crystals and how they interact with one another in polycrystalline materials. Understanding this behaviour has helped the company to understand the strength of different crystals and how they can be best configured to optimise performance.
- Studying how metal powders used in additive manufacturing interact with different surfaces. Aircraft blades can be constructed via a technique known as blown powder additive manufacturing in which metal powder is blown coaxially into a laser beam, melting the particles on a base metal to bond when cooled. By studying the mechanics and physics associated with this technique, the company is now better able to improve the properties of its materials, and ensure components remain durable.
- Using Diamond to understand the residual stress profile of engine component materials. Diamond's beamlines allow them to measure, in a non-destructive manner, the internal stresses and strains of components up to 2 tonnes in mass, and beyond 1 metre in length. For example, it has used energy dispersive X-ray diffraction on beamline I12 to assess how well fan blade surface treatments work, including in terms of their ability to prevent cracks at different stress levels.

Using Diamond means that Rolls-Royce can test real materials in situ, rather than relying on predictive models. This testing is also non-destructive, meaning that components can be re-used. Diamond also provides several specific advantages that make it Rolls-Royce's preferred research facility. While most synchrotron beamlines are focused on microscopic samples, Diamond's I12 Joint Engineering, Environmental and Processing Beamline (JEEP) can be used to study larger components up to 2,000 kgs and over a metre long. This is an important feature for an engineering company that designs and builds (large) components for the aerospace, marine and nuclear industries. The quality of Diamond's beamline scientists is also considered important; and Rolls-Royce welcomes the willingness with which Diamond's staff engage with user research activities and support the testing activity that takes place.

Rolls-Royce does conduct some of its research at Diamond through the proprietary route. However, much of their beamline time comes through collaborative research with universities, with the results being made available on an Open Access basis. The company sees this route as a way of gaining easier access to leading academics, while there are also reputational benefits for the company in being associated with research published in leading scientific journals.

Being able to conduct research at Diamond has helped Rolls-Royce see a range of different commercial benefits. For example:

- When bidding for new contracts, Rolls-Royce has presented their research from Diamond as evidence that their systems can reach the performance levels required by the client's brief. This has supported the company in winning additional work.
- Research at Diamond has also helped to reduce the size of repair bills for existing contracts. Typically, addressing faulty fan blades in existing aeroplanes can cost Rolls-Royce tens of millions of pounds, both through additional repair costs and through any wider commercial embarrassment that may affect the company's share price and future sales. Using Diamond has enabled the company to strip products apart and see if they react as planned in a variety of different conditions. This makes it easier for the company to find problems that were not anticipated at the design stage and therefore reduce the risk of costly after-sales problems and even passenger.
- The company also uses the research at Diamond to improve the predictive capability of their parts. This helps ensure that guidance on product lifespans are neither overly conservative nor overly generous. Having more accurate predictions helps demonstrate the company's competence to potential customers and helps maintain the company's reputation.
- The use of Diamond to develop manufacturing processes that lead to new or improved engine architectures is central. However, company representatives also noted that the study of materials performance may also play a role in making production processes quicker and more cost-efficient.

Supporting evidence

- Interview with David Rugg, Rolls-Royce Senior Fellow and lead on research projects at Diamond
- https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Rolls-Royce-fan-blade-strain.html
- Additional supporting slides prepared by Professor Rugg for the interview

A.1.2. Glaxo Smith Kline - small molecule drugs, antibacterial treatments and biologics

Summary: Glaxo Smith Kline (GSK) are a multinational pharmaceutical company, using Diamond through the remote access route to provide X-ray structural characterisation for structure based drug design. GSK, in collaboration with the University of Edinburgh, used Diamond to determine the structure and small molecule inhibitors of the KMO protein in a project that won the Royal Society of Chemistry's Teamwork in Innovation Award (2016). GSK have also used Diamond to support their research into a new antibacterial compound for a gram negative bacteria. Their work at Diamond helped establish the mechanism of action of the new compound, which is now in clinical trials. This work has also served as a foundation for collaboration with the United States Government and participation in an international collaboration for the Innovative Medicines Initiative (IMI). Diamond has also facilitated GSK's work in emerging fields, such as medicines extracted from biological sources (aka biopharmaceuticals or biologics).

Structural characterisation using X-ray is a major part of the research done by GSK at synchrotrons, from protein crystallography, through to small molecule crystallography and high powder diffraction. GSK, like many companies in the pharmaceutical industry, use a number of synchrotrons across the globe, including Diamond. At present, GSK's use of Diamond is mainly via the remote access route. By shipping the crystals to Diamond and operating the experiment from their facilities, GSK's researchers are able to work in a flexible way and capitalise on resources. As such, they are able to conduct small but more regular shifts on the beamlines, providing more timely support for their projects.

Three examples of GSK activity at Diamond are described below.

Small molecule drugs

A successful collaboration between researchers at the University of Edinburgh and GSK used Diamond to help yield a series of new inhibitors to treat acute pancreatitis. Kynurenine-3-monooxygenase (KMO) is an enzyme involved in tryptophan metabolism, which is associated with neurodegenerative disorders and acute pancreatitis. Despite being an important metabolic enzyme and potential drug target, the crystal structure of full length KMO had not been solved. Treatment options are limited for patients with disorders affecting KMO production as there are no clinically approved KMO inhibitors available.

When a drug molecule binds to its target, they often have a particular way to stop the target protein from working. For this molecule to be a viable drug for market, it has to be both effective and safe. Current available inhibitors of the KMO protein, while effective, produce bleach as a side effect.

One of Diamond's Macromolecular Crystallography beamlines (I04-1) allowed the team to picture the protein and its active site and how the drug molecule engaged with the target. Using this visualisation to support structure-based drug design, it was possible to observe that by moving parts of the active site, this side effect was avoided. A drug that uses this mechanism has continued pre-clinical development.

In additional to identifying potential preclinical candidates with unexpectedly high potency, the study also demonstrated the opportunity of harnessing FAD movement in optimising the pharmacological properties of the inhibitors. This novel binding mode was unprecedented and poses a potentially new approach to inhibiting other similar enzymes. This collaborative work also won the Royal Society of Chemistry's Teamwork in Innovation Award (2016) for the strength of industry-academia collaboration.

Antibacterial

In seeking new antibacterial treatments, GSK have been working on a new antibacterial treatment for a gram negative bacteria. Antimicrobial resistance is a serious threat to global health, threatening effective prevention and treatment of an ever-increasing range of infections. Antibacterial resistance occurs when bacteria mutate in response to drugs to the point where they become ineffective, allowing the infection to remain in the body. As resistance is increasing, it is becoming increasingly important to both manage the use of current antibacterial, and develop new treatments. Novel antibiotics are very valuable, however there are relatively few being developed and approved for clinical use.

In exploring a novel antibacterial treatment, GSK were able to elucidate the mechanism of action to show how the active compound worked using Diamond's crystallography techniques. This showed that the detailed mechanism of action differed from other antibiotics - by preventing the replication of the bacterium and 'trapping' a protein responsible for the DNA replication process. As this protein is present within a DNA bound complex, it is challenging for crystallography research. As such, the intensity and automation of the Diamond beamlines allowed GSK to test many crystals to find best for further analysis. The compound is now in clinical trials.

This work has also paved the way for further collaborations with world leaders in the area ,with GSK receiving further funding from United States Government and participating in the COMBACTE-MAGNET project for the Innovative Medicines Initiative (IMI) that seeks to combat bacterial resistance in gram negative infections.

Biologics

Medicines extracted from biological sources (aka biopharmaceuticals or biologics), are a growing market for GSK and the pharmaceutical industry more broadly. Though the propensity to publish findings publicly is less, this is another valuable area of research for the company. One example of this is the work of GSK to better understand the binding site of the VEGF antibody.

Anti-VEGF therapy is the current standard of care in the treatment of wet, age-related macular degeneration (AMD). Wet age-related macular degeneration is where vision is lost quickly over a few months or weeks. However, current anti-VEGF treatments are currently both risky and burdensome to patients, as they require multiple, regular injections. In order to improve patient experience, GSK were looking to develop a new slow-release treatment system. This would require a molecule with an improved binding capacity toward VEGF at low concentrations. Using data gathered at Diamond I04-1 beamline, GSK could visualise and better understand the binding mechanism of the antibodies. This allowed the team to then explore variants of natural antibodies with novel architectures that would also bind to this site with greater binding capacity.

Supporting evidence

- Interview with Chun-Wa Chung, Director Structural and Biophysical Sciences, GlaxoSmithKline R&D UK
- Diamond Light Source, Industry Services Case Study, GSK – drug characterisation. Available: https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-GSK-drug-characterisation.html
- Jonathan P. Hutchinson et al., 2017. Structural and mechanistic basis of differentiated inhibitors of the acute pancreatitis target kynurenine-3-monooxygenase. *Nature Communications*, 8, p.15827. Available: https://www.nature.com/articles/ncomms15827
- Walker, A., Chung, C., Neu, M., Burman, M., Batuwangala, T., Jones, G., Tang, C., Steward, M., Mullin, M., Tournier, N., Lewis, A., Korczynska, J., Chung, V. and Catchpole, I. (2016). Novel Interaction Mechanism of a Domain Antibody-based Inhibitor of Human Vascular Endothelial Growth Factor with Greater Potency than Ranibizumab and Bevacizumab and Improved Capacity over Aflibercept. Journal of Biological Chemistry, 291(11), pp.5500-5511.
- https://www.diamond.ac.uk/Science/Research/Highlights/2017/kmo-acute-pancreatitis.html

A.1.3. AstraZeneca – Determining molecular structures for drug development

Summary: AstraZeneca is a global, science-led biopharmaceutical company that focuses on the discovery, development and commercialisation of prescription medicines. For its UK research, the Diamond Light Source is the first-choice synchrotron and AstraZeneca uses the facility to help carry out a wide variety of drug discovery research. This is exemplified by the published work on novel ERK1/2 inhibitors (proteins that are critical to cancer cell survival) where initial compounds were optimised using information from high resolution protein inhibitor complex structures determined using Diamond's crystallography beamlines. This has allowed the company to quickly design selective covalent compounds and has led to five new chemical entity patents.

AstraZeneca is a global, science-led pharmaceutical business with a particular focus on developing new prescription medicines. As one of the world's largest pharmaceutical companies, with R&D centres across the globe, the company uses a variety of synchrotrons at any given time. However, for AstraZeneca's UK research, the Diamond Light Source remains the first-choice synchrotron, and it uses Diamond's high-quality X-ray beams in a wide variety of crystallography-based drug discovery activities.

Diamond's operational and management procedures are particularly conducive to industrial users like AstraZeneca. A representative of the company reported that it uses Diamond because it is well-managed, reliable, and has a large number of automated processes. Diamond's remote data collection processes are particularly valued, as these significantly improve the efficiency of research.

Much of AstraZeneca's work at Diamond has focused on the determination of molecular structures, used to design new molecules, which then feeds into drug development. A particularly high-profile area of research that AstraZeneca has carried out using Diamond centred on examining ERK1/2 inhibitors; compounds that have the potential to block cancer growth.

Diamond provided AstraZeneca with the necessary tools for the high throughput determination of multiple protein inhibitor complex structures, allowing the company to design novel compounds which can then be assessed with in vitro and in vivo studies. Specifically, Diamond provided high quality data that has supported the invention of compounds described in five new chemical entity patents.

More generally, a representative of the company was clear that there had been a direct link between past research conducted at Diamond, and the discovery of molecules for a range of neurological diseases, cancers, respiratory diseases and cardiovascular conditions.

Supporting evidence

- Interview with Chris Phillips, Associate Director of Structural Biology at AstraZeneca, IMED Biotech Unit
- AstraZeneca survey response
- https://www.diamond.ac.uk/industry/Industry-News/Latest-News/Synchrotron-Industry-News-AZ-Small-Molecule.html

A.1.4. Johnson Matthey – Materials and catalyst characterisation

Summary: **Johnson Matthey is a multinational company, headquartered in the UK, that specialises in chemicals and sustainable technologies. As part of their materials characterisation activities, Johnson Matthey utilise a range of different methods and techniques, including the imaging facilities at Diamond. Johnson Matthey use Diamond as a key part of their characterisation capabilities, particularly for characterisation of energy materials and catalysts, providing unique capabilities they can't provide. The value of Diamond for Johnson Matthey is visibly reflected by the scale of their investment in electron microscopes for the recently opened ePSIC facility.**

Johnson Matthey is a multinational company, headquartered in the UK specialising in chemicals and sustainable technologies. Its cooperate research centre, the Johnson Matthey Technology Centre, is based a 30-minute drive from Diamond. The company's key research areas focus on catalysis, precious metals, fine chemicals and process technology. As part of their materials characterisation activities, Johnson Matthey utilise a range of different methods and techniques.

Johnson Matthey interacts with Diamond facilities in all materials science, but most notably in structural, imaging and surface characterisation techniques for catalysts and energy materials. The company utilises several beamlines at Diamond, employing three main advanced characterisation techniques to better understand materials and chemical processes – X-ray Absorption Spectroscopy (XAS), Small Angle X-ray Scattering (SAXS) and High-Resolution Powder Diffraction. These beamlines are used in addition to a range of other lab-based analytical techniques. As such, Diamond provides an efficient and sometimes unique method within the tapestry of complementary methods and techniques at Johnson Matthey's disposal. This also includes those provided by other facilities on the Harwell Campus. As such, the whole site is of vital importance to the R&D activities of the organisation.

The direct commercial benefit of using Diamond for Johnson Matthey largely arises from the proprietary work they've conducted, much of which is confidential in nature. However, the company also conducts work through the peer-review access route, in collaboration with the UK academic community.

For example, scientists from Johnson Matthey used beamline I20 at Diamond to carry Energy Dispersive EXAFS (EDE) measurements to better understand automotive exhaust catalysts. Unlike many other analytical techniques that require vacuum conditions, this experiment was conducted *in situ*, allowing Johnson Matthey to mimic real industrial conditions and better understand the mechanism and behaviour of the materials while the reactions take place.

The measurements sought to determine platinum oxidation state in NOx absorber catalysts. Automotive emissions standards are tightening around the world and a particular focus in on nitrogen oxides (NOx) which can cause respiratory disease and contribute to smog and acid rain. Nitrogen oxides are a challenge for emissions control systems in diesel engines, especially under cold start conditions. Storage materials, called NOx absorber catalysts and based on platinum, are used to trap nitrogen oxides when the engine is running lean (fuel poor) and then release them when the engine is running fuel rich to be destroyed by a NOx reduction catalyst. The absorber material shows evidence for fast chemical processes occurring during the switch from lean to rich conditions and experiments at Diamond on the I20 beamline using the EDE technique investigated this. This work demonstrated that the mechanism of operation is related to the composition of the NOx absorber material which will help in work to improve these materials and make emissions control catalysts continually more effective.

The strength of the relationship between Johnson Matthey and Diamond has continued to grow in recent years. In some cases, the Diamond and Johnson Matthey relationship has involved co-development, in which researchers from both organisations will come together to push technology and research forward in a mutually beneficial way. This collaborative relation has culminated in and is highlighted best by Johnson Matthey's role and involvement in the I14 beamline. Johnson Matthey have also made further investments at the site at Diamond, including through the purchase of a multi-million (GB) pound JEOL electron microscope, which is be housed at the electron Physical Imaging Centre (ePSIC), sitting alongside Diamond's I14 beamline. Johnson Matthey use the instrument but also support collaborative use by other scientists through Diamond's user services.

For Johnson Matthey, Diamond provides an anchor and focal point for their relationships with academic partners who complement and feed into their proprietary work. For example, a UCL iCASE student, sponsored by Johnson Matthey has been working in collaboration with Diamond and the UK Catalysis Hub to develop a new *in* situ cell to combine X-rays with infrared measurements. This new cell lowers the dead volume within the measurement and Johnson Matthey have since applied the method for their own proprietary work. Their involvement in the I14 beamline is also expected to serve as a foundation for new collaborations with academic partners in future. Johnson Matthey values the opportunity to work at all levels with the beamline scientists and user community at Diamond to express science needs, support technique and capability development, conduct peer reviewed research and purchase proprietary time for near market product analysis.

Supporting evidence

- Diamond Light Source, 10-Year Vision, available: http://bit.ly/Diamond10yearvision
- Interview with Dr Peter Ash and Dr Paul Collier, Johnson Matthey
- https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Johnson-Matthey-Pt-speciation.html

- T.I. Hyde, P.W. Ash, G. Randlshofer, K. Rothenbacher, D.A. Boyd, G. Sankar,(2011). X-Ray Absorption Spectroscopic Studies of Platinum Speciation in Fresh and Road Aged Light-Duty Diesel Vehicle Emission Control Catalysts, Platinum Metals Review, 55(40), 233, (doi:10.1595/147106711X598910)
- E. K. Dann, E. K. Gibson, R. A. Catlow, P Collier, T. E. Erden, D. Gianolio, C. Hardacre, A. Kroner, A. Raj, A. Goguet, and P. P. Wells. (2017). Combined In Situ XAFS/DRIFTS Studies of the Evolution of Nanoparticle Structures from Molecular Precursors Chemistry of Materials, 29 (17), 7515-7523 (doi: 10.1021/acs.chemmater.7b02552)

A.1.5. Unilever - Development of hair care products[1]

The consumer hair care market is rapidly evolving and developing as consumers seek greater sensory experience and functionality from their products. Manufacturers are increasingly seeing rapid product innovation as a way of growing their markets, and this requires a more detailed understanding of product microstructures, dispersion properties, and interaction between different components.

Unilever has used the I22 beamline to help in this area. Working alongside a team of Diamond scientists, a Unilever team used the facility to study the microstructure of a new hair care product once diluted. The experiments helped demonstrate the stability and suitability of the new product, enabling the development of a working prototype product that subsequently progressed to an "in-home trial."

- Using Diamond provided Unilever with several advantages. Firstly, it enabled the company to collect data quickly. Data was translated into findings shared with the project team within a matter of weeks after the original experiment. This in turn quickened the pace with which Unilever could develop a working prototype, and subsequently capitalise on the new market opportunity. Secondly, the Unilever team particularly valued the expertise of the Diamond Industrial Liaison scientists.

A.1.6. Infineum – Developing improved fuel products

Summary: Infineum is a leading formulator, manufacturer and marketer of petroleum additives. It has conducted a variety of research at Diamond, including around the performance of biofuels in cold temperatures, the reduction of friction in engines, and the behaviour of additives in tribological contacts. Some of this research has already fed into projects which have resulted in products that have reached market. The company believes that other work around reducing friction in engines could lead to significant improvements in vehicle fuel economy resulting in significant reduction in CO2 emissions.

Infineum is a leading formulator, manufacturer and marketer of petroleum additives, for fuels and lubricants. The company, headquartered in Abingdon, has conducted a variety of research at Diamond, including on the performance of biofuels in cold temperatures, the reduction of friction in engine and determination of molecular structure of additives. The company values the expertise of Diamond staff and the collaborative nature of the relationship, whereby staff work closely with Infineum on all experiments.

One of the most notable areas of research conducted by the company at Diamond involved the examination of fuel performance in cold temperatures. In cold weather, molecules in fuels can crystalize, forming waxes that then block fuel filters to the engine. The growing use of biofuels complicates the search for a solution; as biofuels are made from living sources, each fuel sample's molecular structure is different, making it difficult to find a common solution that works across fuels.

Infineum used Diamond to conduct real-time molecular-level examinations of the crystallisation process. They examined not only different biofuels, but also studied crystallisation under a range of different conditions (e.g. where there is a sudden temperature drop, or where temperatures fall gradually over time). By increasing understanding of how different additives function at the molecular level, Infineum could better develop more effective solutions to the issue of wax crystal formation.

This research has already fed into wider projects that have resulted in new products reaching the market.

Infineum has also used Diamond to examine the interaction between fuel additives and metals, looking for ways to reduce friction in engines and improve performance. The company believes that its work on reducing engine friction could be transformational. Current technologies result in incremental improvements to fuel economy. Infineum is confident that its Diamond-based research can help produce significant performance improvements, which could help cut CO_2 emissions by millions of tonnes a year.

Collaboration with Diamond is key to continued success in developing future generations of additive systems.

Supporting evidence

- Interview with Peter Dowding, Principal Scientist, Infineum UK
- Survey response from Professor Dowding
- Case study: *Controlling Crystallisation in Fuels and Biofuels.* https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Infineum-oil-additives.html

A.1.7. Lewtas Science and Technologies – Transforming production processes for materials production

Summary - Lewtas Science and Technologies (LST) are licensors and providers of science, technology and product solutions in the fields of crystallisation, oils, fuels, energetic materials and polymers. The company has used Diamond for the past four years, to better understand the fundamental principles of different materials, with a view to developing new materials and manufacturing processes. One advanced area of work is the development of a new (non-migrating and non-toxic) plasticiser replacement for use in polymer-based manufacturing. LST is currently working to commercialise this product, with first sales expected in 2019.

Lewtas Science and Technologies are providers of science, technology and product solutions in the fields of crystallisation, oils, fuels, energetic materials and polymers. Its director has used Diamond (mainly beamlines I12, I13, I15 and I22) for the past four years, both in a commercial and academic setting. This research has revolved around understanding the fundamental principles of different materials, with a view to developing new materials and manufacturing processes. There have been two main areas of focus:

- The first relates to understanding molecular behaviour, and how materials change under different conditions, such as varying temperatures, varying gravitational forces, or varying pressure.
- The second area is at a higher macroscopic scale, and relates to understanding the properties of energetic materials in different process conditions.

This wide-ranging portfolio of research at Diamond has helped LST to better understand the

1 This case study draws primarily on information provided at https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Unilever-hair-care-product-development.html (accessed 22 October 2018)

fundamental principles that underpin material behaviour; knowledge that can be applied to a multitude of different settings and industries – indeed, any process that involves the materials concerned. Once the fundamental principles are understood, it becomes far easier to effectively and efficiently develop solutions to issues that manufacturers encounter in production or operation. For this reason, the company believes its research has diverse potential uses, from finding quicker food manufacturing processes, to developing more efficient car emission control systems.

To give one specific early example, the research carried out by LST at Diamond has been important in the development of new plasticisers. Manufacturers put these into polymers to lower the viscosity and make them more flexible during the manufacturing process, but there have been concerns about their toxicity and the migration into their surroundings. LST examined the molecular structures of different polymers and has developed non-migrating and non-toxic plasticiser replacements. It is currently working to commercialise this product, with first commercial trials planned for 2019.

Going forward, the company is hopeful that their research at Diamond will help open new high-value markets. Because they are engaged in transformative research, their solutions – if taken up by the market – could radically alter the *status quo* in relevant product fields.

The Director of LST argued that Diamond was an important part of the overall jigsaw that enables them to carry out cutting-edge, solution-oriented research. It provides real-time data and high-quality light, without which their research would take place at a much slower pace. Indeed, without synchrotron access, some of their larger-scale research could not have happened at all. As an very small SME, LST does not have the time/resources to travel abroad to use another synchrotron. Having access to worldclass facilities and capability in the UK has therefore been crucial in ensuring that they can carry out cutting-edge research.

Supporting evidence

- Interview with Ken Lewtas, Founder and Director, Lewtas Science and Technologies

A.1.8. Porton Biopharma - Bio-pharmaceutical development and manufacturing

Summary: Porton Biopharma is a bio-pharmaceutical development and manufacturing company that is focused on life-saving products including biologics, vaccines, enzymes and proteins from bacterial fermentation. One of the company's core products, Erwinase, is an enzyme used to treat leukaemia, and Porton Biopharma has used Diamond to collect data on the enzyme's structure. The data helped demonstrate that a minor component seen in the purified product was in-fact a subtle conformational change in the enzyme which did not alter the drug's activity.

As part of their ongoing commitment to fully understanding their product, Porton Biopharma contracted with Diamond to examine the molecular structure of its core product, Erwinase, an enzyme which is used to treat childhood leukaemia. Demonstrating full knowledge of one's product is an important component in reassuring medicines regulators, especially as analytical techniques become more and more sensitive.

Scientists at Porton Biopharma used Diamond's small angle X-ray scattering (SAXS) service to help characterise and understand the different variants, with SAXS helping examine tiny structural changes in the enzymes. Using data collected at Diamond and elsewhere, Porton Biopharma demonstrated that the differences between product variants were minor and therefore would not affect Erwinase's effectiveness. The company communicated this evidence to the US regulatory authorities, reassuring them of the drug's effectiveness.

Diamond therefore provided a quick and easy way of obtaining the information required to help maintain product confidence in one of the company's most important markets.

Given the importance of obtaining the data, Porton Biopharma needed synchrotron access quickly. Proprietary access to Diamond meant the company could secure beamline time at short notice. Its proximity to the company's Porton base also meant no language or time zone barriers, helping further speed up the research process. The expertise of Diamond's staff and the commercially-minded nature of the support offered were also important and welcomed factors.

Supporting evidence

- Interview with Dr Dave Gervais, Head of Product Development, Porton Biopharma
- Survey response from Dr Gervais
- *Characterising variants in clinical grade biopharmaceuticals. Available at* https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-BioSAXS-Porton-Biopharma.html
- Gervais D, King D, Kanda P, Foote N, Elliott L, Brown P, Lee NO, Thalassinos K, Pizzey C, Rambo R, Minshull TC. Structural characterisation of non-deamidated acidic variants of Erwinia chrysanthemi L-asparaginase using small-angle X-ray scattering and ion-mobility mass spectrometry. Pharmaceutical Research 32(11):3636-48 (2015).

A.1.9. Evotec - Supporting greater efficiency in drug development

Summary: Access to cutting-edge research facilities is vital for a contract research organisation like Evotec. Located just five miles from the Harwell campus, Evotec is a regular user of the Diamond Light Source, as well as other co-located research facilities, to support its drug discovery work for pharmaceutical and biotechnology clients. The use of synchrotrons is now routine in the drug discovery industry and Diamond addresses Evotec's needs by providing a range of novel technologies, housed in high quality facilities in one location. Ease of access and efficiency are important factors for the organisation and its clients, and Evotec has become a near bi-weekly user of the facility to support its contract work. Working closely with Diamond staff has also brought additional benefits, in terms of developing skills and knowledge within the company. Their association with Diamond is also thought to have improved Evotec's international reputation, helping to bring in additional contract work over time.

Drug discovery is a complex and challenging process. Researchers need to understand the three-dimensional structure of macromolecular drug targets and the molecules that bind to them, as well as the interactions that take place. The use of synchrotrons to support this process is now routine and Diamond offers world leading facilities that combine cutting-edge technical instrumentation, with the latest developments in automation required to accelerate lead identification and screening processes.

Evotec is a multi-national contract research organisation that works primarily on drug discovery and development with leading pharmaceutical and biotechnology companies, academics, patient advocacy groups and venture capitalists. Its structural biology operations are based primarily in Abingdon, Oxfordshire – less than 5 miles from Diamond Light Source and the Harwell campus – and it uses Diamond as often as every other week, as well as other co-located facilities (e.g. electron microscopes), to support its contract research work for a range of organisations.

The knowledge and expertise gained through conducting regular experiments at Diamond have helped deepen Evotec's understanding of more advanced technologies and methodologies. A prime example of this is XChem, Diamond's platform for streamlined screening of X-ray fragments (associated with the I04-1 beamline). This streamlined process allows Evotec to screen molecular structures for potential ligand binding sites at much higher rates than was previously possible. As a result, it has been able to provide information-rich structures to clients in a more time- and cost-effective manner.

This work has supported Evotec's clients in their drug development work and is thought to have informed new patent applications, as well as the subsequent launch of new products.

More widely, conducting research at Diamond has enabled Evotec staff to develop their experimental and analytical skills. The company has also welcomed the opportunity to work closely with Diamond staff and engage regularly with beamline scientists, as well as develop their wider networks.

The centrality of synchrotron research to their work means that Evotec does use other similar facilities abroad, especially during periods of downtime at Diamond. However, proximity, familiarity and the development of good working relationships over time all mean that Diamond Light Source is the company's preferred synchrotron. The use of other facilities also adds to project timescales and costs.

Their proximity to, and regular use of Diamond, is thought to have also bolstered the international reputation of the company and its services, helping them to win new drug discovery-related contracts.

Supporting evidence

- Dr Paul Alastair McEwan, Principal Scientist
- https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Fragments.html
- https://www.diamond.ac.uk/Home/News/LatestNews/24-11-15.html

A.1.10. Heptares - research into GPCRs[2]

Summary: **Heptares is a biotechnology and drug discovery company that specialises in clinical-stage research into novel medicines that target G protein-coupled receptors (GPCRs), a superfamily of receptors linked to a wide variety of different human diseases including diabetes, obesity, and kidney and digestive diseases. The company has been a regular user of Diamond, using I24 to research how antagonists bind onto GPCRs associated with Parkinson's disease; how peptides bind onto GPCRs linked to diabetes; and studying immune system proteins. This drug discovery work has helped feed into the treatment of life-changing diseases and helped enhance Heptares' reputation in the field. Their standing in the drug discovery sector led to Heptares' acquisition by the Japanese biopharmaceutical firm, Sosei, for up to $400 million.**

Heptares has been a regular user of Diamond in recent years, using it at least once a month for its research into GPCRs. Generating approximately 90% of its structural data there, Heptares is also one of Diamond's largest industrial users in the biomedical area. It has undertaken a wide variety of research at Diamond, as highlighted below:

- **Understanding Xanthine-GPCR binding structures:** The Adenosine A_2A receptor is a GPCR that is a major target of caffeine and is also important in regulating oxygen consumption in heart muscles, coronary blood flow, and central nervous system neurotransmitters. Consequently, there is growing interest in it as a receptor for new drug development. First generation A2A receptor antagonists have for instance, been shown to be useful in treating Parkinson's disease but have been associated with safety and tolerability limitations. In order to generate the next generation of drugs, Heptares looked to see how xanthine-based drugs like caffeine bind onto A2A receptors. Diamond's I24 beamline was crucial to Heptares for this, allowing them to solve the 3D structure of adenosine A2A receptors, and understand how xanthine-based drugs, and the firm's own novel drug candidates bind onto it. The findings, published in the journal, *Structure, will help inform the next generation of drug treatments.*
- The structure of insulin stimulator: Type 2 diabetes is a condition associated with poor glucose control, people being unable to respond adequately to the GLP-1 hormone which stimulates insulin release from the pancreas in response to food. One way of treating Type 2 diabetes is to stimulate the GLP-1 receptors but current avenues for this are expensive, and use long peptides (molecules) which can only be administered by injection. The goal is to create small molecules which can be taken orally. Heptares approached the problem by using the I24 beamline to determine the full-length structure of the GLP-1 receptor and how peptides bind onto it. Using this knowledge, Heptares was able to design a series of peptides which have subsequently been found to work well in mouse models of diabetes. It is hoped that this will eventually lead to transformative new diabetic treatments.
- Finding a new binding site on immune system proteins: Chemokine receptors are a type of GPCR that aid immune responses by mediating the migration, activation and survival of immune cells. They also play a role in viral entry and tumour growth. Agents typically targeting chemokine receptors have a high failure rate, often believed to be because of limited information on receptor structures. Heptares used Diamond's I24 beamline to study the structure of the chemokine receptor CCR9 when bound with one of its antagonists. This for the first time, proved the existence of a specific unusual binding site (intracellular pockets) in some chemokine receptors, something which will ultimately help develop better targeted drugs.
- As shown, Diamond has been crucial to Heptares being able to carry out high profile drug discovery work which in turn will feed into the development of treatments for life-changing diseases. Using Diamond has also helped Heptares test and prove the effectiveness of its StaR ® methodology, a technique used to stabilise GPCRs and subsequently allow handling and crystallisation for experiments. Heptares' Diamond-based research, and its development of StaR ® led it to be recognised as an outfit undertaking world-class science. This reputation led to the 2015 acquisition of Heptares by the Japanese biopharmaceutical company, Sosei, for up to $400 million.

Supporting evidence

- https://www.heptares.com
- *Beating the sugar rush – Diamond Science Highlights 2017. Available at* https://www.diamond.ac.uk/Science/Research/Highlights/2017/insulin-stimulator.html
- *Heptares – GPCR research: Xanthine-GPCR binding structures herald new Parkinson's treatments. Available at* https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Heptares-GPCR-research.html
- *Drug discovery goes intracellular. Available at* https://www.diamond.ac.uk/Science/Research/Highlights/2016/I24-heptares-intracellular.html
- House of Lords Science and Technology Committee (2013) *Second Report: Scientific Infrastructure. Available at* https://publications.parliament.uk/pa/ld201314/ldselect/ldsctech/76/7605.htm

2 Please note that this case study draws entirely on published material

A.2 Academic case studies

A.2.1. University of Portsmouth (John McGeehan) - A plastic digesting enzyme

Summary: The discovery of a new, plastic digesting bacterium offers new opportunities to deal with the ever growing, global plastic waste problem. However, questions still remained about how the enzyme digesting the plastic, PETase, actually worked. By solving the 3D structure of the enzyme and its active site using Diamond, researchers are better able to understand how the enzyme may be adapted to industrial applications.

The widespread use and disposal of plastic is a significant and growing environmental issue. Only 9% of plastic is recycled and the vast majority of it ends up in land-fill or the ocean, dispersed by currents[3]. Most does not biodegrade, but instead breaks down into smaller pieces (microplastics), which are then irretrievable. Should current consumption patterns and waste management practices continue, there will be around 12 billion tonnes of plastic litter in landfills and the environment by 2050[4].

A recently discovered bacterium, *Ideonella sakaiensis* 201-F6, has demonstrated the ability to grow on Polyethylene terephthalate (PET) - one of the most abundantly produced plastics - using it as source of energy and carbon. Central to this ability is the production of PETase; an enzyme that is capable of digesting PET. Investigating this newly discovered enzyme is a team of scientists from the University of Portsmouth, the National Renewable Energy Laboratory in Colorado, the University of South Florida, the University of Campinas in Sao Paulo and Diamond Light Source.

Using Diamond's unique Long-Wave Macromolecular Crystallography (MX) beamline (I23) and Diamond's other MX beamlines (I03 and I04), the team has been able to understand and solve the 3D structure of the enzyme, as well as visualise the active site of the enzyme and how it consumes plastic. As a result, researchers are now able to investigate how the enzyme could be engineered to become more effective or even adapted to digest other types of plastic beyond PET.

The outputs of the research were published in the journal Proceedings of the National Academy of Sciences USA as well as receiving widespread recognition in the mainstream media. Articles have been published in the Economist, the Times, the Guardian, National Geographic, as well as reported on television news to an audience of over 200 million and featured in UKRI's strategy paper as a case study of successful research and innovation in the UK.

Patents for the enzyme have now been filed in many jurisdictions and there has been a great deal of interest in the solution from industrial stakeholders. Companies are now more keen to explore the technologies further in order to help improve their public perception and reputation. As environmental awareness and action is a growing amongst consumers, a greater responsibility for environment impact can help a company with sales, market share and share prices etc. The project team are currently working with several multinationals to further develop the research over the next five years. Industrial experience of enzyme research in other fields (e.g. for medical and detergent applications) will prove useful for the further development and tailoring of PETase for industrial recycling processes.

The potential environmental impact of this research is significant. In addition to contributing to the reduction of plastic waste it also opens opportunities for better recycling of plastic. The enzyme will break down any PET but also highly crystalline ones like those seen in plastic bottles. The main advantage of the enzyme is that it breaks down the constituent polymer chains into their original building blocks so that they can be used to make recycled PET with the same properties as petroleum-based virgin PET. It is hoped that these building blocks can be further utilised for upcycling waste plastic by creating new polymers with improved properties and higher value. This would be a major step forward to turning plastic waste into a valuable commodity.

Following the work on PETase, Professor ***John McGeehan*** at the University of Portsmouth has been invited to numerous conferences across the world (e.g. Hong Kong, Iceland, Singapore) which he feels has helped enhance the reputation of his team in the field. Portsmouth University have also provided further backing to support projects focussed on enzyme research and have recently established a new Centre for Enzyme Innovation. Going forward, the study team will continue to work with Diamond to develop enzymes that can work on other polymers (e.g. cellulose, lignin and other plastics) and this work has served as a solid foundation for application for larger research grants. The Centre was most recently awarded £5.8 million from the Research England Expanding Excellence in England (E3) Fund.

The reputational benefit has also extended to the wider research team, helping them to compete internationally. The profile of crystallography research more generally has also benefited.

From the perspective of the study team, Diamond provides some of the best facilities in the world. While other synchrotrons were available for the research, the innovative technology and exceptional resolution of the beamlines at Diamond were the core reasons they chose to use this facility. Within a day of using the beamlines, they had the highest resolution image of the enzyme the research team had seen.

Furthermore, as the facility is world class, they are also able to attract world class staff and contribute their expertise to such projects. Without the Diamond staff contributing to this study it would have been very difficult to run the experiments. For this reason, the research was co-authored with Diamond scientists. The team also received support from Diamond's Press Office who have been helpful in dealing with press enquiries.

The proximity of Diamond to some of the research partners (i.e. Portsmouth) has been important for the research team.

Supporting evidence

- Interview with Professor John McGeehan, University of Portsmouth
- Diamond Light Source, 2018 News, "Solution to plastic pollution on the horizon". Available online: https://www.diamond.ac.uk/Home/News/LatestNews/2018/16-04-2018.html
- Publication: http://www.pnas.org/content/early/2018/04/16/1718804115

3 Geyer, R., Jambeck, J., Law, K.L. (2017). Production, use, and fate of all plastics ever made. Available online: http://advances.sciencemag.org/content/3/7/e1700782.full

4 United Nations Environment Programme (2018) Single-Use Plastics: A Roadmap for Sustainability. Available online: https://wedocs.unep.org/bitstream/handle/20.500.11822/25496/singleUsePlastic_sustainability.pdf?isAllowed=y&sequence=1

A.2.2. University of Manchester (Sam Shaw, Katherine Morris) - Nano-scale processes in radwaste management

The Problem

Management and disposal of higher activity radioactive wastes is a significant issue across the developed world as many countries with a history of nuclear power generation and military activities seek long term solutions for these materials. The most common disposal choice is containment within a deep geological disposal facility (GDF). To remain effective over the long term, the design of a GDF must limit the mobility and migration of radionuclides.

The Challenge

The interaction of radionuclides with geological materials is key to understanding the mechanisms by which radionuclides can become mobile. Most designs for GDF involve extensive use of cement to seal the wastes as well as engineer and backfill the site ready for closure. Over time, groundwater will interact with the cement to form a plume of hyperalkaline leachate. While high pH can prevent solubilisation of uranium, a key radionuclide in wastes, by sorption / precipitation of hydroxide phases these extreme conditions may lead to the formation of U(VI) colloids which could, in contrast, enhance the mobility of U.

The Solution

A team from The University of Manchester worked with Diamond scientists to apply both in situ and ex situ X-ray techniques to characterise the formation of U(VI) colloids in synthetic cement leachate systems. Small angle X-ray Scattering (SAXS) was used to characterise U systems. Nano-particulate U-colloid formation was observed occurring within hours and by measuring aged samples, the colloids were stable for several years under some conditions. X-ray absorption spectroscopy (XAS) showed that the U-colloids had a sodium uranate-type crystallographic structure.

The Benefits

Understanding the potential for U-colloid formation at high pH is important in understanding U-behaviour in deep geological disposal. This current work highlights the potential importance of U-colloids and further work is ongoing to understand their interactions with cements. More broadly, these techniques are being applied to understand colloid behaviour in radionuclide impacted environments and systems: current work includes studies looking at iron oxide floc formation in a radioactive effluent treatment system.

"We are really beginning to access a full range of synchrotron techniques at Diamond using radioactive samples by working closely with the team on site. This is allowing

us to make real progress in understanding radionuclide and colloid behaviour in really important radioactive treatment and waste disposal systems. This information will be

used to underpin management, decommissioning and ultimately disposal of these radioactive materials and we are keen to develop further work with industry in these areas."

Prof Katherine Morris, University of Manchester

Supporting evidence

- https://www.diamond.ac.uk/industry/Case-Studies/Case-Study-Radwaste-Management-Manchester.html

A.2.3. University of Birmingham (Owen Addison) - Identifying how medical devices fail

Summary: Implanted materials and devices are used routinely in healthcare and can fail for many reasons. Understanding why or how they fail is essential for the development of better products and manufacturing processes to improve outcomes for patients. In this particular case, the University of Birmingham, in collaboration with NHS surgical specialists were able to use the Diamond Light Source to obtain high-quality chemical imaging of biological tissues associated with a newly introduced implant that was exhibiting unexpected early failures. The data generated helped the product manufacturer identify an improved manufacturing process and provide surgeons with updated guidance on how to insert the device. More broadly, the research findings of the Birmingham group and others using Diamond for similar studies, have significantly improved understanding of how metal implants behave in the human body, which is feeding into further research.

When a manufacturer of osseointegrated implants **new product was having a much higher failure rate than expected**, an international panel of experts was brought together to try to understand why this was happening. They looked at patient and surgical factors alongside carefully studying the failed implants and the tissues neighbouring them.

A research team from the University of Birmingham turned to the chemical imaging capabilities at **Diamond's I18 to identify whether the implant material itself was implicated in these failures**. Synchrotron light was essential to provide high-quality imaging of dilute materials in biological tissues that was needed for this inquiry. Using these high-quality images, the team were able to quickly determine an unexpected behaviour of the device.

The impact of the research was immediate, with the company able to **modify their manufacturing process** for its product. More broadly, this research is a small part of a larger program which has significantly improved our understanding of how metallic implants behave in the human body. The importance of this work has been recognised, with the findings featured in a number of important publications. It will also be the subject of an impact case study for the 2021 Research Excellence Framework. Furthermore, the findings are feeding into further research projects, in collaboration with both academic and industrial partners, which will further contribute to improving patient outcomes in the future.

The use of methods using synchrotron light, primarily at the Diamond Light Source has also had **significant impacts for the primary investigator,** Professor Owen Addison (University of Birmingham) as it was instrumental in securing him a prestigious NIHR fellowship with £900,00 of funding to study metallic implants further. Professor Addison is a clinician scientist who has used his work at Diamond to broadened his exposure to a wider scientific research community. In line with this, one of the benefits of Diamond from his perspective was its role in encouraging cross-university collaborations. This exposure has also provided him with clearer understanding and direction for both his research work and his career path as a whole. Diamond has also played a role in supporting the career development of junior staff working with Professor Addison. The opportunity has helped his PhD students gain further experimental, analytical and team-working skills, facilitated by collaborations with Diamond staff.

For Professor Addison, one of Diamond's selling points is that it is a UK-based facility that is internationally competitive in the measurements it can provide. In particular, for measurements of biological tissues, particularly when human in origin, it is much easier to preserve sample integrity when they do not have to travel very far. There are also considerable savings in terms of the additional work that would be involved in transferring biological samples across international borders (e.g. requirements to chemically fixing samples, completing additional materials transfer and biohazard paperwork). Furthermore, the co-location of Diamond with other facilities and services at Harwell is valuable. Indeed, Professor Addison noted that proximity to Diamond would be a key consideration in any future relocation he might make.

The **reliability of Diamond's beamlines** is seen as another valuable aspect of the facility, with Professor Addison rarely losing time to technical issues. This is important because the tissue samples need to be prepared for a fixed date, after which they begin to deteriorate. The technical and scientific staff at the facility were also reported to be deeply engaged with the research and helped to improve the quality of the outputs.

Supporting evidence

- Interview and survey with Professor Owen Addison, University of Birmingham

A.2.4. University of Bristol (Mahmoud Mostafavi) – Proving the safety of nuclear plants

Summary: **Dr Mostafavi is a mechanical engineer whose work focuses on structural integrity. His main research interest is in materials damage, namely fatigue, fracture and creep. Previous research at Diamond has included studying the structural integrity of blimps in cold temperatures, and characterising solidified nuclear core from Fukushima accident. One of his most notable research projects using Diamond has been on assessing the safety of extending nuclear power plant operations.**

Nuclear power plants that were built in the UK in the 1970s and 1980s were originally intended to have an approximately 30-year lifetime. Adhering to these timescales would mean closing much of the existing stock of reactors, with significant impacts on current UK electricity supply capability. The loss of nuclear power would have major implications for the UK power grid, especially while renewable energy infrastructure is insufficiently developed to help bridge any shortfall. As such, plant owners have looked to determine whether they can safely extend the life of current plants.

As part of this effort, Dr Mostafavi has carried out research that examines the nature of creep failure in nuclear power plants' boiler tubes, and the extent to which boilers can continue to operate safe levels. Using Diamond, he examined the behaviour of existing boiler parts when subjected to conditions similar to those seen in the plants. This was possible through *in-situ*, time resolved X-ray tomographic imaging and diffraction available at Diamonds I-12 beamline. These experiments provided 3D images of strain and damage inside samples.

According to Dr Mostafavi, ESRF could have provided similar facilities to the I-12 beamline, however Diamond was the only one that was operational when he was looking to conduct his research. In his view, complexity of the experiments required close interaction with the beamline team which was considerably facilitated by the proximity of Diamond Light Source and University of Bristol and would have been significantly less fruitful had the experiment been done at ESRF. He added that the quality of Diamond's staff was also a major draw and he felt that the I12 beamline scientists demonstrated huge commitment to maintaining the beamline, as well as providing valuable technical support and a willingness to help at all hours of the day. The knowledge and understanding of beamline staff was critical in ensuring the experiment was designed correctly which could only be archived through a close collaboration between the staff and the experimental team.

Dr Mostafavi's research validated models that suggested that the expected 30-year lifetime of nuclear plants was overly-conservative, showing instead that plants could continue to operate safely for longer periods. The results are currently peer-reviewed for publishing in a prestigious academic journal. The study, once peer reviewed, will be used as part of the evidence supporting the Safety Case presented to the Office for Nuclear Regulation demonstrating that a nuclear power plant could continue operating safely well into the future.

The time-resolved high-speed change in materials and the techniques he learnt during his time at Diamond is knowledge Dr Mostafavi would have not been able to gain without Diamond. More generally, he believes the support from Diamond has significantly improved the quality of his research and in turn influenced his international standing. This is supported not only by the quality of the experiments, but the added benefit of working in an in an intense, collaborative and vibrant environment with other academics that inspires his critical and innovative thinking. He also believes that his wider research group has benefited from being associated with the Diamond work, helping to enhance their wider reputations in relevant research fields.

Furthermore, the type of measurements made possible with access to Diamond Light Source formed the backbone of further EPSRC grants as they allow for a step-change in their understanding and provided answers to long standing questions. Dr Mostafavi was also confident that the quality and speed of research that had been possible at Diamond would encourage his industry partners to consider making greater use of synchrotrons in future. For example, a recently funded project for the Department for Business, Energy and Industrial Strategy (BEIS) to better understanding of the structural integrity of Advanced Joining Technologies for application in the nuclear industry budgeted for four days of industry Diamond access.

Supporting evidence

- Interview and survey with Dr Mahmoud Mostafavi, University of Bristol

A.2.5. University of Reading (Kim Watson) – New prebiotics with thermally stable enzymes

Summary: **Professor Watson's research uses X-ray crystallography and computational methods to undertake structure-based analyses and computer-aided drug design. She has been a regular user of the Diamond Light Source, since it first opened. One of her most notable research projects involving the facility was in collaboration with the prebiotics technology developer and manufacturer, Clasado Biosciences. Professor Watson worked with the company to develop more thermally stable enzymes for use in the production of prebiotics. The research led to a novel enzyme being adopted by the company in the manufacture of their flagship product Bimuno®, which enabled higher yields, reduced downstream processing and produced less waste.**

Professor Kim Watson of the University of Reading's School of Biological Sciences specialises in protein function and how that function translates to health, with particular focus on the use of X-ray crystallography and computational methods for structure-based and computer-aided drug discovery. Most recently, her research has focused on understanding how enzymes interact with small signalling molecules at the atomic level. This expertise on how to affect changes in these interactions through protein engineering has stimulated a number of research collaborations aimed at transforming industry-relevant enzyme-controlled processes.

Professor Watson has been a regular user of the Diamond Light Source, but one of her most notable projects using the facility has been in collaboration with the prebiotics technology developer and manufacturer, Clasado Biosciences. This partnership started in 2012, with the aim of finding a more thermally-stable enzyme for use in the manufacture the company's flagship product Bimuno - a daily food supplement with prebiotic properties to support healthy gut bacteria and improve overall health.

Professor Watson used the facilities offered at Diamond to design a series of different enzyme constructs and determine how they worked. Using Diamond gave several advantages. Synchrotron access helped quicken the pace of the research. Additionally, the wider on-site facilities enabled the research group to carry out work in a high throughput, parallel manner over four weeks, which might otherwise have taken up to two years. From there, she could identify which enzyme constructs would be the best candidates for commercial scale-up. The research team found one enzyme construct that was particularly stable and favoured the desirable product, again using Diamond to solve the structures of the different variant enzymes, and gaining a thorough understanding of their structure-function properties at the molecular level.

The research results have brought significant commercial benefits for Clasado. By 2015, the company had switched production to the new thermostable enzyme, leading to more efficient Bimuno production. Operating the production process significantly higher has helped the company to increase yield of the prebiotic product, while simultaneously reducing the need for additional processing, and reducing waste water. This increased purity also enabled Clasado to increase their product range, now selling Bimuno as pastilles in addition to powdered form.

Ongoing research involving another group at the University of Reading is exploring whether Bimuno could be helpful for children with autism spectrum disorders. Gastrointestinal symptoms are of particular interest in this population due to the prevalence and correlation with the severity of behavioural traits, therefore interventions that can help to address imbalances in the gut bacteria and metabolism could prove beneficial. With their first study now published showing some beneficial effects, it is hoped that this may stimulate additional R&D into more tailored prebiotic formulations to support good gut health, mood, behaviour and sleep in children with autism spectrum disorders.

Professor Watson and colleagues are also now exploring the potential to use their enzyme, and related family members of this class of enzyme, for other uses. Her research group has secured a BBSRC/IPA grant of £521,352 to further tailor their enzyme for the production of specific carbohydrates that could supplement infant milk formulas so that they more closely resemble human milk.

For Professor Watson, the Diamond-based work has helped improve the understanding of new research techniques, and enhanced the group's reputation in the area of protein engineering and biotechnology. Professor Watson also commented that the quality of Diamond's staff was as important as the infrastructure itself, with clear benefits from her research team being able to interact with like-minded individuals sharing similar research interests and with other experts in the wider field of structural biology.

Supporting evidence

- Interview with Professor Kim Watson, Professor in Structural Biochemistry, University of Reading
- Survey response from Professor Watson
- University of Reading Staff Profile for Professor Watson, available at
- http://www.reading.ac.uk/biologicalsciences/about/staff/k-a-watson.aspx

A.2.6. University of Sheffield (Jon Sayers) – Studying flap endonucleases (FENs)

Summary: **Flap endonucleases (FENs) are a class of enzyme responsible for maintaining the double helix structure of DNA by trimming of unnecessary "branches" during DNA replication and repair. Using Diamond, professor Sayers of the University of Sheffield was able to precisely define the mechanism of this interaction. As DNA replication occurs in all life, FENs could serve as novel targets for antibiotics or anti-cancer therapeutics and understanding this mechanism is a key part of future drug development. To further explore this, Professor Sayers founded DeFENition, a company focussed on identifying small molecule inhibitors of FENs to tackle antibiotic resistant bacteria.**

Traditionally, DNA is thought of as having a double-helix structure. However, it in fact adopts a range of different shapes as part of normal biological processes, with "branched" DNA molecules being present in all living organisms. Indeed, these DNA branches are crucial intermediates formed when DNA is copied. Enzymes known as flap endonucleases (FENs) then trim branched DNA molecules after cell division, helping to restore the double-helix and reducing the risk of harmful mutations.

Dr Sayers is Professor of Functional Genomics at the University of Sheffield. His research focuses on the interaction between small molecules and DNA proteins, which has included using the Diamond Light Source to help better understand precisely how FENs trim branched DNA molecules.

After he secured funding, Professor Sayers crystallised a particular FEN enzyme and then using Diamond's IO3 X-ray beamline and MX beamlines IO2 and I24, Professor Sayers was able to more precisely characterise how it bound with DNA. This also showed how branched DNA modules are removed from the double-helix and more specifically, that FENs were able to "thread the free end of the branch through a hole in the enzyme before sliding along to the trunk where it acts like a pair of molecular secateurs, trimming the branch and restoring the iconic double-helix."[5] The research results were high profile. His findings fed into a paper that was published in *Nature Structural & Molecular Biology* (2016) and also gained exposure in the popular press, given links to an ongoing plot-line in the popular SciFi TV series *The X Files*.

Because the enzymes involved in removing branched DNA modules are also involved in tumour progression and mutation, the research team hoped that the discovery would pave the way for better diagnostics and improved drugs, including new drugs to fight bacteria that have become resistant to antibiotics. In fact, Professor Sayers formed a spin-out company, DeFENition, in May 2016 in order to commercialise and enhance his research on FENs to this end.

The company focussed on identifying small molecule inhibitors of FENs, with the intention of developing a new class of antibiotics for highly resistant bacterial infections. The continued rise in antibiotic-resistant bacteria suggests that by 2050, 10 million lives a year will be at risk due to superbug infections. To help tackle this crisis, the company's initial focus has been on bacteria that the US Center for Disease Control and Prevention view as the biggest drug-resistant threats.

The research at Diamond helped demonstrate that the development of FEN inhibitors to tackle highly drug-resistant bacteria was based on clear and sound scientific foundations. This was crucial in helping to secure an initial investment of £400,000 from IP Group (an intellectual property commercialisation company) just three months after the *Nature Structural & Molecular Biology* publication. By December 2017, DeFENition had secured a further £1m of investment, plus funding from Innovate UK for follow-on research (including further work at the Diamond Light Source). The company now employs two full-time post-doctoral researchers, 1.2 full time technicians, and a number of external consultants.

5 https://www.wired.co.uk/article/branched-dna-x-files-scully-replicate

According to Professor Sayers, without the Diamond-based research that helped secure the initial investment, DeFENition could not have grown as quickly as it has. "*Our work and publications on flap endonucleases provided our initial investors with the confidence to invest in a new spin-out".*

Using Diamond offered a number of different advantages to Professor Sayers and his research team. Some elements of their work could not have occurred in the absence of a synchrotron – using university facilities would have meant using lower quality structures, in turn leading to poorer quality data and thus slower scientific progress. Specific characteristics of Diamond itself also made it appealing. This included the quality of Diamond staff and the proximity of the facility to the research team's university (Sheffield).

Supporting evidence

- Interview with Professor Jon Sayers, Professor of Functional Genomics/Deputy Head of Department of Infection, Immunity & Cardiovascular Disease, University of Sheffield
- Survey evidence from Professor Sayers
- *University of Sheffield spin-out secures investment to develop first-in-class antibiotic (16 November 2016). Available at* https://www.sheffield.ac.uk/news/nr/sheffield-new-antibiotic-secures-funding-1.662057
- Professor Jon Sayers profile for the Sheffield Institute for Nucleic Acids. Available at http://genome.sheffield.ac.uk/people/professor-jon-sayers/
- Groundbreaking research Direct observation of DNA threading in flap endonuclease complexes. *Nature Structural & Molecular Biology. 2016 23:640-6. https://dx.doi.org/:10.1038/nsmb.3241*
- *'X-Files' mystery of how DNA replicated itself is solved. Available at* https://www.wired.co.uk/article/branched-dna-x-files-scully-replicate

A.2.7. University of Warwick (Joanna Collingwood) - Transition metal ion and Alzheimer's disease

Summary: Dr Collingwood's research centres on the imaging and quantification of transition metal ion distribution and chemistry in human brains, using these to identify changes in neurodegenerative disorders such as Alzheimer's. One of the highest profile research projects has used Diamond to help understand the processes that lead to Alzheimer's disease, including strong indications that atypical chemical reduction of iron in brains contributes to the pathogenesis of Alzheimer's disease. The study's findings could inform the creation of more effective Alzheimer's therapies, and at a time when trials of iron modifying drugs are already underway, this work will be important in interpreting the trial findings.

One of the hallmarks of Alzheimer's disease pathology is the formation of plaques of amyloid-beta protein, which form insoluble deposits in the brain and impair its function. There is also evidence that regional brain iron levels change in Alzheimer's disease, and that some studies have associated iron foci with amyloid plaques. Well-regulated iron metabolism is crucial for health, and it is hypothesized that interactions between iron and amyloid-beta can adversely affect iron chemistry at sites of plaque formation in the brain, leading to overproduction of reactive species.

Dr Collingwood of the University of Warwick has collaborated with colleagues in the UK and USA to test this hypothesis by characterising in unprecedented detail the iron species found within amyloid plaques in the human brain. The research team used STXM beamline I08 at Diamond in tandem with the STXM 11.0.2 beamline at the Advanced Light Source in the USA to apply X-ray microscopy to the brain samples of two deceased Alzheimer's patients, to better understand the specific iron oxide compounds present. Access to the Diamond synchrotron was central to this effort, enabling the research team to examine the samples at tens of nanometres resolution, to non-destructively analyse organic and inorganic materials (here, transition metals) within a specific part of a sample, and – uniquely at I08 – to determine the magnetic properties of the iron oxide inclusions using X-ray Magnetic Circular Dichroism.

The research team found that the amyloid plaques had many types of reduced iron forms, including the iron oxide magnetite, which is not normally found in the human brain. From this, the research team deduced that atypical chemical reduction of iron occurs at a significant level at sites of amyloid deposition, supporting the hypothesis that this contributes to the pathogenesis of the disease. The research also uncovered evidence of multiple calcium compounds in the amyloid plaques, which may in future contribute to understanding disrupted calcium metabolism in Alzheimer's disease.

This research is helping to improve understanding of candidate treatments for Alzheimer's. For instance, clinical trials of iron modifying drugs to treat Alzheimer's are already underway, and it is expected that Dr Collingwood's work will help researchers better interpret the findings of these trials worldwide.

Dr Collingwood also noted wider benefits of using Diamond. For instance, she highlighted the effectiveness of Diamond's outreach and engagement work, noting that the organisation works hard to publicise its users' research through high quality public engagement and the showcasing of work to funders and stakeholders. This helps raise the profile of users and their research, and is particularly supportive and encouraging to early career researchers who are establishing independence.

The reach of their work at Diamond has helped Dr Collingwood's research collaborations increase their scale and impact, with increased citations, increased funding (using Diamond-based research as the basis for further research funding proposals), and increased funding to support early career researchers in the group. It has also has raised Dr Collingwood's profile, leading directly to collaborations with industry (and subsequent joint-funded projects), invited talks at international conferences, her term as chair of the Diamond User Committee, her service on the I08 beamline working group, and her recruitment to an overseas synchrotron beamtime review panel. She recognises that these factors arising directly from her research at Diamond have been instrumental in supporting her career progression within academia.

Supporting evidence

- Survey response and further engagement from Dr Collingwood
- Joanna Collingwood profile at University of Warwick. https://warwick.ac.uk/fac/sci/eng/staff/jfc/
- *Metallic drivers of Alzheimer's disease.* https://www.diamond.ac.uk/Science/Research/Highlights/2018/Metallic-drivers-of-Alzheimer-s.html
- Everett, J., Collingwood, J., Tjendana-Tjhin, V., Brooks, J., Lermyte, F., Plascencia-Villa, G., Hands-Portman, I., Dobson, J., Perry, G. and Telling, N. (2018). Nanoscale synchrotron X-ray speciation of iron and calcium compounds in amyloid plaque cores from Alzheimer's disease subjects. *Nanoscale*, 10(25), pp.11782-11796.

A.2.8. The Pirbright Institute (Bryan Charleston) - Foot and Mouth Disease Vaccine

Summary: **Foot-and-mouth disease (FMD) is a highly contagious, acute viral disease of cloven-hoofed, domesticated and wild animals. There are many variants of FMD which cause a global economic impact, estimated at US$21 billion per year. Vaccines do exist but are in short supply because of the need to grow large volumes of the live virus in high containment facilities and is expensive. Synthetic alternatives offer a possible solution by triggering an immune response without using live material.**

The search for an effective and practicable process for producing a synthetic vaccine suitable for mass distribution led researchers from the Pirbright Institute to the Diamond Light Source, where they have been able to determine the structure of different strains (serotypes) of FMDV (FMD virus) and gained a detailed understanding of the structural characteristics of a synthetic vaccine. In particular, the synthetic vaccine under investigation was less stable as its outer shell was prone to falling apart.

This research has provided proof of concept for a new low-cost vaccine which can be effective in protecting cattle against multiple serotypes of FMDV. The stabilised FMDV capsid has been patented in 13 countries. This has provided the basis for further funding from the Wellcome Trust and Bill and Melinda Gates Foundation to support the development of a commercially viable product with MSD Animal Health. This is progressing well and is expected to be available within the next few years.

The Diamond research should also enable the development of a wider range of vaccines, and research teams are currently applying similar approaches to Polio and Hand, foot and mouth viruses of humans.

Foot and Mouth Disease Virus (FMDV) is a pathogen that affects various domestic and wild animals, including cattle, sheep, pigs and goats. It causes a high fever, followed by blisters in the mouth and feet, which may rupture and cause lameness, and even death. It is highly contagious, and can be spread via contaminated equipment, clothing and feed, or directly between animals. Containment is also difficult, often requiring vaccination, monitoring, trade restrictions, quarantine and /or culling.

The disease can have severe implications for farming and there have been a number of major outbreaks of FMD globally since the disease was first recognised. This includes several outbreaks in the UK, including in 1967 when 442,000 animals were culled, in 2001 when 6 million animals were culled, and further localised cases in 2007 which resulted in a nationwide ban on cattle movement. The 2001 UK outbreak alone is estimated to have cost the economy £8 billion.[6]

FMDV remains endemic in many parts of the world and the research community has been seeking a better means to control it. Current vaccines are produced by growing large volumes of live virus before deactivating it to make the vaccine. Vaccines *do* exist, but they are in short supply because the production process requires producing large quantities of the live virus and are extremely sensitive to temperature and pH and can become ineffective if stored incorrectly.

To circumnavigate this problem, **scientists at the Pirbright Institute and the Universities of Oxford and Reading** - working in collaboration with the Diamond Light Source – have been developing a new synthetic form of the vaccine; a version of the virus' outer shell that can trigger an immune response without use of the live virus. This synthetic vaccine doesn't require a live infectious virus and is therefore much safer to produce and can be engineered to be more stable and therefore easier to store. Diamond was chosen because of the quality of its beamlines and because of the expertise available on site. One of the facility's scientist in particular is recognised as a leading voice on the structure of the FMDV.

While synthetic vaccines offer the potential for commercially viable mass distribution, they are often less stable because the outer shell is prone to falling apart. A primary aim of the research undertaken with Diamond was therefore to gain a more detailed understanding of the structural characteristics of the synthetic vaccine and of why these structures break. This was vital information in the development of a vaccine that is more stable, during production, storage and transportation, and that is therefore more commercially viable. At the same time, the research undertaken at the Diamond Light Source has also played a key role in determining the structures of the different strains of the FMD virus.

The development of the synthetic vaccine is progressing well, and it is expected that a commercially viable product will be available within a few years. The stabilised capsid has 13 patents in place across 10 countries and Europe. The initial research programme has also served as the foundation for a long-standing partnership between The Pirbright Institute and Oxford University, which has recently received a further £3 million from the Wellcome Trust and an award from the Bill and Melinda Gates Foundation to support further development towards a commercial product.

Without the facility and expertise, it is highly likely that the research would not have progressed so far. The success has been contingent upon this access. Indeed, other research groups have attempted to replicate the research elsewhere, but without the same level of success.

It is worth noting that there are seven serotypes and multiple strains of each serotype of FMDV, and a number of different vaccines, suitable for use against different strains will be needed. The Diamond-based research into the structures of these different strains will therefore also be important in enabling the development of a wider range of targeted vaccines. The work also opens the door to vaccines for other human viruses within the same family. Notably however, while the approach is similar, the diversity of viruses means that the details of how to make a stable synthetic vaccine are different.

An international team have already successfully applied the same technology to the Polio virus and identified a candidate for a synthetic polio vaccine. The team that includes staff from Diamond Light Source used the cryo-electron microscopy at Diamond's Electron Bio-Imaging Centre to confirm the structure of the synthetic vaccine and have demonstrated its viability in small scale laboratory tests. These results have paved the way for a new synthetic vaccine to help eliminate the polio virus.

The research has the **potential for very significant impacts**. FMDV outbreaks can be extremely costly to the economy and a method of disease control that avoids mass culling of livestock would be a major step forward. Therefore, an effective vaccine would be an essential tool for outbreak control of FMD in countries that are currently free of FMD, such as the USA and Europe. An effective FMD vaccine that is readily available will also significantly improve food security as FMD outbreaks hit low and middle-income countries hardest by reducing the availability of milk and meat, as well as dependence on animals for transport and cultivation.

Supporting evidence

- Interview with Dr Bryan Charleston, Director of Immunology, Veterinary Practitioner, Virology from The Pirbright Institute
- Diamond Light Source, Latest News (2013) "Food-and-mouth-disease vaccine" http://www.diamond.ac.uk/Home/News/LatestNews/27_03_13.html
- Diamond Light Source, Latest News (2017) "FMDV-host interactions mapped" https://www.diamond.ac.uk/Home/News/LatestNews/2017/02-06-17.html

6 Knight-Jones, T. J.; Rushton, J (2013). "The economic impacts of foot and mouth disease – What are they, how big are they and where do they occur?

- Diamond Light Source, Latest News (2017) "New synthetic Polio vaccine candidate" https://www.diamond.ac.uk/Home/News/LatestNews/2017/15-08-17.html
- The Pirbright Institute, Foot-and-mouth-disease virus fact sheet https://www.pirbright.ac.uk/files/quick_media/Foot-and-mouth%20fact%20sheet%20DL%20leaflet_FINAL.pdf

A.2.9. University of Edinburgh (Colin Pulham) – Phase-change materials and Sunamp Ltd.

Summary: Professor Pulham uses the Diamond Light Source to examine the properties and behaviour of different materials over a range of pressures and temperatures. One of his highest profile research areas has been the crystallisation of phase-change materials and their role in heat storage. Working in collaboration with Sunamp Ltd, his research into the properties and performance of phase-change materials has contributed to the development of the company's "heat batteries" which can store thermal energy at higher energy densities than more traditional methods (e.g. hot water tanks). The research at Diamond has helped provide the evidence needed to help develop a more controllable and commercially-viable product, which has the potential to reduce both CO2 emissions and domestic fuel bills.

Forty-two per cent of UK energy consumption is in the form of heat and so there is growing interest in finding more efficient heating solutions, especially through heat-storage systems.

Sunamp Ltd. is a small, but rapidly growing Scottish company that designs and manufactures thermal batteries for heat storage. These use phase-change materials (PCMs); chemical compounds that can store and release large amounts of energy (heat) through melting and solidification (and importantly much more energy per unit volume than traditional methods of heat storage, such as hot-water tanks). The technology therefore has the potential to reduce CO2 emissions and domestic fuel bills, thereby making a contribution to the alleviation of fuel poverty.

Initially, Sunamp bought off-the-shelf PCMs, but inconsistent performance led the company to link up with the University of Edinburgh to understand more about PCMs and improve the reproducible performance of the PCMs used in their heat battery technology. The company worked with David Oliver, then a materials science PhD candidate at the University; and Professor Pulham, Professor of High-Pressure Chemistry at the University of Edinburgh, who regularly uses the Diamond Light Source to examine the properties and behaviour of various materials (pharmaceuticals, fuels, energetic materials) under a range of pressure and temperatures.

Mr Oliver used his understanding of the underlying science that causes salt hydrates to fall apart to shortlist some potential PCMs for Sunamp. He and Professor Pulham used X-rays on the I11 beamline to examine the crystal structures of PCMs – how the atoms are arranged and how these change during crystallisation – as well as to explore possible degradation pathways. The high intensity of Diamond's X-ray source (especially relative to laboratory X-ray sources) meant that data could be collected in a matter of seconds, allowing Professor Pulham, Mr Oliver and the research team to study changes to crystal structures in real time under variable temperature conditions. University facilities would only have enabled them to study solid state materials.

The research determined the temperature at which one particular PCM formulation developed by Mr Oliver would cease to function properly and identified the various crystalline species present during heating and freezing cycles. One 48 hour session of beamline time at Diamond helped confirm that the particular PCM formulation worked as intended and could be commercially viable.

The work at Diamond has had several important commercial benefits for Sunamp. For example, the research has helped the company's product development. Knowing the temperature that PCM formulations begin to degrade has meant that Sunamp could build in appropriate temperature cut-offs to their batteries. The research has also provided clear scientific evidence that the novel PCM formulation works and that the enhanced phase-change materials will continue to function over extended periods, some 40,000 cycles. This has helped to reassure investors as to long-term battery performance and hence appropriateness for domestic installation. The data from Diamond helped Sunamp secure a several million-pound investment from a venture capital firm, something which has been one of the cores bases upon which Sunamp has grown. It meant that Sunamp could progress the technology while there was still demand and a market gap which they could exploit. The company is now valued at tens of millions of pounds. Their heat batteries are currently in 1,000 UK homes, and have a memorandum of understanding in place to supply Chinese homes too. Mr Oliver subsequently joined Sunamp following his PhD, and Sunamp is now one of the global leaders in salt-hydrate PCM knowledge. The data from Diamond has also been shared with OEMs with a view to working with them in the future.

Professor Pulham's research team has also benefited from the project through the direct demonstration of the socio-economic impact of the research. The relationship with Sunamp means that the University of Edinburgh receives royalties from battery sales. The PCM research has also helped Professor Pulham (in partnership with Sunamp) to secure follow-on funding from organisations such as Innovate UK, the Energy Technology Partnership, and the Advanced Propulsion Centre to continue related research work. The work has also gained international interest, which has resulted in Professor Pulham being approached by other potential partners and collaborators who are keen to work with his team in future.

Supporting evidence

- Interview with Professor Colin Pulham, University of Edinburgh
- Survey response from Professor Pulham
- Interview with David Oliver and Andrew Bissell, Sunamp
- Enhanced Phase-Change Materials for Heat-Storage Applications, presentation slide pack prepared by Professor Pulham and Sunamp
- https://www.diamond.ac.uk/Home/News/LatestFeatures/Issue-5/28_12_15.html

A.2.10. University of Manchester (Alberto Saiani) – Characterising molecular materials

Summary: Professor Saiani's research focuses on the characterisation of molecular materials across length scales. His particular interest is the study of the correlations between chemical architecture, structure / morphology and physical properties in complex polymeric systems. His Diamond-based research has included examining the self-assembly of short peptides into fibres and their subsequent hydrogelation. Diamond has helped in developing the fundamental knowledge allowing the precise design of these materials that resulted in the establishment of Manchester BIOGEL™, a start-up company that offers engineered, self-assembling peptide hydrogels for use in biomedical applications. Work perform at Diamond has also contributed to Professor Saiani's career development by supporting the publication of high-profile research papers.

Alberto Saiani is Professor of Molecular Materials in the School of Materials at The University of Manchester. His research focuses on the characterisation and development of polymeric materials, with a particular interest in the study of the correlations between chemical architecture, structure / morphology and physical properties in complex polymeric systems. He has used Diamond many times to help characterise the morphology of thermoplastic polymers and explore the fibrillar structures resulting from the self-assembly of short peptides as well as their assembly into fibrillar hydrogels.

Over 15 years ago, Professor Saiani – along with his colleague Professor Aline Miller – synthesised a family self-assembling peptides, with interesting gelling properties. They used Diamond to gain a better understanding of how peptide design affects the fibres' structure and how these fibres assemble together to form hydrogels. These hydrogels are commonly used for cell culture and tissue engineering applications, providing structural support and a natural physiological extracellular environment for cells. They also offer additional opportunities, including in the development of more effective drug delivery systems and biosensors.

Industry and academic demand for the peptide hydrogels led to the c0-founding by Professors Saiani and Miller and Dr. G. Saint-Pierre of Manchester BIOGEL™ (originally PeptigelDesign) in 2014. This start-up licensed the technology from the University of Manchester and now offers a range of self-assembling peptide hydrogel products (PeptiGels®), suited for use in 2D and 3D cell culture, 3D bioprinting (PeptiInks®) and incorporation into medical devices. These off-the-shelf formulations are now sold to a range of clients working in the biomedical field (e.g.: disease modelling, tissue engineering and regeneration, drug delivery). The company also offers more bespoke services, whereby they are able to tune the mechanical and functional properties of their gels to suit the individual needs of specific clients (e.g. for pharmaceutical purposes). The Diamond-based research contributed to the fundamental knowledge allowing developing the product and process control required for the design of these hydrogels with precise properties.

Diamond's beams are especially bright, which for example allowed real-time flow experiments that were crucial for the study of cell injection processes. Equally as important as the quality of physical infrastructure, was the expertise provided by Diamond staff. Their post-analysis support has been especially important as well as their support to PhD students. Diamond's proximity to other facilities at Harwell used by Prof Saiani group, such as ISIS, is also particularly advantageous.

In November 2017 and May 2019, the company received significant investment from Kero Group™ (industrial investors backing cutting edge technologies) and DeepBridge Capital™ (venture capital fund investing in the biomedical sector). This has enabled growth of the team, bringing marketing, sales and intellectual property specialists on board, as well as expanding the company scientific expertise. A new larger team is now widening the company's remit – offering the companies unique hydrogels to the pharmaceutical, biotechnology and cosmetic industries, in addition to academic users.

The research conducted at Diamond has also helped Professor Saiani and his research team achieve notable personal benefits. The data collected led to the publication of high impact papers, helping Professor Saiani establish himself as an expert in his research field. This in turn played an important role in securing promotions and the award in 2015 of a prestigious EPSRC 5-years research fellowship. His wider research team also benefitted from using Diamond, for example in helping secure post-doc positions in other leading UK and oversee institutions for several of the PhD students involved.

Supporting evidence

- Interview with Professor Alberto Saiani, University of Manchester
- Survey response from Professor Alberto Saiani
- Prof Saiani website: www.polymersandpeptides.co.uk
- Manchester BIOGEL™ website: www.manchesterBIOGEL.com

A.2.11. The Mary Rose Trust – Informing conservation techniques

Summary: The Mary Rose was a Tudor warship that sank in the waters of the Solent in 1545. In 1982, archaeologists raised the wreckage from the seabed and since then, there have been considerable efforts to conserve both the ship and artefacts from it. Diamond has hosted several research projects centred on determining the effectiveness of various conversation efforts, and their suitability for continued use, both in relation to the Mary Rose and with other UK heritage assets. For example, Diamond has been used to study the corrosion profiles of cannon balls that have been treated with a range of different conservation methods, helping to inform preservation techniques going forward.

The Mary Rose was a Tudor warship that sank in the waters of the Solent in 1545. In 1982, archaeologists raised it from the seabed and, since then, there have been considerable efforts to conserve the wreck and associated artefacts. Between 1994 and 2013, the ship's timbers were been sprayed with the water soluble wax, polyethylene glycol (PEG), to help seal the wood and structural stability to the wood where it has already degraded.

The Mary Rose Trust, the organisation responsible for preserving and displaying the warship, has conducted experiments at Diamond since 2008. While traditional lab based methods can provide an indication of the material composition of an artefact, the techniques available at Diamond provide greater detail to better support their development work. Initial projects focused on using X-ray beams on I18 to determine the distribution of sulphur and iron compounds in ship timber samples, and how these substances interacted within the wood.

In 2013, the Trust stopped spraying the ship, and started drying out residual moisture from the wood. Researchers exposed slivers of ship timber and used Diamond to determine precisely which elements were present in the drying wood, and to spot potential oxidation (and resultant acid build up) that could occur during drying. Understanding whether there is molecular level damage can help identify a need for corrective action before longer-term damage occurs. Moreover, this research has also helped development other treatments.

Further research in 2014, using the I18 beamline at Diamond, helped show that PEG itself had promoted the oxidation of iron in acidic solutions. While this is still the standard treatment used, this research has allowed the team to be more mindful of these methods and their effects on the artefacts.

More recently, research led by Eleanor Schofield (now Head of Conservation and Collections at The Mary Rose Trust) at Diamond has also helped understand conservation techniques for non-wooden artefacts from the Mary Rose. Some 1,200 cannon balls were recovered from the wreckage, but given their long-term exposure to corrosive sea water, preserving the artefacts has become a real concern. The cannon balls have been treated with a range of different conservation methods. Using Diamond has allowed the Trust's researchers to study the corrosion profiles of the different cannon balls and trace them back to the different treatments applied. This work has contributed significantly to their decision-making about the best conservation techniques going forward as it helps conservators to understand the true effects of the conservation methods. As this cannonball collection is very repetitious, the Trust is able to conduct techniques that other collections may not be able to. In this sense, other conservation efforts are looking to the Trust and their outputs of the work with Diamond to better understand iron preservation of their own collections.

The research on cannonballs is supported by a joint PhD student through UCL's Doctoral Training Centre and Diamond, who is investigating the different iron conservation treatments. Through the work at Diamond, the project was able to connect with a number of other researchers and broaden the scope of work which was thought to benefit not only the scope of the project, but the PhD student's experience too.

As a charity, they are dependent upon interest from the public and ticket sales, which in 2018 amounted to around £2.4m. As such, the PR generated through the work has been highly valuable for the trust. While the impact of the research conducted at Diamond will not be evident for some years, it is valuable to ensure the longevity of the collection. For that reason, the work conducted at Diamond is a useful part of the investments made into conservation (in which the trust spends around £1m per year). The Mary Rose achieved second place in the 2018 European Museum of the Year award. The Mary Rose is one attraction at the Portsmouth Historic Dockyard which in 2017 attracted a record number of 850,000 visitors and an economic impact of £110.40 million per year.

The improved understanding and techniques developed with Diamond in relation to the Mary Rose will have wider implications, helping to better protect and preserve other heritage assets. These are key aspects within the UK tourism industry offer and therefore important for the UK economy (UK tourism is worth ~£80 billion per year). The conservation team at The Mary Rose Trust are expecting to continue using Diamond to explore the chemical composition of other items in their collections.

Supporting evidence

- Interview with Professor Eleanor Schofield, Head of Conservation and Collections Care, Mary Rose Trust
- Science Ahoy! Preserving the Mary Rose with Diamond light. https://www.diamond.ac.uk/Home/News/LatestFeatures/20_04_15.html
- High-tech conservation for old warship. https://www.diamond.ac.uk/Home/News/LatestNews/7February2008.html
- Preston, J., Smith, A.D., Schofield, E.J., Chadwick, A.V., Jones, M.A., Watts, J.E.M. (2014) The Effects of Mary Rose Conservation Treatment on Iron Oxidation Processes and Microbial Communities Contributing to Acid Production in Marine Archaeological Timbers. PLoS ONE 9(2): e84169. https://doi.org/10.1371/journal.pone.0084169
- Science meets conservation on Mary Rose cannonballs. 'Eureka!' magazine, March 2018. http://www.eurekamagazine.co.uk/design-engineering-news/science-meets-conservation-on-mary-rose-cannonballs/170599/
- The Mary Rose Trust, Annual Report 2018. https://maryrose.org/annual-reports/
- https://www.archaeology.co.uk/articles/a-shot-at-conservation-using-the-latest-technology-to-save-the-mary-roses-cannonballs.htm
- Simon, H., Cibin, H. G., Robbins, P., Day, S., Tang, C., Freestone, I., Schofield, E., (2018) A Synchrotron-Based Study of the Mary Rose Iron Cannonballs. *Angew. Chem. Int. Ed. 57*, 7390. https://onlinelibrary.wiley.com/doi/full/10.1002/anie.201713120
- Record-Breaking year for Portsmouth Historic Dockyard https://www.historicdockyard.co.uk/news/item/912-record-breaking-year-for-portsmouth-historic-dockyard

A.2.12. Cambridge University (Alan J. Warren) – Understanding neurodegenerative disorders[7]

Professor Warren's research activity includes examining the causes of neurogenerative disorders. Using Diamond Light Source has helped inform his work (in collaboration with the lab of Dr. David Ron) on the Integrated Stress Response (ISR), a cellular stress response common to all cells with a nucleus enclosed within a membrane (eukaryotes). ISR is a signalling pathway present in eukaryotes and is activated in response to a range of physiological changes and different pathological conditions. Although ISR is essentially a way to help cell survival, excessive exposure to ISR can lead to cell death.

A chemical inhibitor of the ISR, the experimental drug ISRIB (Integrated Stress Response Inhibitor), works by reducing the effect of eIF2B, a multi-subunit protein that is critical for the initiation of protein synthesis and in turn cellular changes. ISRIB has previously been shown to protect mice from neurodegeneration and traumatic brain injuries. Professor Warren has used Diamond's electron microscopy facilities to study the structure of eIF2B, and how ISRIB binds to it. By understanding the structure of e1F2B, the research group was able to identify a site on the structure that ISRIB could exploit to regulate eIF2B translation, and therefore the ISR.

According to Professor Warren, the research undertaken at Diamond, which has helped identify ways of inhibiting the ISR, will have major implications for the development of new therapeutics for neurodegenerative disorder treatments. His research group has already had discussions with venture capitalists with a view to forming a spin-off to bring new small molecule therapeutics into clinics.

On a personal level, the research has also had important benefits. It has been particularly high profile, featuring in reputable journals, helping Professor Warren secure additional funding, and his appointment to grant panels and editorial boards.

Supporting evidence

- Survey response from Professor Alan J. Warren
- Zyryanova AF, Weis F, Faille A, Alard AA, Crespillo-Casado A, Sekine Y, Harding HP, Allen F, Parts L, Fromont C, Fischer PM, Warren AJ & Ron D. (2018) Binding of ISRIB reveals a regulatory site in the nucleotide exchange factor eIF2B. Science 359 (6383):1533-1536

7 This case study draws exclusively on a survey response and published material

A.3 Supplier case studies

A.3.1. Kurt J. Lesker – Supplying specialist vacuum technology

Summary: Kurt J. Lesker is a specialist manufacturing and distribution company providing bespoke vacuum chambers to facilities including the Diamond Light Source. The construction of vacuum chambers and associated hardware has increased Kurt J. Lesker's experience of working with the technical requirements of synchrotrons and improved the reputation of the company. As a result, the company has seen increased exposure and sales to new markets (including Diamond's other suppliers and other synchrotrons abroad).

Kurt J. Lesker manufactures and sells high-quality vacuum technology. The company has had a number of ongoing contracts with Diamond to supply different pieces of vacuum hardware, including one-off bespoke vacuum chambers (which remove absorption of beamlines by air scattering effects and thereby improve the end results of experiments).

The high technical standards and the specific nature of Diamond's requirements has stimulated a better understanding of different solutions within the company, encouraged the development of better quality products and increased the company's capacity to innovate.

Working with Diamond has also provided Kurt J. Lesker with opportunities to access new markets. On the one hand, Diamond has connected them with other suppliers involved in the UK synchrotron market. For example, they have been able to secure a number of contracts with another of Diamond's suppliers, FMB Oxford. On the other hand, their experience of working with Diamond has improved their understanding of synchrotrons, including their price and technical requirements, which has aided their entry into other markets (e.g. synchrotrons in France, Germany, and Sweden). Diamond has also provided the company with reputational benefits, supporting their other sales.

Diamond is a key customer for Kurt J. Lesker, but this is a global company working with a range of institutions (e.g. CERN). Working with Diamond has accelerated their traction into these other European projects and resulted in around £100k of increased sales.

- Supporting evidence
- Survey and interview responses from Marc Poulsom, Regional Sales Manager, Kurt J. Lesker

A.3.2. T-Squared – Design, construction and servicing of controlled environments

Summary - T-Squared is a specialist engineering company that provides design, construction and servicing for controlled environments. Over the past ten years, T-Squared has provided Diamond with a range of different services, including upgrades to beamline cabin structures, and numerous mechanical and electrical services installations that support it. Diamond has been an important client, providing repeated work, as well as links to other customers based on the wider Harwell campus.

T-Squared is a specialist engineering company that provides design, construction and servicing for controlled environments. It has provided a range of services to Diamond over the past decade, but the size and significance of these contracts has increased significantly in the past five years.

For example, one notable contract concerned beamline I15 in late 2014. To enable the upgrade of experimental equipment, a number of modifications were needed to the structure of the beamline cabin, and the various mechanical and electrical services installations supporting it. Diamond appointed T-Squared to carry out these works, which included:

- Modifications to cabin wall, floors, doors, windows and roof
- Installation and extension of pipework for air, gases, and water
- Cabling and earthing installations
- Replacement of lighting systems
- Modification of safety and alarm systems

Diamond is a valued customer for T-Squared. Not only has it provided the company with repeated custom, but staff particularly enjoy assignments for the facility and the opportunities this provides to interact with Diamond staff. The work for Diamond has also helped showcase T-Squared to other potential customers on the Harwell Campus, with contracts having since been awarded to supply other organisations on site. Being a supplier to such a well-known organisation has also helped to enhance T-Square's reputation and it uses Diamond as a key reference when bidding for other jobs.

Although T-Squared works for a range of clients, the company did note that working with Diamond has helped to at least safeguard some jobs and revenue at its Swindon office. It also highlighted that its Diamond contracts had helped keep sub-contractors busy, nearly all of whom are based in the UK.

Supporting evidence

- Interview with Mike Shurmer, Director of T-Squared P3 Ltd
- Survey response provided by the company
- http://www.tsquared.co.uk/projects/index/id/56

A.3.3. Faraday Motion Controls – High performance motion control systems

Summary: Faraday Motion Controls (FMC) specialises in ultra-high-performance motion control technologies. Their contracts with Diamond have given the company access to new markets, an enhanced reputation, and led to additional employment. Sales to foreign facilities have increased by around £750k per year, a benefit which would have been unlikely without initial work for Diamond.

Diamond Light Source has over 1,000 axes of motion that require manoeuvring to high levels of precision. For example, guiding light, focusing the beam and directing it towards instrumentation. Motion control systems are also required for holding, positioning and manipulation of samples. The angles and positions in each case are guided by electronic motion commands developed by Delta Tau.

Faraday Motion Controls (FMC, formerly Delta Tau UK), have delivered several contracts to Diamond in recent years, with the facility using many of FMC's control technologies for mechanical handling equipment. For example, as light enters the beamlines at Diamond, it is guided through a series of slits, lenses and crystals, the angles and positions of which are guided using electronic motion commands generated by FMC's unique "MACRO" communications protocol, licensed from Delta Tau.

The company was very small when it won its first contract with Diamond, but they continued to win further contracts with the facility, which has contributed to FMC's growth. The company has hired additional staff, four of which (including one apprentice) are directly attributable to Diamond contracts. The Diamond contracts have also allowed the company to gain momentum and impetus upon which further contracts, both with Diamond and further afield, have been based.

Though Diamond's contracts, FMC have also been able to increase awareness of their company and bolster their reputation. Prior to working with Diamond, FMC worked predominantly with UK clients. Diamond contracts have opened the door to wider international markets, providing the necessary knowledge and expertise to access high energy physics clients globally. This includes contracts with synchrotrons, fusion laser, free electron lasers and Neutron sources in Brazil, Australia, North America, Canada, Germany, France and China, as well as third party suppliers to these facilities.

Without the contracts with Diamond, FMC believe they would be a radically different company. Given the narrow vertical market within which they work, the reputational benefits and references provided by Diamond have been very valuable. Sales to foreign facilities have increased by around £750k per year, a benefit which would have been unlikely without FMC's initial work for Diamond. Access to this niche market has been central to the company's success and now accounts for 50% of their turnover.

FMC's contracts with Diamond have also helped further R&D activity within the company, including new products that have been developed following feedback from Diamond. This includes their fourth (and current) generation of control systems. From the company's perspective, their ability to innovate, design and produce new products has been the most important benefit of being a supplier.

Supporting evidence

- Interview and survey responses from Andy Joslin, Director of Faraday Motion Controls
- http://faradaymotioncontrols.co.uk/diamond-is-in-motion/

A.3.4. DECTRIS – Supplying specialist X-ray detectors

Summary: DECTRIS develops and produces high-quality, high-performance hybrid photon counting X-Ray detectors. Since its establishment in 2006, the company has been developing and selling different detector systems to the Diamond Light Source, innovating to meet the ambitious demands of the facility and its user community. Given the strong international standing of Diamond, supplying them with specialist detectors has had strong benefits for the reputation of the company and helped it grow more rapidly.

DECTRIS was established in 2006. It develops high-quality, high-performance hybrid photon counting (HPC) X-ray detectors. Diamond bought their first large-area detector system from DECTRIS in 2008, and since then it has purchased a number of different detector systems, including the company's first MYTHEN 6K detector and the PILATUS 12M-DLS - the largest and most customer specific PILATUS detector built.

While some of the instruments that DECTRIS provides to Diamond are more 'standard', the company also provides more bespoke products. In doing so, the relationship with Diamond has stimulated further innovation within DECTRIS and eventually encouraged it to also commercialize more advanced detectors.

A prime example of this is the development of the Long Wavelength Macromolecular Crystallography (MX) Beamline, I23. This I23 beamline was one of the most ambitious MX beamlines in the world and remains unique to Diamond. The specialist requirements of the beamline posed new challenges for DECTRIS and required them to provide innovative solutions.

The PILATUS 12M detector DECTRIS built in response was possible due to their extensive experience of detectors, custom geometries and special energy calibrations. This was the first in-vacuum detector DECTRIS developed and the first in such complicated custom geometries. Diamond also hosted the initial tests of a Pilatus detector in vacuum and later performed the first in-vacuum experiments at the Diamond test beamline B16. This new innovative detector allows users to perform experiments in a wavelength range not accessible at any other MX beamline world-wide, allowing direct access to the three-dimensional structure of their samples without the need to modify them beforehand. The detector is *unique* to Diamond and strongly supports the facilities' competitiveness in the MX space.

Diamond is ambitious to stay at the cutting edge of research and is pushed by its user community to provide the newest methods and services. This has translated to the products it requests of DECTRIS, encouraging and supporting them to develop new products and services and providing testing facilities. After these first successful tests, in-vacuum products have become a significant part of the DECTRIS product portfolio and a unique selling proposition that enables new applications.

Given the strong reputation of the Diamond Light Source on the international research scene, there are benefits to being associated with the facility. DECTRIS is keen to capitalise on this and it uses its work with Diamond to showcase the company's capabilities on social media and in advertising campaigns. DECTRIS also uses Diamond as a reference for other potential customers. The Diamond user community also tends to visit other synchrotrons, and DECTRIS believes that this has helped spread the word about the company to these other facilities. Certainly, DECTRIS has succeeded in winning contracts with other synchrotrons across the globe and believe that this is, at least in part, a result of Diamond contracts.

While DECTRIS now has an international customer base, it is clear that the early collaboration with Diamond was a significant boost to DECTRIS's continued growth and success.

Supporting evidence

- https://www.dectris.com/
- Interview with Johannes Durzok, Head of Sales, DECTRIS
- Support from Armin Wagner, Principal Beamline Scientist I23
- Novel crystallography beamline takes delivery of in vacuum X-ray detector (Diamond Science Highlights, 2014). Available at: https://www.diamond.ac.uk/Science/Research/Highlights/2014/I22-detector-install.html

A.3.5. Orbital Fabrications – Specialist welding and fabrication

Summary: As specialists in the design and manufacture of Stainless Steel high purity gas delivery solutions, we provide repeatable fabrication for high tech companies as well as one-off fabrications or prototyping of bespoke and unique systems. Over the past 30 years, Orbital Fabrications have served a range of clients in the semiconductor, pharmaceutical, aerospace, chemical and allied industries. Over the course of the last decade, the company have had 9 contracts with Diamond, providing significant revenue for the company and the capacity for increased employment. Furthermore, Diamond's high standards have encouraged and stimulated Orbital to improve the quality of their products and their internal capabilities. The company has benefited from the reputational benefits of being associated with the facility, with new clients in the scientific sector.

Orbital Fabrications pride themselves on being one of the "best in class" specialist welding company in the UK. Orbital welding is a technique whereby a tube or pipe is held in place while the electrode rotates (or orbits) around it. It offers higher levels of control over precision welding and can therefore produce more reliable components. Typical clients for this technique include companies in the semiconductor, pharmaceutical, aerospace, chemical and allied industries.

Orbital Fabrications have worked with Diamond since 2007, when the facility was in its initial construction phase. Since then, the company has had continuous contracts with the facility to provide welding services. Their first contract was one of the largest in their history (£1.5M), which proved to be very successful. Subsequently, Diamond went on to appoint Orbital Fabrications for a further eight projects.

Prior to its first contract, Orbital Fabrications were a small company of 15-20 staff, based on a tiny industrial estate. The additional revenue from Diamond contributed to the company being able to buy their own premises in St Ives, just outside of Cambridge, and to employ five more staff. The benefits to the company extend beyond the specific contracts though.

For instance, Diamond's welding inspector recommended the company to other clients. The company was also exposed to other opportunities with new clients on the Harwell campus when working with Diamond. More generally, Diamond's high-profile and reputation for quality has been of some help to Orbital Fabrications when approaching new clients. As a result, Orbital Fabrications, which used to focus mainly on semi-conductor and pharmaceutical industries, has moved increasingly into the scientific sector.

Contracts with Diamond have also had an impact on skills, capabilities and processes within the company. As they have had to work closely with Diamond's welding inspector, Orbital Fabrications have been pushed to improve their own capabilities. This included not only the quality of their products and services, but also the skills level of their staff. As a result, the company is better able to maintain its global competitiveness and is more experienced in working with Weld Inspectors and Qualifications.

Partly as a consequence of its contracts with Diamond, Orbital Fabrications have also introduced more systematic document traceability mechanisms to help ensure that information and documentation requests can be more easily and more efficiently provided. These improved efficiencies have affected their interactions with all their clients for the better.

Diamond has been beneficial to Orbital Fabrication's development, playing a noteworthy role in the company's growth over the last ten years.

Supporting evidence

- Interview and survey responses from Ian Pearson, Chairman of Orbital Fabrications
- https://www.orbitalfabrications.co.uk/

A.3.6. Hivac Engineering – Specialist vacuum chamber manufacturing

Summary: Hivac are a UK based manufacturing company specialising in ultra-high vacuum chambers. Through their contracts with Diamond, Hivac have not only benefited directly from increased turnover and employment but also via the reputational benefits of being associated with Diamond. Diamond has provided the motivation and specifications to produce innovative, high quality products, as well as opportunities to tap into new markets across Europe.

Hivac are specialist manufacturers of ultra-high vacuum chambers and equipment. They secured their first contract with the Diamond Light Source in 2004 and have since delivered a further 150 contracts.

The first contract involved vacuum chambers that required oven bake & RGA scan. As this was not something the company had produced before, they set about developing a bake out unit in house to allow the tendering on future Diamond projects guided by the detailed specifications provided by Diamond. This has been repeated in subsequent work with specific, high-end solutions being required by Diamond, which have encouraged innovation and technology development within the company, pushing for a quality of product that Hivac may not otherwise have sought. In many cases, the resulting new or improved products have found application elsewhere.

The 10+ year history of contracts with Diamond have been very valuable for the company. This has been an important source of revenue, with additional employment also created to cater to the project work. It has also helped enhance the reputation of Hivac as a highly technical manufacturing company. Their connection with and reputation within the international synchrotron community has grown, and their experience with and references from Diamond have helped to bolster their bids to other scientific companies and research facilities across the world. The company believes that perhaps £200k-£300k of turnover each year is attributable to their work for Diamond.

Diamond remains a key client for Hivac, although the majority of their sales are now elsewhere in Europe and the rest of the world. It is possible the company would have moved elsewhere, if it were not for the continued opportunities at Diamond, which would also have had implications for its UK-based supply chain.

Supporting evidence

- Interview and survey responses from Paul Lennard, Managing Director, Hivac

Appendix B - Methodology

In this section we set out the requirements for the study, followed by details of the approach taken.

B.1 Requirements

Diamond commissioned Technopolis to undertake a socio-economic impact study with the aims of:

- Measuring and demonstrating the facility's economic and social benefits to stakeholders
- Contributing to the available evidence base to help secure further funding for Diamond
- Helping to better understand what Diamond's future impact might be
- Developing an evaluation framework that Diamond can use in the future.

The study was asked to include three distinct, but inter-related and overlapping stages, covering evaluation scoping, the evaluation itself, and the development of a benefits framework/plan for the future. The key aims, tasks, and requirements for each of the three stages are outlined below:

Stage 1: Scoping and methodology development for the assessment of Diamond

- Review initial data and documentation provided: This should form the basis for the development of an evaluation logic model, which should detail the logical sequence and causal relationships among: Diamond's rationale, aims and objectives; the resources used and the activities undertaken; and the results, outcomes and ultimately impacts that will be realised as result
- Identify gaps in the data currently available: To determine whether there is sufficient information available to enable a full and robust evaluation of Diamond. If there isn't, then additional monitoring and evaluation tools (e.g. surveys or further data) need to be considered and planned
- Design a monitoring and evaluation framework: Finally, the evaluation approach should be developed, based on the learning of the scoping phase, as to what the most appropriate methodology is. This should be presented to the Project Board for approval

Stage 2: Socio-economic Impact from Diamond – Evaluation

- Gather evidence of user benefits: Quantitative and qualitative evidence should be obtained on the actual and projected economic and non-economic benefits to the main user groups of Diamond
- Gather evidence of wider impacts: Quantitative and qualitative evidence should also be obtained related to wider socio-economic impacts of Diamond, beyond its users. This will include the benefits to Diamond's suppliers, and the enhancement of the UK's reputation in science
- Quantify and aggregate the impacts: the impacts should then be quantified and aggregated – and then monetised as far is possible. Wider benefits of Diamond should also be captured.

Stage 3: Development of a monitoring and evaluation plan for Diamond

- Create a final monitoring and evaluation framework for future use: Drawing on the experiences and findings in Stages 1 and 2, a finalised monitoring and evaluation framework should be produced. This will include any additional regular data or tracking methods that are deemed to be of significant benefit to future socio-economic studies into Diamond.

B.2 Evaluation scoping phase (Aug-Dec 2017)

The first phase of the study focused on planning and preparation for the main phase of evaluation. Through initial discussions, document/data review, and desk-based developmental work, the study team sought to establish key contextual issues for the study, understand what relevant data and information were already available (or not) and devise a logic model and evaluation framework to guide the next phase of the study. This included further developing the approach and methodology outlined in the original proposal for the study, along with associated data collection tools and templates. Details of the main activities undertaken during this phase are summarised below.

B.2.1. Study inception meeting

An inception meeting was held on 8th August 2017 between the study team and representatives from Diamond and STFC. This was used to provide further details as to the background to the study, as well as relevant contextual issues relating to Diamond's operations and activities. The meeting was also used to discuss various aspects of an initial information request issued to Diamond by the study team.

B.2.2. Review of key documentation and data

Based on our previous experience of carrying out socio-economic impact assessments of large-scale research infrastructure, we had a reasonable understanding of the core data and information that would be needed and might already be held by Diamond (in annual reports, user databases, financial records, etc.). We therefore issued an initial request for data and information, which covered:

- Various background information on the facility (annual reports, strategies, case studies, etc.)
- Financial data, including key aspects of income and expenditure, as well as employment
- Contact databases for various stakeholders, staff and users, for use in interviews and surveys
- Other data to inform the assessment (beamtime, usage, publications, training/events, visitors)

A considerable amount of content was then collected by Diamond and transferred to the study team over the subsequent weeks. An initial review of each item was undertaken, so as to understand its relevance and usefulness in the next stages of the impact assessment, as well as to identify any remaining gaps that would need to be filled through further data collection activities (surveys, interviews and other means) and which were then built into our evaluation methodology and tools.

In addition to cataloguing the material, a selection of these documents were reviewed in more detail to better understand the underlying rationale and objectives that have shaped Diamond, helping to frame the overall evaluation logic model and plans for the evaluation.

B.2.3. Scoping interviews

A programme of initial interviews was undertaken with nine senior stakeholders, who were selected from a longer list of key discussion partners provided by Diamond. This included representatives from Diamond, STFC and the Wellcome Trust, as well as the academic and industrial user communities.

The focus of scoping interviews was intentionally quite open but guided by four broad topics. This allowed for positive and fruitful early discussions, providing the study team with a good understanding and overview of Diamond's activities and achievements, as well as helping to identify important areas for inclusion within the study (e.g. areas of impact to be explored via desk research and consultation).

B.2.4. Development of logic model and evaluation framework

Technopolis has been closely involved with the development of BEIS's and STFC's approach to impact assessment in the context of research infrastructure, having carried out a series of studies over the past few years. For instance, our Big Science and Innovation study in 2013[8] reviewed methodologies used to measure the innovation and economic impacts of large-scale research infrastructure, and through this we developed a generic intervention logic for science capital investments. This model outlines how investments in research infrastructure enable research and related activities that lead to various outputs and outcomes relating to science, innovation, human capital and public outreach.

This generic framework served as the starting point for the development of a logic model specific to Diamond, which has been refined and expanded based on the information obtained through our initial review of Diamond documentation (especially the current 10-year Vision and the business cases for the three main phases of development) and discussions with Diamond staff and key stakeholders.

As well as providing clarity as to Diamond's ambitions and activities, the identification and classification of activities and benefits (outputs, outcomes, or impacts) in the form of a Logic Model set the basic framework for evaluation monitoring. We therefore took the content and structure of the model as the basis for the development of our evaluation framework, with key indicators and sources of evidence (pre-existing or to be collected) identified against each element. This guided our plans for data collection and analysis, so as to ensure we were able to arrive at a complete view of the full breadth of achievements that Diamond has enabled, encompassing all of the important types of scientific, skills and economic benefits (direct and indirect) likely to have been realised.

The logic model and framework have been further revised and are presented as part of the future monitoring and evaluation framework in Section 8.1 of the report.

B.2.5. Finalisation of approach and method

The first phase of the study ended with the delivery of a scoping report. This presented the results of the initial document and data review, set out the proposed evaluation framework and methodology, and the presented drafts of the research tools (i.e. survey questionnaires). A draft version of this report was discussed with the Advisory Board in December 2017 and then revised to reflect the feedback and inputs provided, with a finalised version accepted at the end of January 2018.

The report was also submitted to BEIS Expert Peer Review for assessment. This considered the appropriateness, validity and quality of the overall methodology, including the comprehensiveness and robustness of the proposed cost-benefit analysis. Comments from this process were discussed at the Advisory Board meeting, although the assessment was largely positive, with "no major concerns".

8 https://www.gov.uk/government/publications/big-science-and-innovation--2

B.3 Evaluation phase (February – October 2018)

The Evaluation phase of the study largely consisted of the further analysis of secondary information, the collection of primary data through interviews and surveys, and the development of case studies. This phase also included the presentation of an interim report to the Advisory Board on the 17th of April. This report presented further review and analysis of the pre-existing information and data provided by Diamond, and analysis of the initial survey results. Based on this, the interim report also presented a list of potential case studies for development in the second part of the evaluation phase.

B.3.1. Desk-based review

During this period, the study team undertook a more detailed desk-based review of the pre-existing information and data provided by Diamond. In part, this work was intended to provide contextual information for various aspects of the current report, such as an overview of the facility and its development, or explanations of different access routes, training and engagement activities. As such, it included a review of various background documentation such as the Diamond businesses cases, ten-year vision, annual reports and website. However, the exercise was also intended to collate, analyse and present evidence (where available from these sources) to help demonstrate the breadth and scale of activities, outputs and outcomes realised. It therefore included analysis of: financial data (accounts, contracts and tender database, HR data, construction costs); data on peer-reviewed access (applications, awards, delivered beamtime); and training data (events, attendees, students). We have also looked at two bibliometric studies undertaken recently (by Clarivate Analytics and the University of Leiden) that measured the bibliometric performance of Diamond research over the past decade.

B.3.2. Surveys

Surveys were run with three different groups - academic users, industrial users and suppliers. Following the acceptance of the overall scoping report (which included draft plans and questionnaires), the individual surveys were further iterated between Diamond and the study team, before being piloted and finalised at the end of February. Invitations to participate were sent out directly by Diamond during early March, with a request for inputs by the end of the month.

Data was then downloaded from the online survey tool at the end of March and an initial analysis undertaken in the first week of April. This initial analysis was presented in the interim report. Following the presentation of the interim report, the surveys were kept open for a further two weeks to allow for additional responses, and a reminder email was issued by Diamond to non-respondents.

In Appendix D we provide the final profile of the questionnaire respondents. This includes 343 useable responses from academic users, 24 responses from industrial and commercial users and 62 responses from suppliers. The analysis of results from each of the surveys is presented in Appendix E.

B.3.3. Interviews

Although not initially proposed, it was agreed that the study should include a programme of interviews with key stakeholders, representing different groups of interest (senior stakeholders, Diamond staff, academic/industrial users, and representatives from the international synchrotron community). With the help of Diamond and the Advisory Board a long list of 45 individuals were identified. To take account of any initial questionnaire input, interviewees were contacted following the closure of the survey. Where suggested interviewees were also identified as subjects for case studies, interviews to support the case study development were prioritised. The study aimed to secure 20-30 interviews.

The purpose of interviews was quite open (allowing flexibility to adapt to the knowledge and experience of the individual), but guided by four broad topics: key aspects of Diamond facilities, activities and evolution; views on the importance, added value and strategic benefit of Diamond; types of benefit / impact generated; and notable examples of achievements, benefits and impacts.

In total 36 interviews were conducted. The list of interviewees consulted is presented in Appendix D.

B.3.4. Impact case studies

To better illustrate the added value of the facility and exemplify the range of benefits and impacts that Diamond has helped to realise, we developed a series of in-depth case studies, covering a selection of achievements made possible by Diamond. The mixed method approach to these case studies (namely, survey evidence coupled with interviews and wider desk-based research) helped us understand better some of the more diffuse impacts that Diamond-based research has enabled.

Based on evidence provided through the user and supplier surveys, as well examples emerging from the desk research, we provided a long-list of 5o potential cases. This list was presented as part of the interim report, screened with the Advisory Board and Diamond and narrowed down to a shorter list. We then combined semi-structured interviews with the 30 academics, companies and other relevant individuals, with further desk research to compile a ~1 page presentation for each case, covering where relevant and feasible the following broad questions: the rationale and objectives of the Diamond research; the immediate benefits of the research to participants; wider benefits; expected future benefits; further investments in complementary research and development; and Diamond added value.

Appendix A sets out the 28 case studies developed (12 academic, 10 industrial and 6 supplier). We have sought final validation of each case from the individual or organisation concerned. In some instances (particularly for the industry cases), this has resulted in the redaction of certain information, previously presented, which the contact did not wish to be published (e.g. for reasons of commercial sensitivity).

Appendix C - Economic impact from Diamond operations

We estimate that **Diamond generates £3.6 million in net economic impact to the UK each year because of its operational expenditure. The calculation is detailed further below.**

We start our analysis by looking at the gross economic impact. We follow a similar methodology to that used in the ISIS Lifetime Impact Report (Technopolis, 2017) and the Sci-tech Daresbury Campus Impact Study (SWQ, 2017). Based on this, the total gross impact of the Diamond's operations each year is estimated to be £84.1 million. This includes:

- Direct impacts of £31.5 million, arising from the payment of salaries to Diamond employees each year (based on 2016/17 staff costs);
- Indirect impacts of £40 million, triggered by Diamond's operations, which generate additional economic value in the supply chain through the purchase of goods and services (based on Diamond's ~£40m a year purchase of goods and services from its suppliers).
- Induced impacts of £12.6 million, resulting from Diamond employees spending their incomes in the economy, thereby helping to create further economic activity (based on a standard income multiplier of 1.4[9] applied to 2016/17 staff costs)

We then take account of a series of parameters to arrive to an estimate of **net impact:**

- Leakage (applied to indirect impacts) – this is the extent to which the public investment benefits those outside the geographical area of intervention. This factor is concerned with discounting any economic activity that takes place outside the 'area of intervention', in this the case the UK economy. All Diamond staff are resident in the UK (i.e. level of leakage outside the UK is equal to 0). Diamond's contracts and tenders database suggests that (where known) 68% of total expenditure (2003-17) was allocated to suppliers based within the UK. This means that leakage of the indirect impact is 32%.
- Deadweight/counterfactual (applied to total gross impact) – a key element when assessing the impact of a public investment is to understand what difference it has made. Put simply, we need to calculate what proportion of the outcomes may have happened anyway in the absence of the support provided. That proportion is called the deadweight factor. In the case of Diamond, one could argue that a substantial share of its expenditure would have happened anyway, as STFC and the Wellcome Trust would have allocated the resources available to Diamond somewhere else in the economy. However, some small proportion of Diamond expenditure is funded through other national and international sources (e.g. proprietary income), most of which would not have materialised in the absence of the facility. Diamond's annual report for 2016/17 suggests that ~95% of annual revenue is UK grant income[10] and so we have applied this 95% deadweight factor, which means that we assume that only 5% of the total gross impact generated by Diamond operations would not have happened in the absence of the facility. This is quite a high discount, however there are many potential investment routes for STFC/Wellcome funding, that these seem appropriate.
- Displacement (not applied in this case) – this corresponds to the extent to which the public investment has reduced other activities and benefits elsewhere in the economy. Displacement could happen when, for instance, public investment helps certain organisations upgrade and expand while their (unassisted) competitors within the same industry may see a resulting loss of income and competitiveness. This is not a zero sum game of course and the selective allocation of government assistance is generally designed to incentivise the wider industry to seek to innovate or otherwise improve performance. Notwithstanding this ambition, it is important to gauge those wider effects to ensure that the positive outcomes within the assisted group is not merely a redistribution of market shares within the economy overall. Given the unique nature

9 Research to improve the assessment of additionality. BIS occasional paper no. 1 (October 2009).

10 The remaining 5% includes revenue from the sale of synchrotron services, other income, and overseas grants

of the Diamond facility within the UK research landscape, we have assumed that there is no displacement, which is to say STFC support for Diamond is not displacing activity at another light source facility elsewhere in the UK, and as such we have rated displacement overall as 0.

Applying these parameters to total gross impact (as shown in the formula below), we estimate that Diamond currently generates a **total *net* impact of £3.6 million a year from its operational expenditure.**

Total Net Impact (£3.6m)	=	Direct impacts (£31.5m) + Indirect impacts (£40m) x [100% - Leakage (32%)] + Induced impacts (£12.6m)	x	100% - Deadweight (95%)

Appendix D - Profile of survey respondents

Below we outline details of respondents to the three surveys conducted during March-April 2018 and analysed in this report. We first profile the responses from Diamond users (academic and industrial), before introducing the supplier organisations that responded to a separate questionnaire.

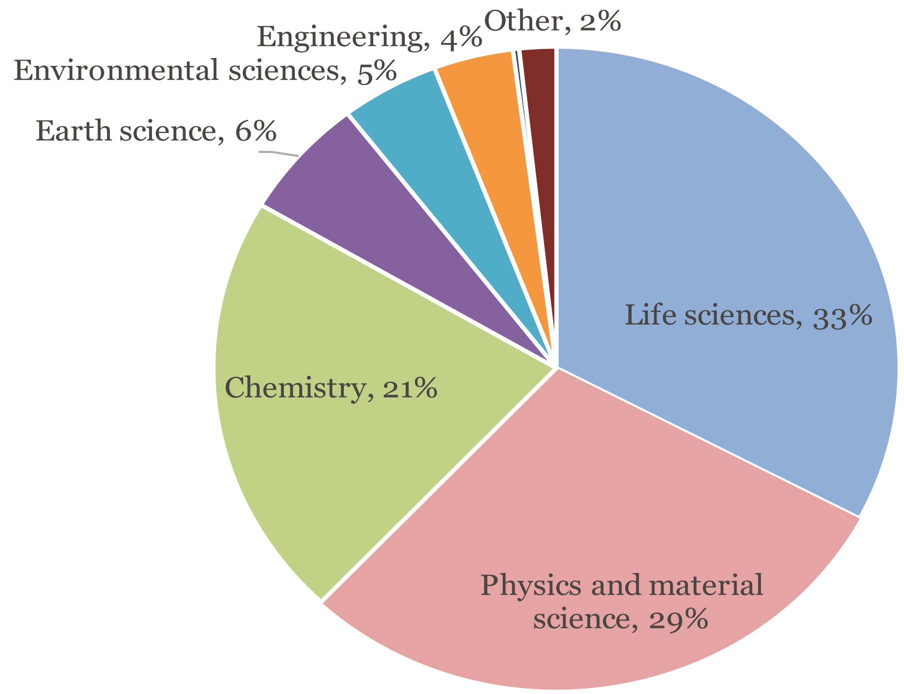
D.1 Responses from Diamond users (academic and industrial)

There were **369 responses to the user surveys** in total[11]. Nearly all respondents (343, or 93%) were from academic institutions (e.g. universities or research centres), while just 24 (7%) were from industrial or commercial organisations[12]. The latter operate in a range of different sectors, but the greatest number (n=9) were from the pharmaceutical industry (reflecting wider usage statistics).

User respondents were located in 25 different **countries**, including 14 EU Member States and 11 others. However, the majority (71%) of individuals were located within the UK. The next most frequent country mentioned was Germany (5%), while Italy and Sweden each accounted for a further 3.2% of respondents, followed by Spain (2.9%). All-but-three of the respondents from commercial organisations indicated that they were based in the UK, while the remainder were in Ireland and Sweden. However, it is worth also noting that most of the industrial users responding to the survey were multi-national (58% indicated that their organisation had staff based in the UK and elsewhere).

Academic respondents were asked to select their **primary area of research** from a predefined list (see Figure 25). The majority indicated that they worked primarily within one of three areas: life sciences (33%), physics and material sciences (29%) and chemistry (21%). The other areas shown (earth science, environmental sciences, engineering and cultural heritage) were mentioned collectively by just 15% of respondents. Just 6 respondents indicated their primary area of research fell outside of these categories – they indicated that their research focused on space or planetary science (4), veterinary science (1) and 'technique development' (1).

Figure 25 Primary area of research



Survey of academic users (n=345)

11 This excludes those respondents that only completed their basic details and no further questions. It also excludes the small number of respondents that did not explicitly give their consent for their response to be used. The responses from these individuals are also excluded from the analysis later in the report.

12 A further two respondents indicated that they from *another type of organisation (not academic or industrial/commercial). There were asked to complete the questionnaire designed for academics.*

Industry respondents were also asked to briefly describe the **main areas of research** where they have made use of Diamond. Their responses are shown in Table 11, grouped by industry sector.

Table 11 Main areas of research undertaken at Diamond – industry users

Industry sector	Type / purpose of research
Pharmaceuticals / Drug design	• Structural characterisation and imaging of processes • Routinely obtaining crystal structures of target proteins in complexes with small molecules • Macromolecular Crystallography / Structure-based Drug Design • Protein crystallography • Determining protein structures with ligands for the pharma industry • Macromolecular Crystallography • Macromolecular Crystallography - Structure Based Drug Design
Medical devices	• To establish structure-processing-properties of polymers with medical applications
Petrochemicals	• Diffraction to study crystallisation of fuels and the crystal structures of calcium carbonate, plus the size and chemical structure of oil additives
FMCG	• 3D imaging of ice crystal size and distribution in ice cream
Nanotech	• Structure determination of biological molecules and imaging molecules
Defence	• The behaviour of materials (mostly metals) at high pressures and temperatures
Metallurgy	• Microstructural analysis of aluminium alloys
Materials	• *In situ* spectroscopy • Imaging of complex materials; single crystal analysis of materials; scattering analysis of complex fluids; high pressure analysis of complex materials
Measurement / Scientific research	• Developing techniques that will allow for more accurate radiation treatment of cancer • Metrology

Survey of industry users

D.2 Responses from Diamond suppliers

There were **62 responses to the supplier survey**[13]. These organisations have sold a range of products and services to Diamond over the past decade. Based on descriptions provided, this includes:

- Machined (metal) components (n=15)
- End station instruments, machines and detectors (11)
- Vacuum components, chambers and systems (9)
- Beamlines, beamline components and control systems (8)
- Mirrors (3)
- Optics and imaging technology (3)
- ICT products and systems (3)
- Magnets (3)
- Gases (2)
- Radiation shielding (2)
- Construction and installation (2)
- Design services (1)

Supplier survey

Half of the suppliers surveyed (48%) were wholly UK-based, while 21% were multi-national (including a UK presence) and a third (31%) have no UK presence at all. They all (100%) anticipate selling to Diamond again in the future.

13 This excludes those respondents that only completed their basic details and no further questions. It also excludes the small number of respondents that did not explicitly give their consent for their response to be used.

Appendix E – Analysis of user and supplier surveys

E.1 Results from a survey of academic users

This section presents the main results from a survey of 345 Diamond users who are located at universities, research centres and other similar institutions. The subsequent sections report on the results obtained from surveys of industry users and Diamond suppliers.

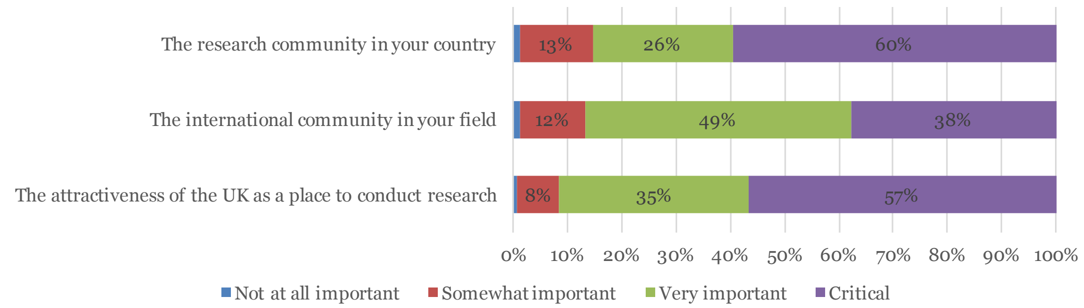
E.1.1. The importance and value of Diamond for research

Academic users were asked to rate the **importance of Diamond for their research**. The vast majority (87% of 345) stated that the facility was either 'very important' (45%) or 'critical' (42%) to their research. A further 12% claimed it was 'somewhat important' and <1% that it was 'not important'.

They were also asked how important Diamond is for different scientific communities and for the attractiveness of the UK as a place to conduct research (see Figure 26). Again, the vast majority (85%) reported that the facility is 'very important' or 'critical' for the research community in their country. An in fact, if we were to look only at those located in the UK, then 75% said Diamond is 'critical' and a further 19% that it is 'very important' for the research community in their country (93% in total).

Similar proportions of academic users (87%) report that Diamond is 'very important' or 'critical' for the *international community* in their field, while 92% indicated it was very important / critical for the attractiveness of the UK as a place to conduct research.

Figure 2 The importance of Diamond for UK research and research communities (academic users)



Academic survey (n=309-310)

Academic users were asked further to explain briefly ***why* they might choose to use Diamond rather than another facility.** Nearly all respondents suggested one or more reasons, which we have grouped and summarised below (with an indication of the number of responses in each case). A selection of quotes is also provided (in boxes) to illustrate the type and range of comments given in relation to each of the main reasons given for choosing Diamond.

The overall quality of facilities – source, beamlines and instruments (n=194) – Diamond's facilities were considered state-of-the-art / cutting edge and constantly improved and developed to stay so. The beamline performance (energy, intensity, flux, resolution, reliability) and quality of resulting data were highlighted in particular. In many cases, users identified the unique capabilities of particular facilities or the specifications of the beamlines they used as being the most appropriate for their work. A selection of examples from the feedback include:

"Over the years we have used several European Synchrotron radiation sources but have always found Diamond to be the most efficient, reliable and suited to our studies. We have always been impressed with the quality of the data that we can obtain from the beamlines"

"Diamond provide outstanding and reliable scientific infrastructure"

"The quality of the beamlines in our area of interest. Our experience is that it is increasingly best place to get our data (having worked at 5+ synchrotrons in Europe & North America)"

"Diamond has high specification beamlines with high reliability"

"Because it is the best facility in the world to do this work"

"Diamond enables to apply broadly synchrotron-based techniques in the field of catalysis and energy. No other synchrotrons offer all together such broad range of techniques"

"Essential part of my research work as it is the only facility in the world to have a micro beam synchrotron CD facility. This feature of the beamline is a requirement in my research work and cannot be done elsewhere"

The location of the facility (n=131) – Diamond's proximity to the respondent's location and the consequent ease, convenience and low cost of access, transportation (of samples, environments and equipment) and data collection. For example, a selection of the more expansive comments included:

"We often take quite a lot of kit and samples to beam time and it's really handy to be able to drive rather than fly"

"The location means I can access it when critical data are needed to finalise papers"

"There is benefit derived from its location in this country, which make transport of user sample environments much easier than other sources"

"The proximity of the Research Complex eases the design and delivery of complex experiments immensely"

"Without Diamond the research must be carried out at other facilities around the world at much higher expense to the group"

"Convenience particularly around avoiding transport of biological samples internationally"

The level of expertise and support provided by staff (n=115) – Diamond's staff were commended in relation to the professional, high-quality, expert, flexible and responsive nature of the support, advice, technical assistance and collaboration that they provide, both in planning, designing and implementing experiments and in relation to data analysis. Several respondents also commented positively on well established relationships with Diamond personnel ("long term collaborators"), and on the critical mass of expertise in one location. Some examples of feedback include:

"The beamline scientists are happy to assist with the co-development of environmental cells"

"We have always been impressed with the expertise available to assist us in data collection and the development of new study designs"

"The engagement from the staff is in many ways essential for our research"

"The staff are extremely helpful, knowledgeable, and responsive to user needs"

"It's perfect for what we do and has really excellent, proactive beamline staff"

"Easy access to information concerning technical details of the beam line and support from beam line scientists during the preparation of proposals"

"Highly qualified and well-trained scientists and engineers - collaborative staff with significant expertise in my area of research"

"The communication and interaction between the different beamline teams allows us to use Diamond as a complete facility rather than the specific beam line as it is for me in other synchrotron"

"Collaborators in the UK, including Diamond staff scientists and the quality of support"

The accessibility and availability of beam time (n=52) – The overall ease with which the facilities can be accessed and used was highlighted. This included the clarity and speed of application and beam time allocation processes, and the range of modes of access available (remote /mail-in / rapid / block allocation). The remote access option in particular was widely praised. Specific comments included:

"Ease of access compared to overseas sites"

"The process to submit proposals is clear and user friendly. The scheduling is very well done"

"There is a relatively short period of time from applying for measurement time and actually doing the experiment. Communication with beamline scientists is also great"

"Access to block allocation time allows for high-risk, high-reward strategies"

"It is a world leader in offering a remote data collection service, which we use all the time"

"We get frequent access with short remote shifts, allowing sample evaluation and data collection to keep up with the wet-lab aspects of our projects"

"The set up is perfectly optimised to perform remote data collection, which is so important"

"The remote collection works like a dream – we get massive amounts of high quality data"

"The data we collect is high quality, and the performance of the beam lines is top notch"

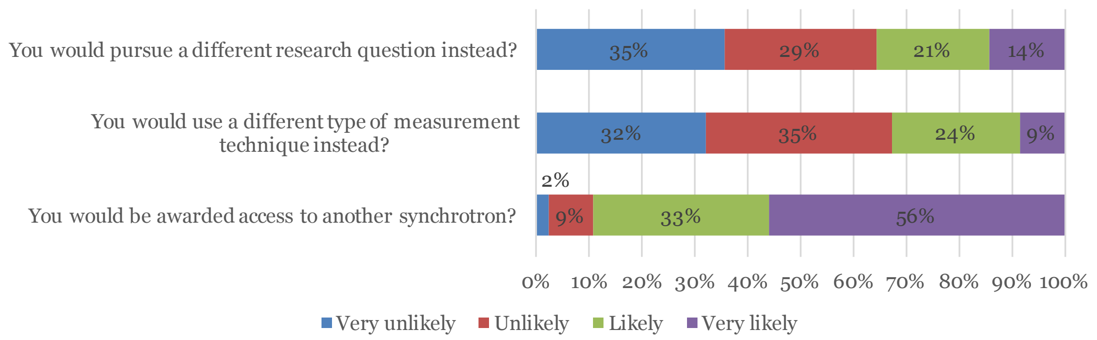
"Transport of materials to site is straightforward"

In addition, a small number of respondents highlighted other reasons for choosing Diamond, including the funding provided for travel and accommodation (n=8) and the fact that Diamond is licenced for restricted materials (n=3) such as explosives, propellants and radioactive samples.

Users were also asked to consider the **possible implications of Diamond not existing**. Specifically, they were asked about the likelihood (under this hypothetical scenario) that they would be awarded access to another synchrotron, use a different measurement technique, or pursue a different research question instead. As can be seen in the figure below, the majority (89%) of academic users believe that it is likely (or very likely) that they would be awarded access to another synchrotron.

Nevertheless, a sizeable minority also indicated that the non-existence of Diamond would likely mean that they would use a different technique (33%) or pursue a different research question (36%).

Figure 3 If Diamond did not exist, how likely are the following alternatives (academic users)



Survey of academic users (n=323-339)

Users were then asked to provide further detail about the **implications for their research work** of Diamond's non-existence. The following table summarises the main points that were highlighted, and gives a flavour of the specific comments provided in each case.

Table 2 Implications of Diamond's non-existence for the quality and efficiency of research work

n	Implication	Example quotes
141	A reduction in research efficiency / productivity / throughput / output	• "We would be limited to lab sources which would greatly reduce throughput, and prevent in situ measurements entirely. Research would be much slower" • "Our efficiency would be significantly reduced (by at least a factor of 3)" • "Other synchrotrons do not provide access so efficiently. If Diamond did not exist, my research would slow down" • "Likely to experience lengthy delays in data acquisition" • "Access to other synchrotrons can be laborious and have waiting times of over a year - not ideal when grants typically run for three years" • "Capabilities at Diamond for my research field are unique. Using other synchrotrons could significantly slow or weaken my output" • "My research portfolio would be smaller and my scientific output would be lower"
95	Lower volume / quality of data and thus a reduction in the quality of research	• "The data quality we get is excellent - I've had trips to other beamlines where we've come away with literally nothing" • "The quality of our data would also suffer due to non-ideal environmental control and lack of ability to collect experimental data" • "The quantity and the quality of the data would be reduced" • "The quality of my publications would drop significantly; I rely on the technical expertise and intellectual leadership available at Diamond" • "It would inhibit development of the materials studied" • "Quality would be less as certain measurements would not be possible" • "I do not believe that I could publish work in high ranking journals without the results obtained from Diamond (and other central facilities such as ISIS): the quality of research would be noticeably lower in terms of impact and how it is viewed by peers"
72	Inability / challenge to pursue (part of) research; a change of research direction	• "I would be forced to avoid the more challenging experiments. I would not be able to pursue some aspects of technique development" • "I simply could not do the same research and uncover the same detail in my experiments" • "There would be experiments that we simply could not do, or could not guarantee that we could do due to costs associated with travel to facilities outside the UK" • "Closure of two currently active research themes" • "If Diamond did not exist I would probably not have pursued my current line of inquiry"
58	Less access to beamtime and associated support through other sources	• "I would probably apply to ESRF and get less beamtime over a year" • "Increased pressure on beam time at the ESRF" • "We would be unlikely to get the same level of access and support at other synchrotrons" • "We would have to go to other synchrotrons, whose technical specifications are not optimal for our work; and with whom we might not have ideal scientific collaboration"
23	Reduction in international competitiveness	• "We would not have the critical insights we gain from in situ work making it difficult to compete internationally" • "My research would lose its frontier edge, and be less competitive" • "This would have a catastrophic impact on us, setting us back 10 years"
18	Increase in time and costs accessing other facilities	• "Regular access would most likely not be possible because of additional costs of travel" • "I would find it incredibly difficult to continue my research. As an ECR I do not yet have the funds to travel to other facilities internationally"

n	Implication	Example quotes
12	Other:	• "Our block allocation group helped bring together researchers from diverse areas which don't often overlap" • "I would need to relocate a significant portion of my research team out of country" • "There would be reduced ability for students to engage with the science" • "It would make it more difficult for me to attend beam time to assist students and help train them in the techniques we use"

Academic survey survey. Technopolis coding. Individual respondents may be coded against more than one 'area'

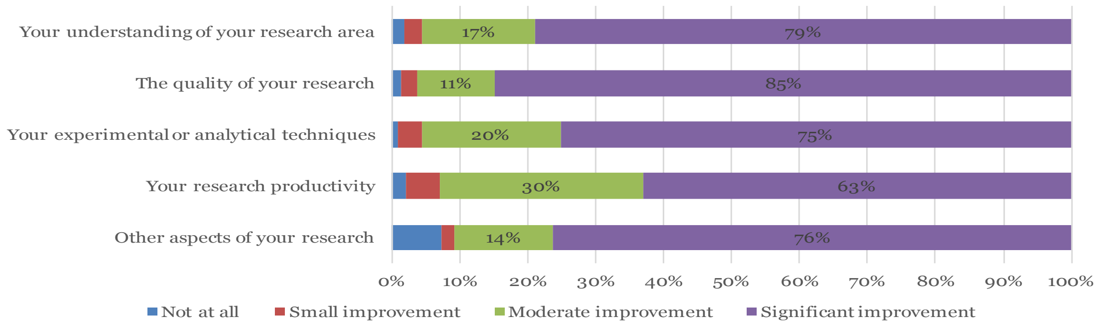
Nearly all academic users (98%) **anticipate using Diamond again in the future** – with 90% indicating that they would 'definitely' do so. Only 6 out of 310 academic respondents indicated that they would probably / definitely not use Diamond again in the future, and in four of these cases this was due to a change of job or retirement. There were just two respondents indicating possible dissatisfaction – one respondent (from a UK university) who indicated that ESRF beamlines would be used instead, and another indicating that they were not satisfied with the service offered in their area[14].

E.1.2. Scientific impacts

Academic users were asked to indicate the extent to which their use of Diamond had led to **improvements in various aspects of their research**. As the figure below shows, the response was very positive, with a majority claiming a significant improvement across all areas (and most other respondents claiming a 'moderate improvement').

Significant improvements were most widely reported (85%) in relation to the *quality* of the users' research. More than three-quarters also reported significant improvements in their *understanding* of a research area and in experimental (79%) or analytical *techniques* (75%). A slightly smaller proportion (63%) has seen significant improvements in their research *productivity*. Those indicating that it had led to improvements in *other* aspects of their research, specified aspects such as collaborations, the scope of their research, new methodologies, interdisciplinarity, outreach and the translation of research.

Figure 24 Extent to which use of Diamond has led to improvements in user's research



Academic survey (n=97-322)

All academic users were asked to point to the **single most important scientific advance** that was attributable to their use of Diamond. The majority did so, providing anywhere between a few words and several paragraphs of explanation – often with reference to a particular publication. We have limited ourselves here to presenting a small selection of the examples where the respondent has gone a little further in explaining the importance or impact of the scientific advance.

14 No further details were provided.

"We discovered that the anticoagulant activity of major human serum protein, antithrombin, with the major pharmaceutical heparin, could be predicted based on its thermal stabilisation and not (as had been thought previously) as a function of changes in its secondary structure. This result paves the way for a new approach to finding improved anticoagulant drugs, and provides an easy way to screen them"

"Using beamline B23 we could show the changes in structure and stability of nanoparticle-protein complexes. This has opened a very important new method that can be applied to several important systems used in the next generation of targeted nanomedicines"

"The high-quality beamlines at Diamond were critical to helping us unravel how the clathrin adaptor AP2 ties cargo recognition to clathrin polymerisation - an essential step in cellular endocytosis that is critical for all eukaryotes"

"First crystal structure of a plant intracellular immune receptor domain bound to its target, which is a milestone in understanding the molecular basis of plant immunity"

"The structure of a metal reducing outer membrane cytochrome was determined in 2011. This dramatically helped our understanding of how microbes interact with insoluble minerals and has been cited over 160 times according to Web of science"

"We have recently assessed the structural integrity of a reactor pressure vessel steel during a thermal shock which may arise during a loss of cooling accident: Measurements of stress during thermal shock in clad reactor pressure vessel material using time-resolved in situ synchrotron X-ray diffraction, PVP2018-84676, Proceedings of the ASME 2018 Pressure Vessels and Piping Conference PVP2018 July 15-20, 2018, Prague, Czech Republic This was done for the first time and has a significant impact on the assessment of operating pressurised water cooled reactors"

"One of the most important scientific advancement is the high throughput circular dichroism measurement obtained which is unprecedented that opens up to not only larger number of samples but also faster data collection for analysis and screening of bio products capabilities"

"We have through collaborative working with Diamond opened up pathways for analysis of radioactive materials at the facility. This has led to increased knowledge on clean up and management of the UK's nuclear legacy. Work has included radioactive waste disposal, spent fuel ponds management, radioactively contaminated land, radioactive hot particle behaviour in the environment, contamination and decontamination of steels and effluent treatment"

"Recycling and efficiently converting waste carbon dioxide into useful products is one of the challenges in modern chemistry but converting it could give power generation a carbon-neutral environmental footprint. By means of operando Q-EXAFS carried out at the Core X-ray Absorption Spectroscopy (B18) beamline of Diamond it was possible to reveal the mechanism of the carbon dioxide reduction reaction activity of iron oxyhydroxide nano-structures (ferrihydrite-like structure). It's an important result towards being able to make the chemicals we need in a more environmentally-friendly

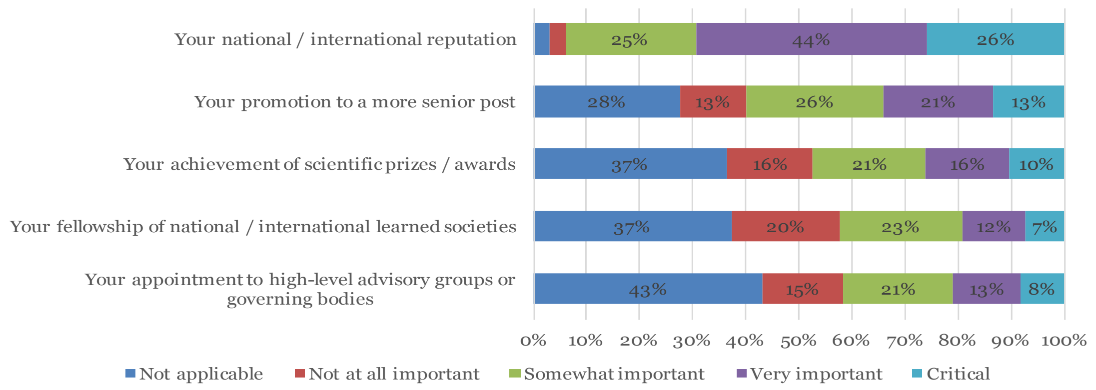
way, recycling carbon dioxide and powering the chemical reactions with renewable energy"

"Determination of the mechanism of hydrogen splitting and formation by an enzyme containing only cheap metals, Iron and Nickel, instead of expensive catalytic metals such as Platinum and Palladium. The implication is that the new understanding could lead to design of better, and cheaper, catalysts for a hydrogen economy"

E.1.3. Benefits to academic users – knowledge, skills and opportunities

Academic users were asked about **importance of Diamond in relation to the achievement of various academic benefits** (e.g. to funding, recognition and collaboration) (see figure below).

Figure 5 Importance of Diamond use for personal recognition



Academic survey (n=315-321)

Nearly all (94%) of the academic respondents claimed that their use of Diamond had been beneficial for their national or international reputation, including a majority (69%) who said that it had been very important or critical. These respondents were asked to provide details of this reputational benefit and the role Diamond had played. A small selection of the responses given are shown below.

This has advanced our reputation internationally and led to invitations at international conferences (on porphyrins and pthtalocyanines, Electrochemical society USA)"

"A key part of my reputation is that I can access Diamond to perform experiments"

"My work with Diamond has allowed us to develop a reputation for a particular set of experiments. I have given invited talks at national and international conferences on the experiments which were developed with Diamond"

"90% of my research involves scattering, spectroscopy and tomography at Diamond. This has allowed me to obtain the highest possible details out of my experiments and increase my (inter)national reputation"

"My use of synchrotron radiation has been a key component on which my scientific reputation is based. Although much of this predates the operation of Diamond, the development of appropriate beamlines at Diamond has now allowed me to significantly advance the originality and volume of this work"

"Diamond does exceptional work to publicise the work of its users which in turn increases research profile and reputation. Everything from press releases to high quality public engagement and ensuring the work is well-represented to governing bodies so that the value of Diamond's contribution is properly understood"

In relation to the other, more specific types of academic recognition asked about (see previous figure), the benefits were less widespread amongst respondents – but this is mainly because they were 'not applicable' in many cases. For instance, one-third indicated that they had not been made a fellow of a learned society – and so could not rate the importance of Diamond in achieving this.

If we only consider those that *have* realised each form of recognition, then the role of Diamond is much more evident within this population. Specifically:

- 83% of those promoted to a more senior post claim that their use of Diamond was beneficial (including 47% who said it was critical or very important)
- 73% of those appointed to high-level advisory groups or governing bodies, claim that their use of Diamond was beneficial (including 37% who said it was critical or very important)
- 75% of those achieving scientific prizes or awards, claim that their use of Diamond was beneficial (including 41% who said it was critical or very important)
- 68% of those gaining fellowships to learned societies, claim that their use of Diamond was beneficial (including 31% who said it was critical or very important)

Those reporting that Diamond had been very important or critical to one or other of these forms of personal recognition were asked to provide further details. Over 100 respondents gave additional information on their particular circumstances, from which a selection of specific and concrete examples are shown below in relation to prizes/awards, fellowships and appointments (we have excluded promotions, as comments here often only specified 'professor', 'senior lecturer' or similar.

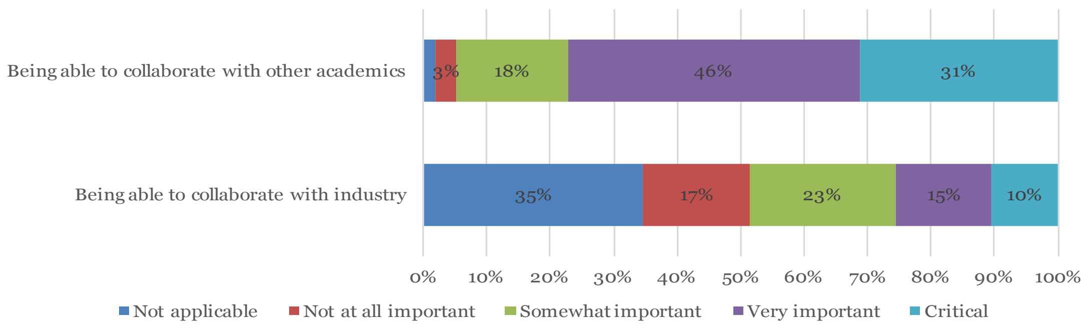
Table 13 Examples of academic recognition where use of Diamond played a very important / critical role

Type	Examples of achievement attributable (in large part) to use of Diamond
Achievement of scientific prizes / awards	• EAG Houtermans Medal for outstanding contribution to geochemistry, early career scientist • RSC Rita & John Cornforth Award (2016) • Imperial's President's Award for Outstanding Research Team (2015) • National young academic prize • Colworth Medal • Hooke Medal • Queen's Anniversary Prize for Higher and Further Education (for University) • Young Researcher in Experimental Physics Prize 2015, Spanish Royal Society of Physics
Fellowship of national / international learned societies	• Elected FRSB and FRSC • Membership of eMBO and made FRS and FMedSci. • Fellow of the American Physical Society • Academy of Medical Sciences • EPSRC Fellowships including (e.g. Established Career Fellowship) • Exhibition of 1851 Fellowship • ERC Consolidator Fellowship • Royal Society University Research Fellowship

Type	Examples of achievement attributable (in large part) to use of Diamond
Appointment to high-level advisory groups or advisory bodies	• Advisory panel membership for Diamond and STFC - both technical and public engagement • Election onto the European High Pressure Research Group • A number of Scientific Advisory panels around the world, in the US, Spain and Sweden • Reviewing and refereeing applications for international synchrotron facilities, journals and grant applications • STFC Physical/Engineering Sciences Advisory panel • Grant advisory board member for a UK funders (e.g. NERC, ESRF) • The SAC of SOLEIL (French synchrotron) • DESY (German synchrotron) Scientific council • Grant panels and editorial boards • International (e.g. EAG Council) committees • Chairperson of German Photon science community (KFS) • ISIS facility access panel member

Nearly all academic users (95%) reported that their use of Diamond had been beneficial to their ability to **collaborate** with other academics (including 79% who said it had been very important or critical). Around half (49%) reported that it had also been beneficial for their ability to collaborate with industry. However, if we exclude those that indicated they do not have industry collaborations, then the proportion citing benefits from Diamond rises to nearly three-quarters (74%). This includes 39% who claimed that Diamond had been very important or critical to collaboration with industry.

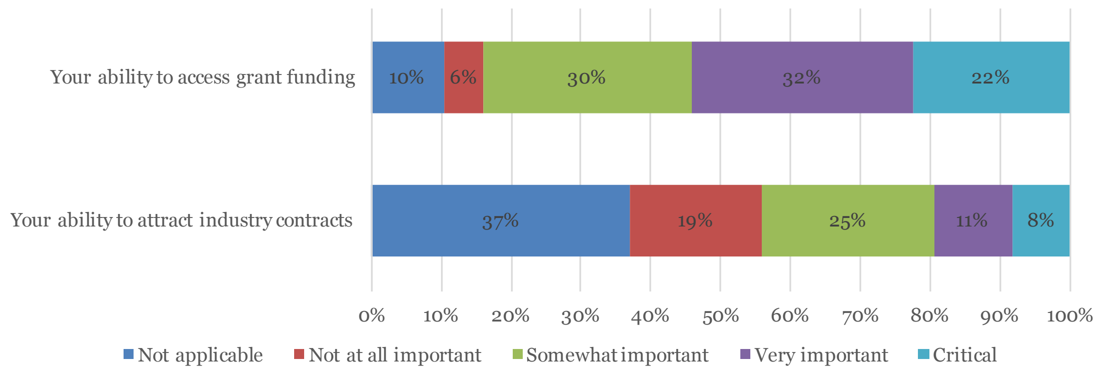
Figure 6 Importance of Diamond use for collaboration



Academic survey (n=317-320)

Just over half of academic users (54%) reported that their use of Diamond had been very important or critical to their ability to access grant **funding**. A further third of respondents said it had been 'somewhat important'. The impact in terms of attracting industry contracts was less widespread. However, even here 44% claimed that there had been some benefit (including 19% who said that their use of Diamond had been very important or critical to attracting contracts).

Figure 7 Importance of Diamond use for attracting funding



Academic survey (n=318)

A small number of specific examples were given of the use of Diamond being critical to attracting industry contracts. These included the following.

Securing industrial/government contracts for collaborative research in fields of energetic materials, heat-storage materials, and fuels/lubricants"

"Contacted by a pharmaceutical company interested in applying the technique to their systems"

"Industry often buys additional days of beamtime during my experiments, where they can retain the IP"

"Directly contributed to our structure based drug design work in collaboration with industry"

"Reputation for work at Diamond led directly to invitation to collaborate with industry partner and agreement of subsequent joint-funded project"

"We work extensively with the nuclear industry and the use of synchrotron techniques are critical to research we perform for these contracts. It ensures we are able to attract this funding"

"I have been invited to participate in an industry iCase award mainly due to my demonstrable experience of data collection at Diamond as this was an area that they were lacking expertise"

"I have been invited to participate in an industry iCase award mainly due to my demonstrable experience of data collection at Diamond as this was an area that they were lacking expertise"

E.1.4. Benefits to wider research groups - knowledge, skills and opportunities

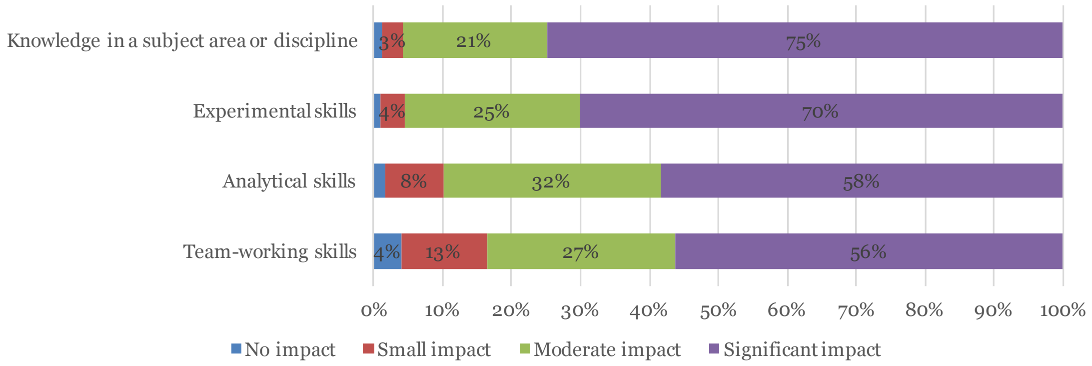
Academic users were asked about the extent to which their use of Diamond had had a **positive impact on various skills and capabilities within their research group**. As the following figure shows, the feedback was extremely positive. In each of the areas listed, the majority (56% to 75%) of respondents claimed that Diamond had had a significant impact on knowledge and skills.

- Nearly all (96%) reported a moderate or significant impact on their research group's knowledge in a particular subject area of discipline
- Most (96%) also reported a moderate / significant impact on their experimental skills
- 90% claimed a moderate / significant impact on analytical skills

- And 84% said there had been a moderate / significant impact on team-working skills

Users were asked whether there were other important skills-related impacts, not covered above. Only a small number of respondents could point to any, but they suggested: interdisciplinarity, working under pressure, data management, project management, writing, communication and design.

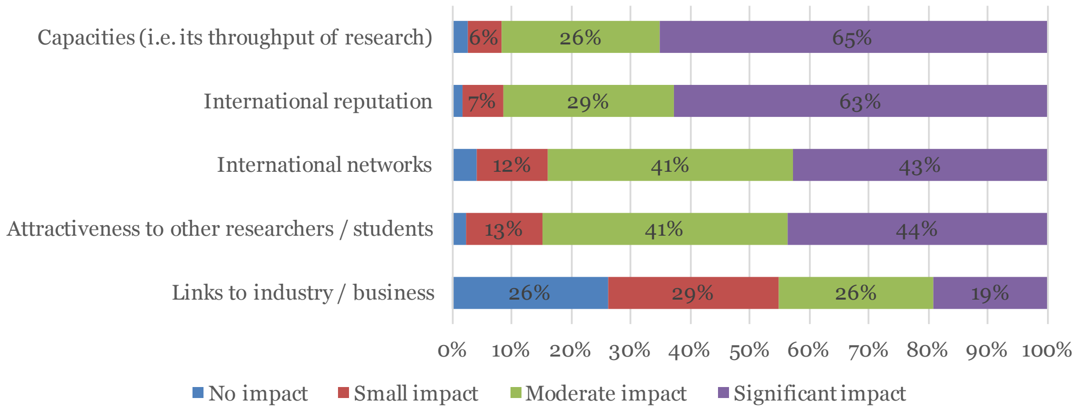
Figure 8 Extent to which Diamond has had a positive impact on research group's skills and capabilities



Academic survey (n=304-312). Excludes those answering 'not applicable'.

Academic users were further asked about the extent to which use of Diamond had **impacted positively on their research group** in other ways. As the following figure shows, the feedback was very positive. In particular, around two-thirds of respondents reported a significant impact on the capacities of their research group (65%) and its international reputation (63%), while most reported either a moderate or significant impact on the group's international networks and its attractiveness to other researchers and students. Indeed, one of the additional comments made alongside this question was that *"the opportunity to carry out experiments at Diamond had been a major attraction for prospective PhD, masters or undergraduate students looking to join our research group".* Another related comment was that "access to the best scientific infrastructure available… is just amazing and extremely cool". Finally, in most cases, respondents reported *some* positive impact on their research group's links to industry, but only in a minority of cases (19%) was this seen as significant.

Figure 9 Extent to which use of Diamond has had a positive impact on other aspects of research group



Academic survey (n=215-310). Excludes those answering 'not applicable'.

There were a couple of additional areas of benefit (not listed) that respondents pointed to. These related to the positive impact of the use of Diamond on the group's public engagement and outreach activities, their exposure to interdisciplinary research and on their ability to maintain scientific cooperation and collaboration with others.

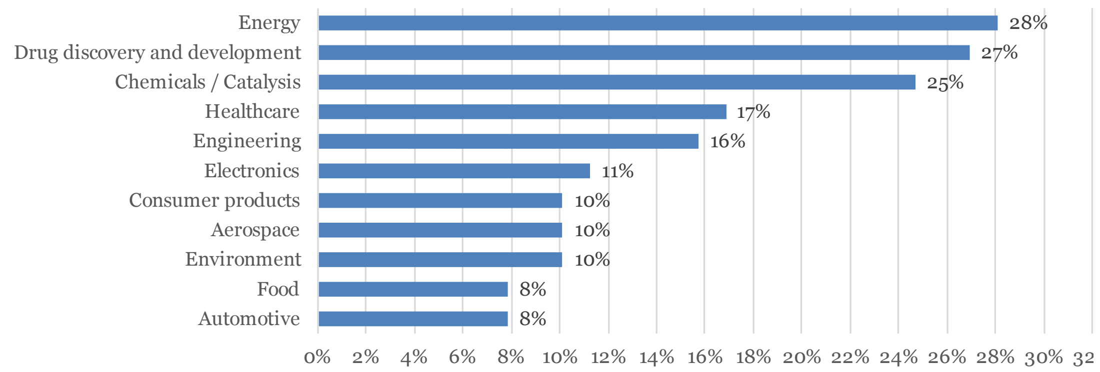
When asked to describe the single most important benefit to skills, knowledge or opportunities, academic users commonly noted improvements to their ability to process and analyse data, improved understanding of research techniques, and their ability to access opportunities for collaboration.

E.1.5. Innovation and commercial benefits

Just over one-quarter (28%) of academic respondents reported that the research they have carried out at Diamond has had some form **industrial involvement** – be that through a collaborative partnership (20%) and / or industrial sponsorship (11%)[15]. Across the three areas of research where we have sufficient responses, there is a slightly higher instance of industry involvement for those working in Chemistry (33%) compared with Life Science or Physics / Material science (both 25%).

There is a wide spread in the **industrial sectors** that these users are involved with, although drug discovery & development, energy and chemicals & catalysis were most commonly mentioned.

Figure 10 Research carried out at Diamond with industrial involvement – relevant industrial sectors

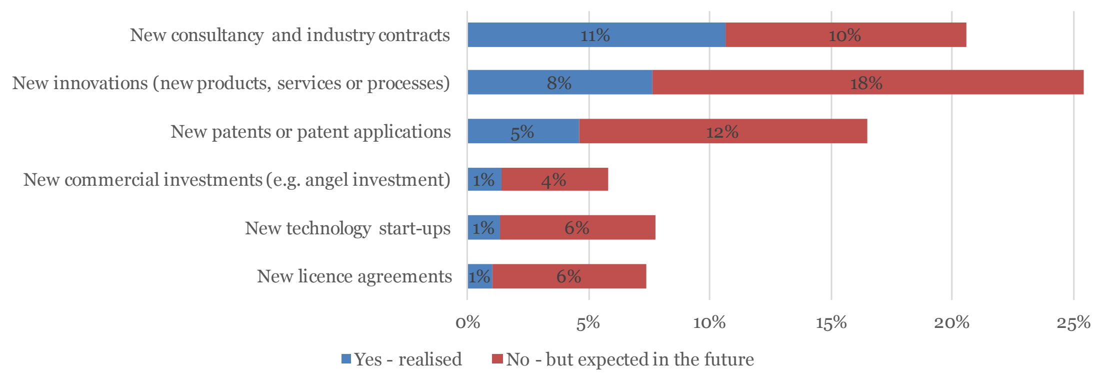


Academic survey (n=89 respondents with industrial involvement / sponsorship of the research they have carried out at Diamond). Does not sum to 100% as multiple responses were allowed.

A minority of academic users surveyed (15% of 303) reported that their research using Diamond had already led to one or more **innovation-related or commercial outputs** (in a third of these cases the respondent selected more than one of the outputs listed). Half of these respondents also indicated that they expected other types of innovation/commercial output in future. A greater number of academic users (28%) have not realised any such outputs yet, but they expect to do so in the future.

The following figure summarises the responses and shows that the most common form of output realised is new consultancy and industry contracts (already seen by 11% of users). New innovations have been realised by a smaller proportion (8%), but are expected in the future by a further 18%. Over 18% also report that new patents or patent applications have been realised / are expected. Start-ups, commercial investment and licence agreements are much less commonly reported, but are still expected amongst a significant minority of users (some 4-6% in each case).

Figure 11 Proportion of academic users reporting innovation-related or commercial benefits



Academic survey (n=298-303)

15 Figures sum to more than the total, because a small number of respondents indicated both types of industrial involvement.

Those indicating an innovation-related or commercial output (realised or expected) were asked to provide **further details**. Most provided some brief additional information. We have limited ourselves in the table below to providing examples quoted in relation to *realised* outputs, but there are several other 'good stories' relating to opportunities still in development.

Table 14 Examples of innovation-related or commercial outputs

Output type	Example of innovation-related or commercial output resulting from use of Diamond
New consultancy and industry contracts	• "I have supported small and medium pharma based on my expertise. They have bought their own beam time rather than using mine" • "Work with Clasado, led to work with Biocatalysts and each of these led to work with Dextra" • "Co-applicant on an H2020 grant with a start-up in Ireland building a benchtop X-ray microscope" • "One long-term industry collaboration which now includes industry funding for a joint project". • "RCaH industrial fellowship scheme" • "An iCASE award and consultancy agreement with Atlas Genetics Ltd followed the publication"
New innovations (products or services)	• "Two patent applications through Sunamp, with new products developed and sold by this company" • "One patent application has been recently filed, which describes a new product in the field of security labels" • "New tomography device was tested at Diamond (RoToPEC)" • "The measurements at Diamond are playing a crucial role in the development of a detailed model of the chemical reactivity of Fe species in water, of potential relevance in important industrial processes, including the production of fuels (methane-to-methanol conversion) and the oxidation of water" • "Refractive X-ray zoom lenses have been characterized and can now be improved" • "Part of my research is on developing new Li-ion battery cathodes, and results at Diamond have played an important role in this work".
New patents or patent applications	• "Our patented work on materials for fuel cell cathodes and separations relies heavily on structural information and understanding derived from access to Diamond" • "The data obtained has helped support patent applications for new alloys" • "Patent application WO2013144628A1 (METAL-ORGANIC FRAMEWORKS (MOF) FOR GAS CAPTURE)" • "Recent patent application for anti-IgE antibodies as therapeutic for allergic disease" • "1 new patent priority filing with potential for further seed funding (with an option of a start-up) and interest shown by potential licensee" • "2 patents" • "2 patent applications, tool compounds in the public domain"
New technology start-ups	• "Based on work done (including at Diamond) we have set-up a company using some of the know how developed. www.peptigeldesign.co.uk" • "Our work and publications on flap endonucleases provided our initial investors with the confidence to invest in a new spin-out (DeFENition Ltd in 2016)"

Respondents were asked to briefly describe the **single most *commercially* beneficial result** that is attributable to their use of Diamond. There were ~35 relevant responses, ranging from a few words to a few sentences of information. Most, however, only went as far as to explain the research result - usually new or improved understanding of a specific material, product or process. For example:

"Development of a better understanding of antibodies as drugs"

"Identifying the binding site for the ISRIB compound on eIF2B using eBIC"

"Development of innovative bone regeneration therapy"

"A better understanding and therefore improvement of catalytic material"

"Investigation of ageing in zeolite catalysts"

"Working on cocoa butter crystallisation"

"Crystallization screens"

"Showing that reduced dead edge detectors work and a viable choice for large scale systems"

"Development of improved detergents in engine lubricants"

"Understanding of hair structure under different treatment conditions"

"Development of X-ray imaging for lab and in-line use"

"Metal-organic frameworks for gas capture"

"Characterize new family of materials: porous hybrid materials"

"Smart photonic sensors for healthcare applications"

A few went further and provided details as to commercial use and benefit. For example:

Development of enhanced phase-change material for heat batteries. This has been instrumental in the growth of 'Sunamp' (the development of products and external investment)"

"We provided a critical contribution to extending the operation of a nuclear power plants' safety case via our Diamond research on graphite and on boiler tube's creep failure"

"Our research into the nuclear effluent treatment process at the Sellafield site has led to a direct reduction in discharges from this site. Also, we are contributing to the decommissioning of key nuclear facilities as part of major national infrastructure projects"

Unilever have patented some of the research we were working on jointly, but our work was only on model systems related to their patent"

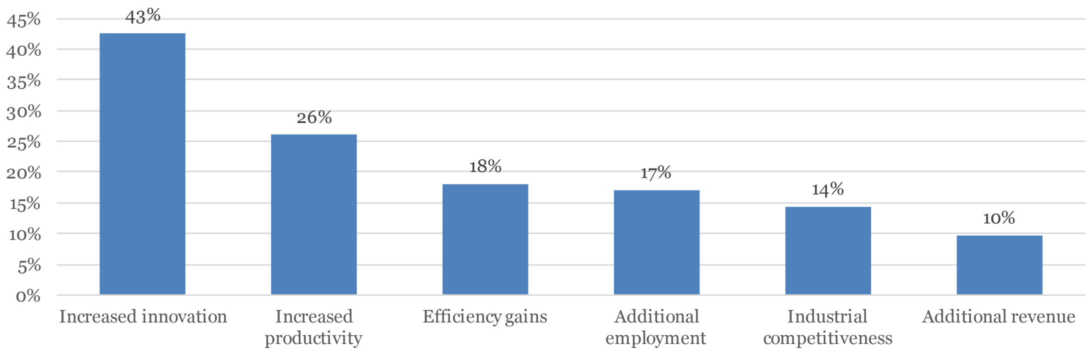
"Our high-pressure work led to a new method from absolute structure determination of light-atom materials. This is used extensively in industry and has been incorporated into widely used structure analysis software"

"Addressing an urgent clinical problem (sensitive) with measurements at Diamond led to identification of a manufacturing fault for a major multinational allowing remediation and subsequently improved clinical outcomes"

E.1.6. Economic impacts

Academic respondents were asked whether they believed that their use of Diamond had helped to delivery any of a series of **economic impacts** (for example, through their links with industry). Over half of the respondents reported at least one of the areas of impact. This included 43% that said that their use of Diamond had helped lead to increased innovation, and a further 26% reporting an increase in productivity. Additional employment and efficiency gains were also reported by 17% and 18% of respondents respectively.

Figure 12 Proportion of academic users reporting economic-related impacts



Academic survey (n=300)

Respondents were asked if they could point to **one concrete example of an economic impact** that has resulted (at least in part) from their use of Diamond. They were also asked to outline the impact further, and to explain the contribution of Diamond and their research. While a number of respondents indicated the potential of their research, very few could provide concrete examples of an economic impact. These included those shown below.

Additional revenue: New solutions for fuel-poverty, grid-intermittency and emissions enabled Sunamp to raise >£5m.

Additional revenue: Without research to prove the safety of current ageing nuclear power plants, they would have been forced to shut down which would have had a significant economical impact.

Increased innovation: The determination of a crystal structure of retroviral integrase has led to a major boost in efforts by a number of pharmaceutical companies to develop novel strategies for anti-retroviral drugs.

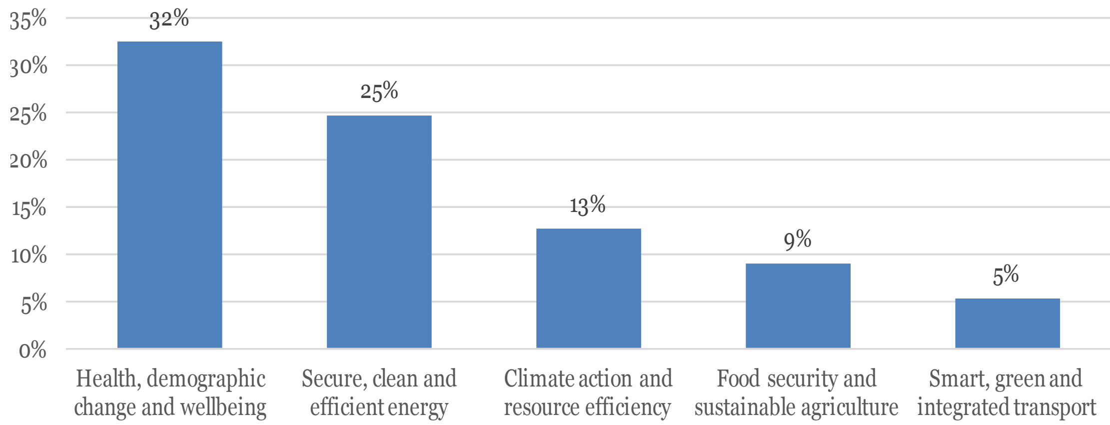
Additional revenue / employment: Our new Bimuno product has provided financial gains to the company Clasado and provided other researchers (at Reading and Oxford) with additional research, testing this new product in the gut microbiome and its effect on health. A new BBSRC IPA grant has the potential to further enhance Clasado's financial position in the food ingredient market, allowing them to enter into new markets - baby formulations and medical supplements. The grant will employ 2 people for 3 years.

Increased productivity of key nuclear treatment facilities at the Sellafield site. e.g. the Enhanced Actinide Removal Plant (EARP)

E.1.7. Societal impacts

Academic users were asked whether they believe that their use of Diamond has helped to deliver **impacts in a range of societal areas**. Around half of the respondents reported at least one of the areas of impact. This included a third that said that their use of Diamond had helped deliver impacts in the area of health, demographic change and wellbeing. A further 25% reported contributions in relation to creating secure, clean and efficient energy.

Figure 13 Proportion of academic users reporting societal impacts



Academic survey (n=300)

Respondents were asked if they could point to **one concrete example** of a social or societal impact that has resulted (at least in part) from their use of Diamond. They were asked to briefly outline the impact, as well as explain the contribution of Diamond and their research to this.

Many respondents could point to the *potential* societal benefit of their research (and new knowledge and understanding gained) – either in very general terms or more specifically. However, in nearly all of these cases it was either too early to point to a concrete example (further research required, results not yet taken up in practice, etc.) or any impact was too indirect to be known (e.g. research has fed into wider body of current knowledge). There were, however, a small number of respondents who were able to provide examples of realised societal benefits associated with their work at Diamond:

Health, demographic change and wellbeing

"Understanding of autoimmune disorders through fundamental science"

"Improved understanding of the relationship between corneal structure and function has helped corneal surgeons develop their surgical techniques and has helped computer modellers to improve the accuracy of their models aimed at predicting the response of the cornea to surgery and pathology"

"Our publication has helped to improve how we screen these medicines so they are safer for delivery to patients"

"Early use of Diamond (experimental method development) partially supported work that changed healthcare policy on the use of metal-on-metal hip replacement"

"Recent use of Diamond has enabled formal contribution to the current debate on the role of iron oxide nanoparticulates (including those attributed to air pollution) in dementia"

"Engagement with patients and their families affected by inherited bone marrow failure to set up a national charity (http://sdsuk.org/)"

Secure, clean and efficient energy

"Keeping the ageing nuclear plants running economically and safely"

"Some of our work is being used to simulate potential accidents in nuclear power plants"

"Our research has led to a reduction in discharges from nuclear facilities (e.g. Sellafield) to the environment"

"Better control of cementation processes for nuclear waste through improved understanding of how cement flows and hydrates"

"The efficiency of 3rd generation solar cells has increased as a result of synchrotron based experiments"

Food security and sustainable agriculture

"In collaboration with DuPont we develop new compounds for food protection"

Smart, green and integrated transport

"Helped support the development of new alloys for the aerospace industry"

Other

"Work on Diamond in the preservation of the Mary Rose"

"Improved methods to store carbon dioxide underground"

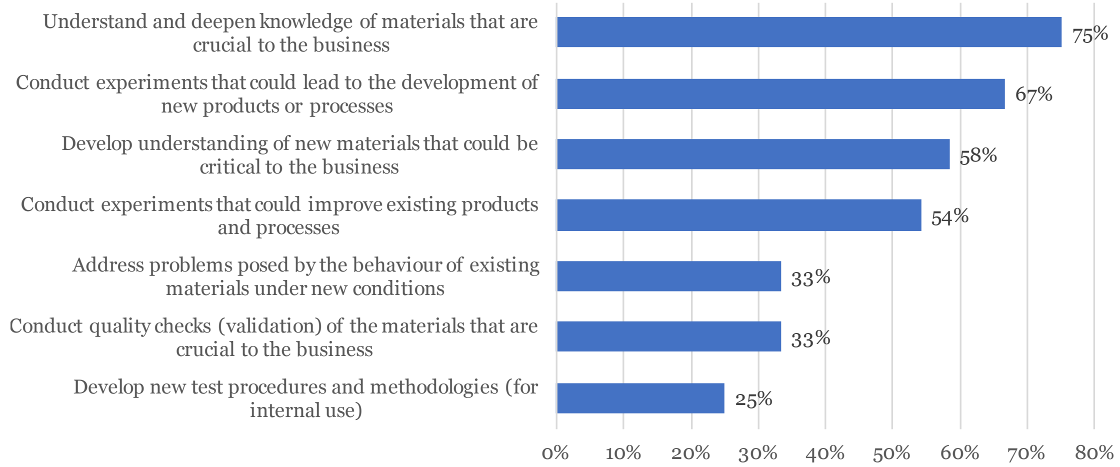
E.2 Results from the survey of industry users

E.2.1. Industry use of Diamond

Industrial users responding to the survey were asked about the importance of Diamond in enabling their company to undertake **various types of research** – either relating to *existing* products and materials (increasing understanding, conducting quality checks, and / or looking to make improvements), or relating to *new* areas (developing new products, understanding new materials, assessing existing materials under new conditions, and / or developing new tests).

The responses, summarised in the figure below, suggest that Diamond is important for all of these purposes, but that four types of research are more common. These are increasing knowledge of both existing and new materials, and conducting experiments to either improve existing or introduce new products and processes.

Figure 14 Proportion of industrial users reporting Diamond has been very important or critical to…



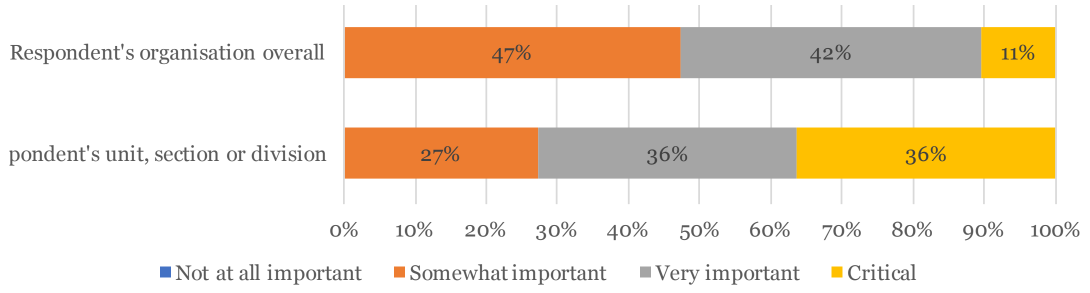
Industry survey (n=24). Proportion reporting type / purpose is 'very important' or 'critical' (rather than 'somewhat important' or 'not at all important').

1.1.1 The importance and value of Diamond for industrial research

Similarly, to the academic users, industry users were asked to rate the **importance of Diamond overall**, both to their own unit, section or division (if applicable), and to their organisation more generally. To this question, all of the respondents (100%) claimed that Diamond was at least 'somewhat important' to both. In addition, two-thirds (73%) stated that Diamond was 'very important' or 'critical' to their part of the business, and half (53%) claimed it was 'very important' or 'critical' to their organisation more generally.

It is perhaps not surprising, therefore that to a separate question the vast majority industry users responding to the survey (95%) also indicated that they **anticipate "definitely" using Diamond again in future.** The remaining 5% anticipated "possibly" using Diamond in the future.

Figure 15 Importance of Diamond for Industry Users' unit/division and overall organisation

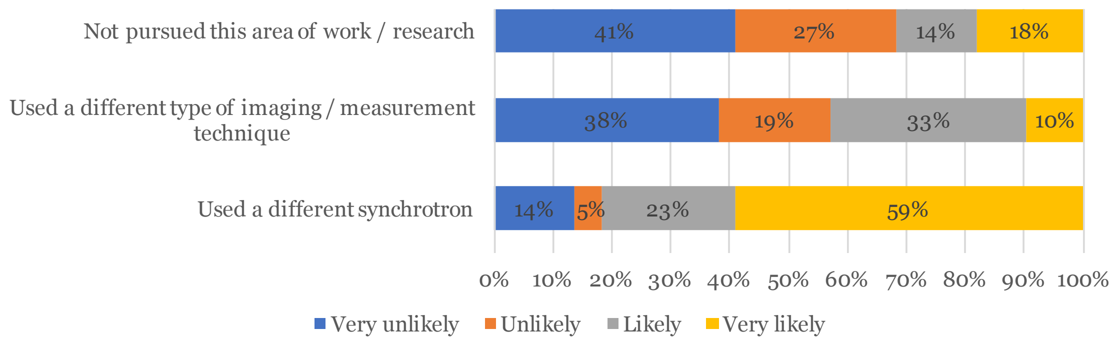


Industry survey (n=19-22)

Industry users were also asked to consider the extent to which the **non-existence of Diamond would have impacted (negatively) on their business**. Respondents were slightly more likely to feel it would impact them to a 'medium' or 'large extent' (54%), compared to those that felt it would have impacted to a 'small extent' (46%). None of the respondents suggested that the non-existence of Diamond would have had no negative impact at all.

To explore further the **possible implications of Diamond not existing**, users were asked about the likelihood (under this scenario) that they would (a) use a different synchrotron, (b) use a different imaging / measurement technique, and / or (c) not pursue the same area of work or research at all. As can be seen in the figure below, the majority (82%) of industry users believed it was likely (or very likely) that they would use another synchrotron. Nevertheless, a sizeable minority also indicated that the non-existence of Diamond would probably mean that they would use a different measurement technique (43%) or that they would not have pursued the area of work or research at all (32%).

Figure 16 If Diamond did not exist, how likely are the following alternatives (industrial users)



Survey of industry users (n=21-22)

Given the apparent possibility for many industry users to access alternative synchrotrons or use other imaging / measurement techniques, the survey asked **why they might choose to use Diamond rather than another facility.** Nearly all the respondents put forward reasons for the choice, which related to the following four main areas:

- The location of the facilities – respondents highlighted the convenience (and cost implications) of the facility being located nearby (n=17)
- The (quality and reliability of) facilities available – respondents mentioned the beamlines, equipment, computation technology/software and robotics – all of which were referred to as being "excellent", "state-of-the-art" and "world-leading" (n=14)
- The (quantity / quality of) user support and expertise provided – respondents mentioned the high-level expertise and support, tailored to user needs, provided by friendly and helpful staff. Proactive efforts to engage and support industry were also mentioned (n=13)
- The accessibility or availability of beam time – individual respondents mentioned free access for non-proprietary work, the reasonable cost of proprietary access, the availability and flexibility of beam time access, and the possibility of remote / mail-in access (n=6)

Relating to the first of these points, industry users were asked whether the existence or location of Diamond (in Oxfordshire, in the UK) had and / or continues to have an **influence on the location choices for their organisation. None of the respondents suggested that Diamond had had an influence on the original location of their business. However, most also indicated that their proximity to the facility was beneficial, and that it could therefore play some role in any (re-) location decision.**

Finally, industry users were asked to point to one **feature that makes Diamond of special value** to their business. Nearly all of the comments reiterated the reasons for choosing Diamond set out above (quality, reliability, accessibility, expertise, etc.). However, it is worth noting a couple of extra features and more detailed explanations that were mentioned in response to this question:

It allows measurements at atomic level"

"The breadth of different instruments and sample environments available"

"It is a unique radiation source that allows for much more accurate calibration of detectors and consequently increased accuracy of measurements"

"XRT is the only technique that allows us to access the 3D structure of our samples"

"Diamond has very high resolution microscopes that would be difficult to access otherwise"

"Diamond's Industrial liaison group"

"The ability to do experiments at or close to working conditions to provide extra understanding"

"Diamond's MacroMolecular Crystallography Beamlines allow us to conduct our everyday research. They are essential when our in-house X-ray equipment is not powerful enough (projects with small, fragile or weakly diffracting crystals). Experiments are moved to Diamond when the volume of experiments required is beyond the capacity of in-house equipment. For the last ~10 years Diamond is an extension of our laboratory. An essential extension"

"The ability to have up-front discussions with Diamond technical staff about the feasibility of experiments, (once we have come up with an idea to solve a particular question, for example). Clear communication up front helps us decide whether an idea is feasible and worth pursuing (especially as proposing a novel experiment takes time and requires customer/internal funding, being an industrial Diamond customer)"

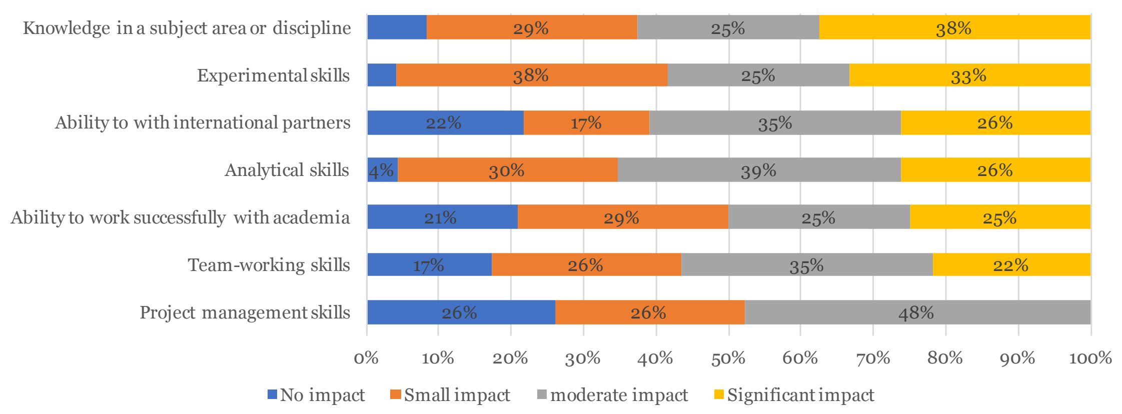
E.2.2. Knowledge, skills and capability benefits (for industry / commercial users)

Industry users were asked about the extent to which their use of Diamond has had a positive impact on the **skills and capabilities of staff** within their organisation. As the following figure shows, the feedback was generally positive, with a majority of respondents claiming that Diamond has had a 'moderate' or 'significant impact' on knowledge and skills in five of the seven areas suggested.

Significant impacts were most widely reported in relation to the development of knowledge in particular subject areas or disciplines and in relation to the development of experimental skills. However, around one-quarter of respondents also reported significant impact in most of the other areas suggested as well. Only in relation to project management skills were impacts not significant.

Other specific areas mentioned by industry respondents as having benefited mainly (beyond those listed in the questionnaire) related to experience and skills developed amongst staff from access to techniques, equipment and expertise at Diamond.

Figure 17 Extent to which use of Diamond has had a positive impact on staff's skills and capabilities



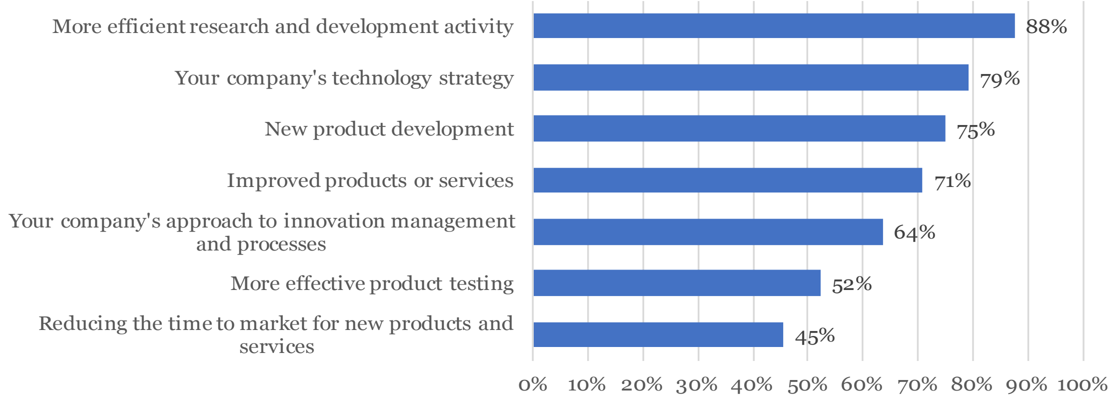
Industry survey (n=23-24)

Industry respondents were further asked to describe the single **most important benefit to skills and capabilities of staff** that is attributable to their use of Diamond. Most of the responses given related to the research that Diamond enabled or the consequent new knowledge generated (e.g. "mechanistic molecular insight into solving industrial problems", "accurate calibration of detectors used in radiation therapy", "investigations at resolution, length, scale and speed not accessible by conventional sources", or "understanding of materials, properties and processes we utilise to manufacture medical devices"). However, several others pointed to a new understanding of 'the possible' (e.g. "new knowledge of what is possible with the right fundamental facilities" or "knowledge of what can be achieved with X-rays at high pressure and temperature"), or to a significant increase in data that could be generated (e.g. "large amount of high quality data, impacting design and the design cycle time", or "the automation of acquiring data in a huge number of projects").

1.1.2 Innovation and commercial benefits

Industry users were asked about the extent to which their use of Diamond has had an impact on various aspects relating to the **innovative capacity, capabilities and activities** of their organisation. As the following figure shows, the most widespread areas of 'moderate' or 'significant' impact were reported around the efficiency of R&D, the enhancement of company technology strategies, and in relation to the development of new and improved products or services. However, moderate and significant impacts were also claimed by a majority in relation to the other areas suggested as well.

Figure 18 Extent to which use of Diamond has had a positive impact on staff's skills and capabilities

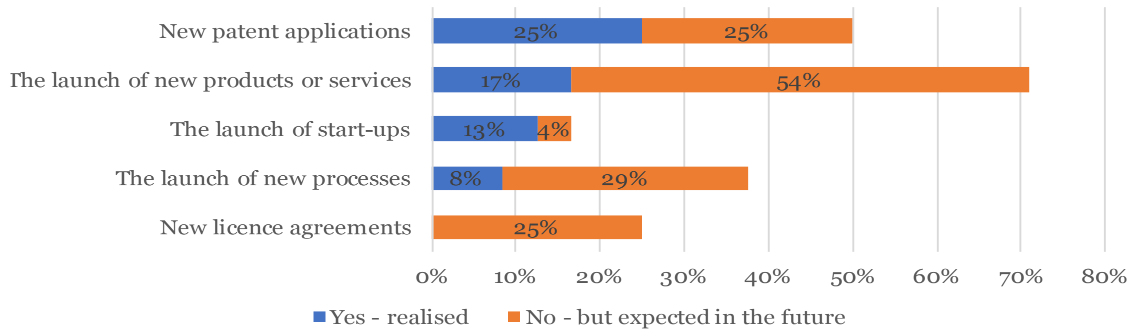


Industry survey (n=22-24). % reporting 'moderate' or 'significant impact' (rather than 'small' or 'no impact').

Just under half of the industrial users surveyed (42%) reported that their research using Diamond had already led to one or more **innovation-related or commercial outputs** (such as patents, products or new businesses). Three quarters of these respondents also indicated that they expected other types of innovation/commercial output to emerge in the future (i.e. given more time). A further 29% of respondents had not realised any such outputs yet, but expected to do so in the future.

The following figure summarises the responses and shows that the most common form of output already realised was new patent applications (seen by 25% of users, and expected to rise to 50%). The launch of new products or services have been realised by a smaller proportion (17%), but these are expected in the future by a further 54%. A small proportion of users (n=4) have also reported the launch of new start-up resulting from their use of Diamond.

Figure 19 Proportion of industry users reporting innovation-related or commercial benefits



Industry survey (n=19)

The following table provides further detail on the outputs realised (where this was provided).

Table 15 Details of innovation-related or commercial outputs realised by industry use of Diamond

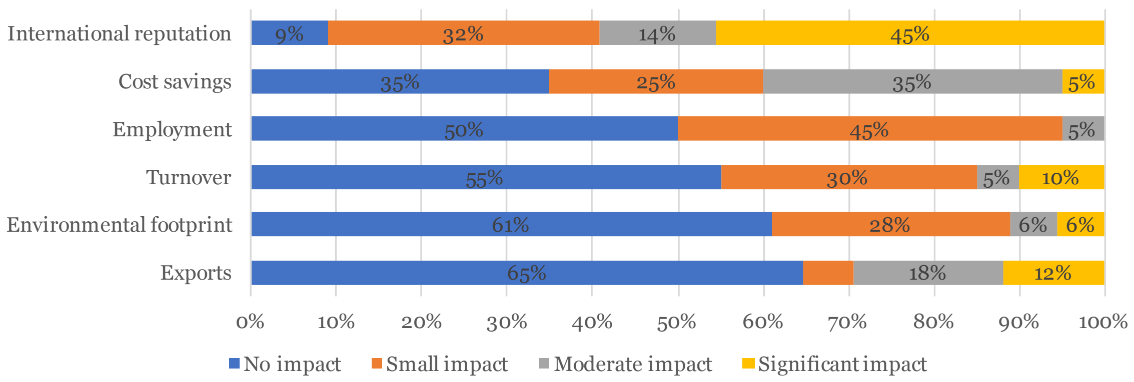
Output	Detail
New patent applications	• "A patent application relating to structural knowledge of crystal forms" • "We have generated 6 development candidates in the past six years [drug discovery] all based on structural information obtained from synchrotron facilities (mainly Diamond)". • "Two patent applications assisted by data gathered at Diamond" • "Diamond has helped in 2 patent applications" • "Data contributions to 5 new chemical entity patents"
The launch of new products and services	• "A new dosimetry service is being established, based on the application of a detectors that was calibrated at Diamond" • "Diamond is one essential part in the R&D jigsaw puzzle. It has helped the development of 3 new products"
new start-ups	• "Start-up of a contract research organisations, which relied on Diamond for data collection (has since been bought by CRL)" • "Establishment of drug discovery company, based on Diamond-based work on membrane protein structures"
new processes	• "Diamond has helped in the development of one new process"

Industry survey

E.2.3. Commercial impact

Industry users were asked to assess the extent to which their use of Diamond has had a commercial impact on their business (e.g. leading to an increase turnover, employment, reputation, etc.). As the following figure shows, all-but-two of the industry respondents (91%) reported an impact on their international reputation (including a majority who felt this impact was significant). A majority of users also indicated some level of impact on costs and employment (though these were mostly small or moderate effects). Impacts on turnover, environmental footprint and exports were less widespread amongst those users responding, but were still significant in one or two cases.

Figure 20 Proportion of industry users reporting commercial impacts



Industry survey (n=17-22). Excludes those responding 'not applicable' (e.g. organisation does not export)

Where possible, users were asked to **quantify the commercial impacts** (specifically any increase in turnover or employment, or reduction in costs) resulting from their use of Diamond. Few felt able to do so (e.g. indicating that it was too early to know and / or that such information was proprietary). However, in the selected cases where data was provided, this includes:

- Three respondents providing quantitative information on increased turnover (£100k, £750k and £2m). These estimates together total £2.85m, or £950k each on average.
- Six respondents providing data on employment (1, 1, 2, 3, 10 and 220). These estimates together total 237 jobs, or 40 each on average.
- Two respondents providing data on annual reductions in costs relating to innovation and new product development. They estimated annual savings of £50k and £250k, so £300k in total across these two organisations, or £150k each on average.

Users were also asked to describe briefly the single **most important commercial benefit** realised through use of Diamond. Again, only a small number of responses were given, but these covered:

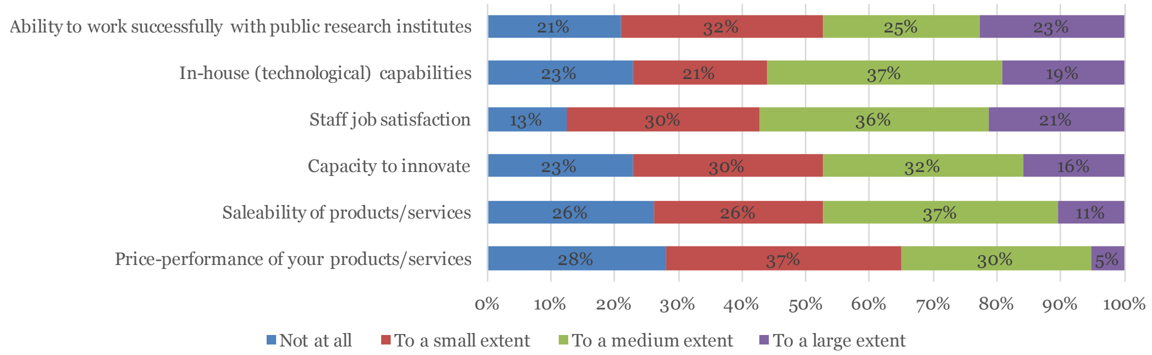
- Improved products and services (e.g. "understanding of molecular level aids better product design with tailored properties" or "new structures could lead to better products in future").
- Faster development of products and services (e.g. "quicker development of new service because Diamond allowed for more accurate calibration of detectors" or "provision of fundamental knowledge to decrease the time to market by many years").
- Increased market competitiveness (e.g. "access to Diamond allows us to remain at the top of the very competitive market for pharmaceutical research. The ease of access and quick reliable results from Diamond form the basis of our competitiveness" or "Frequent access to Diamond beam time was a major contributor in an increased number of customer projects (we are a CRO)").
- Improved reputation (e.g. "ability to demonstrate we work at the forefront of scientific research")

E.3 Results from the survey of suppliers

E.3.1. Effects on supplier organisations

Supplier organisations were asked about various possible **positive effects** on their organisation resulting from past sales to Diamond. The feedback provided was positive, with a majority (70%+) of suppliers reporting some improvements in each of the six areas suggested (see figure below).

Figure 21 Improvement to supplier organisations as a result of past sales



Supplier survey (n=56-57)

They were asked more specifically to describe the single **most important organisational benefit** that had resulted from having Diamond as a customer. The comments provided are listed below, arranged according to each of the 'benefit categories' introduced above:

Ability to work successfully with public research institutes

"It provides good insight into price and technological requirements for other synchrotrons globally"

"Knowledge gained helps successfully supply products into other STFC funded organisations"

"We can access the latest Synchrotron technology trends and needs through the sales to Diamond"

"Understanding of how large organisations undertake detailed project work, control, management, and communicating, the process has been very helpful in improving our management of complex project work"

In-house (technological) capabilities

"This is a long-term relationship with (some) challenging projects"

"High quality requirements push us to improve process control"

Staff satisfaction

"A very good company to work for, with good engineering drawings and interesting work"

"Dealing with Diamond has been a pleasure, as they are people of integrity at commercial and technical levels"

"We have a continuous ongoing positive relationship with Diamond"

"Purely on a personal level the work I receive from your company is interesting and enjoyable"

"Involvement with cutting-edge research and discoveries"

Capacity to innovate

"Our ability to innovate, design and produce has been the most important benefit"

"The challenging instruments delivered to Diamond forced us to innovate and improve our engineering, manufacturing and testing capabilities"

Saleability of products and services

"The saleability of our products to other similar organizations that respect Diamond's supplier selection"

Price performance of products

"It has helped us to remain competitive as a distributor, in terms of pricing and range of our products"

Several suppliers also mentioned the important role that Diamond had played in simply providing a regular and continuous stream of opportunities and income, supporting jobs and investment. One went as far as to say that "sometimes Diamond have ensured our financial survival", while another suggested that they would have relocated elsewhere in Europe if Diamond had not existed.

This sample of 62 suppliers also reported a number of specific **innovation-related outputs** resulting from their work with Diamond. This included: 2 new licence agreement; 13 new products and services; 7 new processes; and the launch of 1 new start up.

E.3.2. Commercial benefits

Survey results suggest that one of the most wide-spread and important impacts for those supplying Diamond is the **reputational benefits** that this brings. Most of the suppliers (81%) reported that past sales had contributed to the reputation or global brand value of their business. This includes over half of suppliers (56%) who said that they had experienced such benefits to a 'medium' or 'large extent'.

Many of the respondents took the opportunity within the questionnaire to further highlight the importance of sales to Diamond in attracting further business. A selection of quotes is shown below.

"Exposure to our products to people visiting Diamond"

"Being on display with our products in the UK's biggest synchrotron source"

"Being part of the supply chain to Diamond opens-up sales opportunities with other companies"

"Being a trusted supplier of Diamond has helped attract new customers"

"It helps to acquire other contracts"

"As a leading research organisation among synchrotron facilities worldwide, Diamond is an important reference for us to acquire new customers and orders"

"Recognition of supplying technical products and solutions to a leader in the R&D market"

"It is a very prestigious organisation, and therefore a great opportunity for us to move in to the scientific equipment design and construction domain"

"Being on display with our products at Diamond is most important for us"

"Diamond is a high-prestige customer for us and a good reference within the whole scientific community. Their scientific research is world-leading"

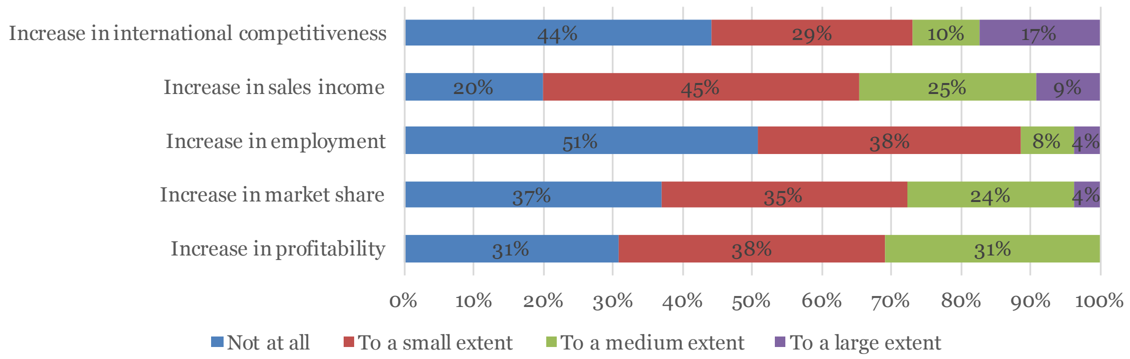
"The association of being a supplier to Diamond has benefits with other scientific companies and research centres thought the world"

"Diamond is an important and well known international customer, references of past projects with Diamond are eminently respectable"

"Diamond are a good reference, and since the job has been done professionally, the more time passes, the more the reference becomes valuable due to reliability of the products"

Suppliers were also asked about the contribution of Diamond sales to **wider commercial benefits** (i.e. going beyond any increased income, employment, etc. directly resulting from contracts with Diamond). A majority (49%-80%) indicated that there had been some impact on each of the elements listed (competitiveness, income, market share and profitability), although in around half of these cases, the contribution was felt to be 'small'.

Figure 22 Extent to which past sales have contributed to wider commercial benefits



Supplier survey (n=52-55)

Suppliers were further asked to **estimate any increase in sales** to *other organisations* that was attributable to past work with Diamond. Only a handful of respondents were willing or able to provide such data, however, these organisations suggested figures ranging from £100k to £750k in additional sales (£100k, £150k, £250k, £500k and £750k). Across the five businesses in question, additional sales attributable to Diamond totalled £1.7m, or £350k each on average.

Several further respondents provided related information, but with insufficient detail to be included within the calculation above:

"From our first project with Diamond in 2007 our business has grown substantially from £3m to a current order book of ~£7m (and growing)"

"Increase of sales of products added to our range as a result of sourcing initially for Diamond"

"Work with Diamond has added approximately 3% to annual sales"

"As a result of the technology developed with Diamond, we have sold similar devices to organisations overseas"

"We have seen increased sales and profitability"

"We have seen increased sales of specific products"

"New sales to other Synchrotron such as CNAO and ALBA"

Appendix F - Complete Financial table, Monetisation of Diamond Publications and List of softwares assessed

F.1. Complete Financial table

	Pre-opening	2007/08	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	2017/18	2018/19	2019/20	Total
Operating Costs	1.6	23.5	28.4	30.5	33.5	36.5	39.9	42.5	44.5	54.6	56.9	62.8	64.5	65.7	585.4
Capital Expenditure - Operation		1	4.5	5.7	8.6	5.1	8	7.5	6.2	8	10.5	12.8	17.4	18.8	114.1
Phase I	264.1														264.1
Phase II	22.1	24.5	25.5	22	16.2	9.9	2.8	0.8	0.2	0	0	0	0	0	124
Phase III		0	0.1	0.3	3	10.3	14.2	17.2	23.7	20.6	11.5	3.7	1	0	105.6
Other Capital Projects		0	0	0	0	0	0	0	4.8	5.6	7.3	4.3	5.3	0	27.3
														TOTAL	1220.5

F.2. Monetisation of Diamond Publications

By first looking at 2019 papers and using the following parameters, we can establish an average value for Diamond publications for the 2019. Then assuming a 1.85% inflation rate every year since 2002 we can estimate the value of knowledge produced by Diamond since the facility became operational.

	Biology	Chemistry	Physics
Number of Diamond paper in 2019 (A)	433	351	333
Average time spent by research on actual research (B)	60%	60%	60%
Average Salary in the UK (C)	38526	32145	43605
Cost of employment in the UK (D)	30%	30%	30%
Average number of publications per year and per scientists (at least based on Diamond data) (E)[16]	1.44	1.44	1.44
Estimated time spent by co-author working on a single paper (F)	30%	30%	30%
Average number of authors per papers (based on diamond data for 2019) (G)	9.82	9.1	9.52
Value of a paper for 2019 (V)	£76,267.42	£59,865.42	£84,191.17
Value of all 2019 papers for the given field	£33,023,793.28	£21,012,762.06	£28,035,657.95

Table 7: Parameters used for the monetisation of Diamond articles.

Using the following formula, we can calculate the value of a single article. In essence, we calculate the cost of the time spent by the main author (salary and cost of employment divided by the number of articles published in a single year) and the cost of the time spent by the rest of the co-authors. We assume that the main author spends all his research time working on the paper and that the other co-authors are spending around 30% of their research time.

$$V = \frac{\big((C \times D) + C\big) \times B}{E} + \left(\frac{\big((C \times D) + C\big) \times B}{E} \times F \times (G - 1)\right)$$

16 Fanelli D, Larivière V (2016) Researchers' Individual Publication Rate Has Not Increased in a Century. PLoS ONE 11(3): e0149504. https://doi.org/10.1371/journal.pone.0149504. Data extracted from the dataset 1. Social sciences are excluded. Average calculated over 15 years for 35029 authors from the United States, Canada, Europe-15 countries, Australia and New Zealand.

For 2019, this gives us an average value for 1 single article of £73,441.33 and a total value of **£82 million** for all articles published in 2019.

Since beginning of operation in 2007, Diamond has been involved in the publications of over 8,600 articles which have a total estimated value of **£590 million**.

Assuming a yearly inflation of 1.85% we can estimate the total value of the articles using the following table:

Year	Number of articles	value of 1 article	Total value for the year
2020	954	£74,800.00	£85,047,599.65
2019	1137	£73,441.33	£83,502,797.89
2018	1091	£72,082.67	£78,642,193.29
2017	1020	£70,749.14	£72,164,123.71
2016	983	£69,440.28	£68,259,797.00
2015	982	£68,155.64	£66,928,835.12
2014	777	£66,894.76	£51,977,226.42
2013	687	£65,657.20	£45,106,499.35
2012	562	£64,442.55	£36,216,710.86
2011	511	£63,250.36	£32,320,933.40
2010	389	£62,080.23	£24,149,208.41
2009	236	£60,931.74	£14,379,891.36
2008	207	£59,804.51	£12,379,532.70
2007	103	£58,698.12	£6,045,906.61
		TOTAL	£677,121,255.76

Table 8: Estimation of the value of knowledge produced at Diamond

F.3. Scientific software and applications

- xia2
- DIALS
- dxtbx
- xia2.multiplex
- screen19
- fast_dp
- fast_ep
- big_ep
- ispyb_api
- python-zocalo
- python-workflows
- DAWN (1500 download/year)
- Project January
- Vivie
- hrpd-rebin
- imod-automation
- txrm2tiff
- StitchM
- gridSNAP
- GDA

F.4. Technical software and applications

- 600 industrial controllers
- EPICS areaDetector
- HDF5
- Odin
- Malcolm
- Scanpointgenerator
- Aioca
- Coniql
- Pmac

F.5. Business software and applications

- UAS
- ISPyB
- SynchWeb
- Diamond RDB
- Jasper Reports
- Legacy DuoPS
- Legacy DuoDesk
- Diamond Publications Database

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