EPSRC Research Grant Final Report
National X-ray Crystallography Service 2001–2006
GR/R33069/01 and GR/R32987/01

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1. Background and Context

The National Crystallography Service (NCS) was inaugurated in 1980, and has been continuously funded since that time. From 1980 until 2001, the Service operated within the rolling grant scheme, with biennial Panel visits and Reviews. The aims and objectives of the Service have developed over the years of its existence. The original requirement to provide a shared diffractometer and single-crystal data collection or full structure determination facility for a small number of named users, developed into a similar operation, but to provide access to all UK researchers eligible to receive Research Council support, and, subsequently, to a brief to engage in further development of single-crystal diffraction methodology and chemical crystallography in general.

Over the years of its operation, feedback from users, referees and reviewers has identified a high degree of support and satisfaction, and, through involvement of its users in international collaborations, together with presentations at conferences and the visibility through the Web site, the Service is currently regarded as a model of its kind, internationally. As a National Service, it has consistently provided core support for many users in small or medium-sized Departments, without local equipment (many of whom, however, have subsequently been able to use their growing Service output to make cases for their own equipment), back-up support at crucial times for busy laboratories with local facilities, and opportunities for special experimentation for users across the spectrum. As a centre for research in the subject, we have consistently sought innovation, and have been directly responsible for passing on a number of new ideas to the national and international communities. The prime example of this is the adoption, in 1989, of the use of area detectors in small-molecule crystallography, as a world first. This led to a revolution in the subject, with considerable knock-on effects in many areas of chemistry, biochemistry and materials chemistry.

In 1999, the EPSRC Chemistry Programme Management commissioned a review, by Segal Quince Wicksteed, (SQW), an independent consultancy agency, to gauge the views of the whole UK Chemistry community on the value of all the National Services then operating, and the level of support for their continuation. This was done through interviews with service providers and a postal survey of heads of UK chemistry departments. The NCS was one of the services recommended for continuation. The report, in 2000, also set out criteria against which the need for a service, the facilities and opportunities it should offer, and its performance should be measured. The subsequent call to tender for the Service indicated that the EPSRC was prepared to consider support for up to five years, to create some stability, and that, since a National Service in a subject should be operating as a centre of excellence, it should provide an ideal environment for training of research students. This had been one of the points raised by the SQW review.

Our strategy, in making our proposal, in late 2000, was thus to focus on three main objectives. The first was to provide users with as efficient a service as possible, including continuation of our earlier theme of developing and providing expertise to work on difficult samples. The second was to seek out and acquire new facilities that ensured a cutting-edge capability in instrumentation, which might not be available in other laboratories. The third was to accept the challenge to provide a first-class opportunity for postgraduate training in crystallography.

A further, most significant development at this time was an agreement to coordinate a submission for continuation of the existing Service with a complementary proposal to provide a formal Service on the Daresbury synchrotron facility to study samples that were still too small to be handled in the Southampton laboratory. This Service would apply for regular allocations on the high-flux single-crystal diffraction facilities at Daresbury Laboratory Synchrotron Radiation Source (SRS), established in 1997 as a user facility as a consequence of a previous large-scale grant awarded to WC in 1994 (GR/J73315). SRS Station 9.8 had a proven performance for small-molecule work by 2000, and users would have the opportunity of having data collected much closer to the time of availability of their microcrystal samples than if they had to go through the time-consuming and delaying process of making individual applications, and would have the work carried out by acknowledged experts. The two operations would be fully coordinated, but separately managed. Access to the unified Service would be assessed at the annual meeting of a Management Advisory Panel (MAP), and approved allocations would be valid for both strands. Moreover, the coordination included the proposal that all samples would be submitted to Southampton for preliminary screening, in case some of them were amenable to data collection on the high-intensity rotating anode laboratory source. The overall objective was to offer to eligible users two levels of powerful crystallographic facilities additional to any they might have locally, with appropriate expert staffing, rising far above any provision currently available in UK University chemistry departments. Full integration of the two components of the Service should present users with a single unified interface, a single point for submission of samples and applications for Service usage, a range of appropriate support and training opportunities, and should lead to an efficient and appropriate use of the equipment and other resources with samples being examined according to their needs as assessed by preliminary screening. Users, whether they have crystallographic expertise or not, are thus provided with either diffraction data or a fully determined and refined structure according to their wishes. We suggested in the grant proposal that this approach was by far the most cost-effective way of using the SRS for crystal structure determination across a broad range of chemistry, not only for end-users but also for the facilities managers and funders, and would provide a Service that is unique in the world, with 'the right people doing the right jobs in the right places.'

The pair of linked submissions, for five-year funding, was supported in full. In the following report, due reference is made to the reporting structure and topics suggested in the EPSRC guidance documentation plus topics which are now core in the responses required by the annual Cross-Panel Reviews of the National Services. We are able to demonstrate that our objectives have been fully met and that both components of the NCS, in the first five years of their combined operation, have comfortably exceeded the initial targets. In particular, for the synchrotron component, the number of data sets measured is 67% higher than proposed; the sample rejection rate (samples not giving a useful data set has fallen from almost 50% to around 35% during the grant period; 73 user groups from 44 institutions have made use of this component of the Service, most of them being people who have had no previous benefit from synchrotron facilities and many being new users of the Service since 2001. Of the publications arising from the Service over this period, more than 60 have used the SRS Service, with a current annual publication rate exceeding 30.

At the conclusion of the five-year grant period, we were requested by EPSRC to submit individual reports (forms and narratives) addressing the achievements of the two components of the Service with reference to the original Cases for Support which were originally submitted and reviewed as two separate documents in 2000. We have subsequently been asked to replace these with a single narrative report on a relatively short timescale, but with a sensible limit of ten pages. The result is this current report, which combines and integrates most of the material of the two separate reports with some removal of overlap and of other text in order to keep within the limit. Inevitably the origin as two separate documents will be evident in places, but we believe it is a fair description of what we have achieved and is in the spirit of the genuinely integrated Service we have developed in the last five years.

2. Achievements: Key Advances and Supporting Methodology

For the Southampton part of the Service, we proposed two main actions. The first was to install a second diffractometer on the rotating anode in Southampton. This was feasible with such equipment, unlike the more common sealed-tube systems. This alone would effectively double the output from the high-intensity source. The new diffractometer was installed in 2002 and was equipped with the last version of detector used by Nonius, prior to their merger with Bruker AXS. The detector proved to be approximately twice as sensitive as the detector on our older KappaCCD (vintage 1997), giving us a corresponding increase in intensity levels.

The second objective was to attempt to increase the flux at the crystal sample by installing a set of confocal mirrors, to be supplied by the Osmic Company, who had made some ray-tracing calculations for us. These had shown that with a set of 100mm mirrors (almost twice as long as those used by protein crystallographers with copper radiation) we might expect an enhancement in X-ray brilliance of some 4–5 times compared with a graphite monochromator. In the event, major changes occurred in the corporate structures of both Nonius and Osmic, causing significant delays in delivery of the mirrors. Eventually (October 2003), we received a set through the newly merged Bruker-Nonius organisation, which were actually made by another supplier. Fortunately, these performed well up to the original specification, with an enhancement in brilliance levels of more than 5×. The mirrors were installed on the new diffractometer, so that effectively we obtained an increase in brilliance of a factor of 10× what could be achieved on the older machine, and we found that the size of crystal we could work with, albeit with overnight collection, was sometimes down to a few microns.[1] The impact of these developments on the output from the Service can be gauged from Section 7 below.

One additional planned enhancement to the Southampton instrumentation was an upgrade to our newest Cryostream, purchased on this grant, to enable operation up to 500K. Overall use of variable-temperature capabilities has been much enhanced by the preparation of software, written by Mark Light of the NCS team, for a fully automatic multiple data collection procedure, including integrated control of the Cryostream.[2]

We may measure the achievements of the new SRS component against the targets set in the original proposal. These estimated that 100 or more samples would find their way each year to the SRS Service, having been screened first in Southampton to ensure that they really did need the much more powerful resource. The samples would come not only from existing NCS users but also from a substantial number of new users attracted by the much enhanced capabilities. We aimed to collect about 3 complete data sets per day for around 30 days of SRS beam-time annually, on the basis of previous experience, providing users with either a set of data for their own processing or a refined structure in a publication-ready form. We also set ourselves the aim of investigating every submitted sample in the available beam-time and to provide data and results to users within a short time of the experiments.

For reasons discussed in Section 6 of this report, we have actually received fewer than 30 days of SRS beam-time in each of the five years of operation of the Service; instead of 150 days in total, we have been able to use just 110. However, because of a combination of efficient working practices to obtain maximum benefit from the available time, additional personnel involvement beyond that funded by the grant, growing experience by the Service staff, and significant improvements to the equipment at SRS during the period of the grant, we have managed to examine virtually every submitted sample (the main exception being a very large series of closely related materials from one user for comparison studies, some of which remain unfinished, though all the highest priority samples have been successfully investigated), and have collected a total of over 750 data sets, including a few that were repeated in an attempt (usually successful) to improve on an initial result. This represents an average of almost 7 data sets per day, compared with the original aim of 3, which would have generated 450 data sets over the lifetime of the grant. Typically, 3–5 data sets were collected each day in the early stages, and this rose to 8–12 per day after new diffractometer and detector systems were installed in 2004. We have consistently set new records for output on SRS station 9.8, above those of other users, and then gone on to break them. It is important to note in this context that we have a policy of measuring complete data sets (with parameters chosen to provide coverage of a whole sphere of reciprocal space in most cases) with high redundancy, and speed in itself is not the primary objective; this is essential for success with the marginal quality of many of the samples with which we have to deal, and a fast data collection, however good it may look in statistics, is useless if it gives a poor result when a more appropriate experimental strategy would delivery a good quality structure.

Another important statistic, which it was not possible to predict at the beginning of the grant, is the rejection rate for samples, i.e. the proportion for which it has not been possible to measure a data set at all, because of inadequate diffraction intensity, obviously non-single-crystal behaviour beyond the scope of the powerful software tools available for handling twins, split crystals and other challenging samples, or samples which appear to have decomposed, redissolved in mother liquor, or otherwise suffered in transit between user and experiment. At the beginning of the grant in 2001, this rejection rate was approaching 50%, but it has subsequently fallen to around 35% on average. A significant rejection rate is, of course, inevitable for this Service, which is the ‘last resort’ for users; almost all samples failing in Southampton are forwarded to the SRS Service for investigation, even when the screening gives little hope of success, and sometimes we have had a pleasant surprise in such cases. Combining the current rejection rate and the productivity in terms of measured data sets per year indicates clearly that the demand for the Service now far exceeds our initial estimate.

Although we have not undertaken any formal assessment of the relative capabilities of the Southampton and SRS components of the Service by carefully controlled comparative measurements from the same sample, and noting that such a comparison is difficult because of a number of contributing and competing factors, we have estimated that the SRS brings a gain of around 3–4 orders of magnitude in overall X-ray intensity over the best performance in Southampton, which itself exceeds standard laboratory X-ray diffractometer systems by about one order of magnitude. This information is now being used in Service promotion. It is of interest to note that the planned single-crystal ‘small-molecule’ diffraction beam-line at Diamond, due to operate from 2008, is expected to be 2–3 orders of magnitude more powerful again, which should reduce the sample rejection rate even further if this really can be achieved.

3. Project Plan Review

In this section we report on developments that were not identified fully in the original applications, but which have been followed up as being of potential value to the operation of the NCS. These have been additional developments, rather than any change of direction, and have been achieved through three special collaborations.

In the first of these, we were invited to join the research programme of the Southampton Combinatorial Centre of Excellence (CCE). This activity was funded by subventions from industry, and the focus was on the development of new methods and technologies in Combinatorial Chemistry. Since discovery of new compounds often involves structural characterization, we were challenged to see if we could automate the process of single-crystal structure determination. Recognising that the creation of a fully automatic process might be of particular value to the operation of the Service, we decided to devote some NCS staff time to build an automatic data collection capability. This involved the installation and development of a robotic sample handling facility. The capital costs for this were provided by the CCE, and the control software was also written by Mark Light. The system has been fully validated, but final implementation into our workflow is awaiting installation of some collision contacts to guard against any possible random movement of the rather powerful robot arm. This has been delayed due to changes in staffing responsibilities (see Section 9 below), but should be completed in the next few months.

Soon after we started the automation project, we also contributed to a multidisciplinary grant proposal to the newly constituted UK e-Science programme. Our collaborators for the project, which was assigned the acronym Comb-e-Chem, were colleagues from Southampton Departments of Electronics and Computer Science (ECS) and Mathematics/Statistics, together with IT Innovations, a spin-out company from ECS. The project name was chosen as a result of the growth in the generation of new compounds and properties as a result of the development of parallel and array synthesis components of Combinatorial Chemistry, and the expectation that e-Science concepts would need to be developed to meet this growth. The objective for our part of this project was to use the operation of the NCS not only as a demonstrator to address a number of points which would be fundamental in the application of e-Science methodology to laboratory work, but also to see if any or all of the procedures developed would provide an enhancement to the operation of the NCS for both users and Service staff. Full details of the outcomes of this project are provided in references 3 and 4; in summary, the activities and outcomes are as follows:

a) creation of an environment to allow full remote access to the laboratory instrumentation – not completed, due to major problems with security issues, to resolve which would create a cumbersome mode of operation, requiring much extra effort by Service personnel and unlikely to be attractive to our users;

b) creation of an environment to allow a remote user to participate in an experiment by visualizing images from the diffractometer in real time, and discussing selection of data collection parameters with a Service operator via voice communication – completed and available to users if requested;

c) creation of a Grid-enabled Service Database, enabling status tracking of a user's own samples during Service processing, and eventual direct access to data or structures and downloading capability – completed and functioning after additional modifications; initial roll-out to selected users in early 2006 with full deployment in November 2006.

A third collaboration, involving researchers from Southampton ECS and the UKOLN team at the University of Bath, was directed at the creation of a procedure to manage the fully provenanced and annotated archiving of the data and metadata associated with the determination of a crystal structure, and the dissemination at source of the contents of the structure archive. This activity was fully funded by JISC (Joint Information Systems Committee), and the development was made in full consultation with the International Union of Crystallography and the Cambridge Crystallographic Data Centre. The resource developed is identified as the eCrystals archive, which has full compatibility with Open Access protocols.[5] Further discussion of this important activity is provided in Section 8.

4. Training

This theme was identified in the 2000 SQW report to EPSRC as a special component of National Services activity, and we have given it much attention during the operation of the NCS. We can report on three sub-headings.

1*. *Studentships. One of the components of our proposals was a request for funding for the equivalent of two project students in Southampton and two in Newcastle, phased over the five-year period of the grants. The Southampton resource was used to provide support for a number of collaborations within the School. In each case, crystallography training up to full operational level was integrated into particular chemistry projects in which structure determination was crucial. In addition, special skills were developed. The following projects were supported:

a) joint funding (the rest from industrial sponsorship to Dr A A Danopoulos) for Mr Nicos Tsoureas with a project 'Phosphine and pyridine functionalised *N*-heterocyclic carbenes and complexes thereof'; special crystallographic skills – working with very air-sensitive, small, often low-melting organometallics; PhD awarded 2005;

b) full funding (co-supervisor, Dr M Grossell) for Mr James Orton with a project 'Directed synthetic and structural investigation of systematic supramolecular assemblies'; special skills – working with crystals with a wide spread of quality, twins, aniso-mosaics etc., crystal engineering; PhD awarded 2007;

c) half funding for 2 years (rest from DTA, to support Royal Society Fellow, Dr Daniel Price) for Mr Tony Keene with a project 'Structure direction and magnetism in transition metal oxalates'; special skills – crystal growth via hydrothermal and gel methods, complex magnetic properties, high-symmetry space groups [at the end of year 2, Dr Price and Mr Keene moved to Glasgow University]; PhD awarded 2006;

d) half funding for 2 years (rest from DTA and School funds) for Ms Samantha Callear with a project 'Systematic study of organic salt and co-crystal formation', supervised by MBH; special skills – crystal growth using robotic liquid handling equipment, Microvate variable-temperature array reactor, handling crystals of widely varying quality, including microcrystals, twins and aniso-mosaics; completion due Sept 2007.

In addition to these specific projects, Service staff have contributed to the regular training of nominated PhD students and Postdoctoral Fellows in practical crystallography procedures, enabling self-handling of crystals from their own projects. Various levels of skills have been achieved, and monitoring of these has enabled approval to be given to some students to book diffractometer time in out-of-hours periods for their own work. Annually, about 6–8 new users from outside the crystallography group have been trained.

The support for two project studentships in Newcastle was divided among three actual students, Mr Luca Russo, Mr Zhanhui Yuan and Ms Kathy Guille, providing funding for 3, 2 and 1 years respectively. All three undertook projects supervised entirely by WC, involving both synthetic and crystallographic research, in areas expected to generate significant numbers of samples requiring the SRS facility. Luca Russo worked on supramolecular coordination chemistry of polycarboxylate ligands with transition metals and Zhanhui Yuan on group 13 metal phosphonate complexes, some of which have microporous structures. Both have successfully completed their theses. Luca Russo moved to a postdoctoral position at Jyvaskyla in Finland, but has now returned to work as a PDRA in Newcastle (50% in the Service). Zhanhui Yuan's thesis has just undergone some revision requested by his examiners and should shortly be approved; he is now seeking employment in a research post, and is likely to return to China for this. Kathy Guille's PhD programme in complexes of s-block metals with ligands of biological and medicinal relevance is now in its final year, supported by other funds. All these students have attended an intensive research training course run by the Chemical Crystallography Group of the British Crystallographic Association (BCA) and an international Summer School in Synchrotron Radiation Science, of which WC is a joint organiser every two years. Mention should also be made of Gary Nichol, a PhD student whose research project has been funded entirely outside the Service, but whose work in s-block coordination chemistry has made substantial use of the Service and who has been a member of the experimental team on several visits, thus contributing directly to its operation; he wrote an excellent thesis and is now Staff Crystallographer at Arizona State University, with a promising career ahead of him.

2. ***Service Staff Training and Development.*** All staff employed on the Southampton Service grant have been encouraged to engage in activities that will contribute to their career development. For example, Simon Coles has been intimately involved in the e-Science and informatics developments, Mark Light has specialised in instrumentation development and control, Thomas Gelbrich has attended advanced courses in computing languages, and Peter Horton has developed special expertise in working with very large structures. Ann Bingham took the opportunity of her part-time appointment to complete a part-time PhD in Crystallography, and to attend a number of University-provided courses, mainly in IT subjects. It is pertinent to comment that the success of our training strategy is demonstrated by the appointment, after competitive interviewing, of Mark Light to the permanent post of X-ray Diffraction Manager in the School of Chemistry, Ann Bingham to a senior administrative post at Southampton Solent University, and the achievement by Simon Coles of national and international recognition for his work on crystallographic and chemical informatics and digital repository work, appointment to the Editorial Boards of three Journals, BCA Council and two steering panels in the Digital Repositories area (SPECTRa and RIN).

Ross Harrington came from a PhD project that involved substantial crystallographic experience in a standard laboratory setting, and has now acquired impressive expertise through his work with difficult samples in Newcastle and (50% contribution) in the SRS Service; he continues with the Service in its renewed funding, together with Luca Russo, and is currently acting as sole supervisor of undergraduate research projects.

3. ***Training of External Visitors***. In response to the recommendations of the original grant review panel, we have organised advanced workshops for researchers from other Universities. Two workshops were organised at Southampton, in 2002 and 2004. In these we provided a mix of lecture presentations and practical sessions, on advanced methods of data processing and structure refinement, by members of the NCS team plus invited speakers from other laboratories who were directly involved in some of the associated software developments. The September 2002 workshop was attended by 13 UK participants, and was organised by Drs Coles, Light and Horton, who led most of the practicals. They were joined by Drs A Duisenberg and A Schreurs from the University of Utrecht, the authors of the highly regarded EvalCCD software for decoding data from twinned crystals, which is supplied by Bruker-Nonius, who attended as presenters and tutors, along with Drs Simon Parsons (Edinburgh), David Watkin and Richard Cooper (Oxford).

The September 2004 workshop, attended by 14 UK participants, provided repeat contributions from Drs Duisenberg, Schreurs, Parsons, Watkin and Cooper, presenting and providing tutorials on twinning and special features in the CRYSTALS software, respectively, and Professor David Rae, of the Australian National University, who demonstrated the very special features in his RAELS refinement program for handling defect crystals. The Skills workshop was followed immediately by a "Crystal Grid" workshop, organised and funded by a special e-Science grant to bring together researchers from the UK, USA and Australia interested in developing e-Science and informatics approaches to service crystallography. Some of the participants of the skills workshop stayed on to attend this workshop also. Both workshops were warmly received by the attendees.

Over the five years of this grant, a number of visits to Southampton have also been made by users, often accompanied by their research students, and students visiting alone, to experience at first hand data collections on difficult crystals.

A two-day workshop at Daresbury in 2003 including some hands-on experience for 8 users on one of our allocated days of beam-time. Other training has included a half-day satellite session at an annual BCA Spring Meeting. We have also provided assistance in interpreting results, especially where these are complicated by aspects of disorder, twinning, etc., frequently encountered for the very demanding samples finding their way to the SRS Service.

5. Service Operation, Management and Performance

These topics are identified as fundamental in the annual review of the Service activity by the independent Cross-Service Review Panel. The management of the integrated Southampton+SRS Service has been as proposed. Applications for use of the Service have been invited annually and have been handled centrally; there has also been provision for interim applications between the major annual exercises. In their applications users have provided a scientific case for support, together with information on local crystallographic facilities and the reasons why these are inadequate, reports on previous Service usage, and information on funding of their research. The applications have been considered by an independent Management Advisory Panel, with members appointed by consultation between the Service directors and EPSRC, and have been graded as high, medium and low priority, with some reductions in allocations compared with requests. These grades have then been used in prioritising work on submitted samples; there has invariably been a queue of samples for investigation at any time. The MAP has met physically in Southampton annually, with an EPSRC Chemistry programme representative present, in order to peer-review the applications from users, and has received and discussed annual reports from both components of the Service. At other times the MAP has carried out its business in virtual meetings by e-mail, particularly for reviewing interim applications from users, advising on training, promotion and significant developments of the Service, and assisting with the preparation of material for the recent funding renewal application.

Samples have been submitted by users to Southampton, where they have been screened and the majority retained there for full investigation. Only samples thus found to be in need of synchrotron study have been forwarded direct to Daresbury in advance of each scheduled SRS experiment; this screening guarantees that the SRS resource is not inappropriately used where it is not necessary and makes our use of this resource particularly cost-effective. In practice we have been able to examine almost all the forwarded samples and scheduling priorities have not been a major issue. On each visit, MAP rankings have been one factor in deciding the priority of samples, together with information on sample stability, effective use of beam-time between electron-beam refills, and experimental requirements such as sample temperature etc.

The principal objective during SRS visits has always been to obtain maximum benefit from the available beam-time, which has meant high-intensity full-time staffing of the experiments, with two people actually engaged in the work at any particular time (this is required by CCLRC for health and safety reasons, quite apart from other considerations). In the early stages of the grant, with 3–5 data sets collected per day, sample preparation and preliminary measurements for each data set were labour-intensive, but data collections themselves took several hours and allowed some respite from the intensive work, so we were able to operate sometimes with a team of three; the grant provided funding for one PDRA (50%) and one research student at any given time (with two students at times, the two funded studentships covering 6 years in total), and WC has been directly involved in the work on every visit. With the acceleration of the work as noted above, it quickly became essential to have four team members for each visit. This has been achieved by providing support from some other PhD students with relevant interests (working on projects that made use of the Service), from two other Newcastle PDRA staff not directly funded by the Service grant, and from some of the Southampton Service staff. This represents personnel involvement significantly beyond that provided in the grant and has ensured the success of this new component of the project. (It should be noted that a somewhat greater personnel funding, entirely at the more experienced PDRA level and directly involving Southampton staff in SRS visits, has been awarded in the recent grants to continue the Service.)

Not all data sets lead to successful structure determination, particularly for the very challenging samples forwarded to the SRS Service. In a small proportion of cases we have complete diffraction patterns from which we have not yet been able to extract reliable unit cells, space groups and integrated data, but we now have more powerful software tools, so hope has not been lost for these. Some samples prove to be quite different from what users expect, unfortunately sometimes including starting materials, decomposition products and by-products of reactions.

Overall, operation of the Service has been as planned, except for the very much higher productivity than originally predicted. The Service has been described as a victim of its own success.

6. Use of central facilities

The SRS Service, clearly, is totally dependent on the use of the single-crystal diffraction facilities at SRS. When this grant started, this meant station 9.8 and the principal access to it was by tickets awarded with grants; 150 tickets were awarded by EPSRC. Subsequent application to SRS for allocation of beam-time in recognition of these tickets was a necessary six-monthly procedure.

In 2003, as a result of the quinquenniel review of CCLRC, the funding and access mechanisms for SRS and other central facilities were completely changed and tickets were abolished. From that point on, after two years of the grant, application was made direct to CCLRC for beam-time. For this particular grant, this involved a further major (six pages) case for support and application form for outline three-year Programme Mode Access, followed by short applications every six months once this PMA was approved. This work has certainly had thorough peer review!

During these five years there have been a number of serious interruptions of the SRS operation. These have included a couple of planned major shutdowns with extended periods for enhancements of the facility, but also several unplanned failures of the system, each of which has usually cost us a visit of 3 or 4 days of beam-time, but one of which wiped out a substantial period of operation towards the end of the grant. This then required major efforts to catch up on the large backlog of samples (this was successfully achieved, though a significant number of samples must certainly have deteriorated in the meantime while waiting). As a result we have received fewer days of beam-time overall than originally intended. However, our high productivity when the system was operating satisfactorily meant that this was not usually a problem; we have sometimes accepted a reduced beam-time allocation by negotiation with the awarding panel, and at other times we have not asked for compensation time to be awarded to which were entitled, as it has proved unnecessary. The markedly lower number of beam-time days used than originally intended is by no means an indicator of difficulties and failure in the project overall. The SRS is definitely showing its age, as the world's oldest operating dedicated storage ring, but it has still been able to provide us with the means of running what we believe is the most productive and successful synchrotron chemical crystallography service worldwide, even in the face of competition from third-generation storage rings.

A major ingredient in the success of the Service despite these operational problems has certainly been the introduction of new diffractometer and detector systems in 2004 (to replace those we originally installed about 8 years earlier), not only on station 9.8, but also on the redesigned station 16.2, developed as a second 'small-molecule' crystallography facility to relieve the massive oversubscription of 9.8 by user proposals. Some of our more recent beam-time allocations have been on station 16.2, which we estimate to have a lower intensity by a factor of about an order of magnitude, so our overall productivity on these visits has been somewhat lower, but the performance is still adequate for the majority of our samples.

Almost all data sets have been collected routinely at low temperature (usually 120 K) with the standard Cryostream and Cobra nitrogen-based open-flow cooling systems at SRS. On one visit we had the use for a day of a helium-based system and were able to collect data down to about 15 K. This was very useful for the investigation of some magnetic phase transitions in iron and chromium complexes, which occur in the range 20–80 K; this work is described later in the Highlights, Section 11.

We remain the largest user group of these facilities at SRS, and without doubt the most productive and cost-effective, with the need for synchrotron radiation being assured by the screening of samples at Southampton.

7. Research Impact and Benefit to Society

Quite clearly, these measures must be viewed in a somewhat different manner from a normal research grant, where the investigators have complete control of all activities and outputs. For a service, there are two quite separate themes to consider.

The first relates to the research proposals of prospective Service users. These are judged by the MAP, which operates essentially as a sub-panel for the EPSRC Chemistry Programme. Decisions made by the MAP are taken by the Service operators as a directive to support the proposed research to the best of their abilities and the capability of available tools. Bearing in mind the prioritisation requirements, mentioned above, Service staff have approached each sample with the same objective – that is to use every available procedure and skill to achieve a positive result. On this basis, it is not unreasonable to suggest that one measure of the effectiveness of the Service provided is represented by the volume of output and the percentage of successful sample handling outcomes. This is represented in Table 1, as an annual summary based on allocation years (i.e. April to March). Note that Southampton papers (i.e. those papers that include Southampton Service personnel as authors) each contain on average 2.8 structures; this translates to a total of more than 600 contributions to the CSD during the course of the grant. A list of posters and peer-reviewed conference papers made by members of the NCS team and colleagues, in crystallography and e-science meetings, can be found at http://www.ncs.chem.soton.ac.uk/confpres.htm

Table 1. *NCS: Sample submissions and processing, and publications details. 2000/1 data, from the last operating year of the previous grant, are provided for comparison.*

	2000/1	2001/2	2002/3	2003/4	2004/5	2005/6
Submitted	642	1017	801	825	977	1224
Full structure	191	346	287	314	243	249
Data collection only	306	510	371	511	734	975
Fails/withdrawals	145	161	143	151	124	116
Southampton pubs	33	41	33	42	41	38
Newcastle/SRS pubs			1	5	12	17
Data users pubs	32	31	30	38	43	45

In this context, the Research Impact is then measured by the output of publications by the users, which is predominantly in their remit, although the input by Service staff to joint publications when full structure determinations are completed in Southampton or Newcastle is also crucial. Details of the outputs from Southampton are available on the Service web site at http://www.ncs.chem.soton.ac.uk/publications.htm Table 1 includes a numerical summary, along with numbers of publications by data collection-only users which we have been able to identify. Much of the Service work now involves data-collection-only provision, and a large proportion of final outputs in this respect are publications prepared and processed without further involvement by Service staff. We have sometimes found that such publications inadvertently omit reference to the use of the Service, and are difficult for us to track, but a more aggressive approach to the question of feedback from users, particularly in the requirements for acceptance of new allocation applications, is improving this situation. The data in Table 1 represent our best effort so far to accumulate the relevant data in this connection. We are now making modifications to the architecture of our new sample tracking database so that we can smoothly initiate a query to users on the outcome of any data-collection-only result sent to them, also after a specific period, and we hope this will contribute to the assembly of a more comprehensive output of results.

It is a particular pleasure to report that 62 publications are so far known to have resulted from the new SRS Service, with many more currently in press. Of these, nearly half (26) are data-collection-only results. It is of interest that the rate of publications is rapidly growing, since the Service was new in 2001, as shown in Table 1. This is a very healthy and encouraging trend. A full list of publications can be found on our SRS Service web site, at http://www.ncl.ac.uk/xraycry/srs_service.htm

The second theme in this section relates to the efforts made by the Service group to progress the technology which we can make available to the Service users, and thus the whole UK chemical crystallography community. This has been discussed in the previous sections, and we would claim that we have more than met our targets in this area. These successes have offered benefits to the whole UK chemistry and crystallography community, and through them, the users of UK chemistry and crystallography research results nationally and internationally. The failure of some UK laboratories engaged in our kind of work to take up the opportunities offered by our efforts is, unfortunately, outside our control – notwithstanding the vigorous efforts we make to publicise our facilities, as prompted by the EPSRC Chemistry Management. These include annual alerting communications to current and past users, Heads of Chemistry and associated departments, together with posters and presentations at many UK conferences; promotional activities are being significantly enhanced in the current grant period.

The synchrotron component of the Service featured prominently in the SRS annual report for 2005 and has been described as the main topic or referred to as a contributing factor in numerous conference presentations (including, no doubt, many of which we are unaware). Users have expressed great satisfaction with the combined Service operation in annual reports and allocation requests, and particularly in their support for renewed Service funding, which has been secured for the next three years to October 2009 with strong endorsement by the panel set up to consider the application. Dissemination has also been through conferences and other presentations, many of which are not directly reported to us by users, though we often hear of them by other routes. Users have told us that results from the Service have significantly influenced the direction of their research and this includes some international and industrial collaborations and exploitation; again, formal details rarely come back direct to the Service staff. The work of the Service has been publicised by its own staff in presentations and posters at national and international chemistry and crystallography conferences attended by current and prospective users and by specific personal contacts with some departments making little or no use of the Service previously. This has already led to some new user applications. One article in EPSRC's *Newsline* and the contribution to one SRS Annual Report will be followed by further articles in similar publications (e.g. RSC's *Chemistry World*, and *Synchrotron Radiation News*). A major article about the SRS Service is being written for an IUCr journal, to serve as a standard reference. The Service web sites at Southampton and Newcastle are being developed and enhanced to feature information on publications, research highlights, and other reports of success and capability.

8. Further Research or Dissemination Activities

In Section 3 we mentioned our development of a procedure to facilitate dissemination of crystal structure determination results. One of the original prompts for taking this route was the knowledge, both from our own experiences, and those of colleagues in other active chemical crystallography groups, that a high proportion of structure determinations are never formally disseminated.[5,6] In order to address this problem for structures which are fully resolved within the Service operation, we have introduced a policy whereby such results are uploaded to the open access eCrystals archive once a certain period has lapsed – currently 3 years. This is fully described on our Web site at http://www.ncs.chem.soton.ac.uk/pub_pol.htm

At the present time, we are operating two archives. One is a private resource, the "green" archive, visible only inside the Southampton firewall, which is used as a comprehensive laboratory management and data archival system, to which we now routinely upload all completed and validated crystal structure determination outputs. The other ("blue") archive is a demonstrator resource, visible externally at http://www.ecrystals.chem.soton.ac.uk, which we use to demonstrate the architecture of the archive, and its usability. The transfer of an entry in the green archive to the open-access blue archive is a simple operation.

Final discussions are now in train with a number of major publishers to gain approval to use the archive as a means of communicating the data and basic results of a crystal structure determination, leaving the relevant chemical or chemical crystallographic discussion to be reported in associated publications which do not need to contain the many data tables conventionally required. A number of crystallography colleagues, in the UK and abroad, have expressed an interest in mounting a similar facility in their own institutions.

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9. Resources and expenditure

For the most part, expenditure was very much in line with estimates. The main variances at Southampton were under three headings:

a) an overspend on equipment (8%) which was due to hire of an Oxford Diffraction Helijet for a special trial period (£6K), payment for the installation of the Mitsubishi robot (£3.8K) and the charging of computer purchasing costs for all staff (£12.3K), which had originally been assumed a component of the consumables budget; this action was used to balance what would have been a major overspend on the consumables budget due to the significant increase in costs of equipment service and repair, following the merger between Nonius and Bruker AXS;

b) an underspend on travel and subsistence (34%) which were originally calculated at grant submission time using the PDRA/PG "standard sum" approach then in train; MBH and SJC were also able to take travel costs for conferences from generous e-Science grants;

c) an overspend on studentship costs (8%) due to use of some of the surplus travel costs to extending the half funding of Ms S Callear by one year (additional to the one year made available by the move to Glasgow of Mr T Keene.

It is pertinent here to comment on the staffing and related arrangements for the period of the grant at Southampton, summarised in the Report proforma. At the start, Simon Coles, Thomas Gelbrich and Mark Light continued working for the Service, having been in post on the previous grant. After one month of the new grant, Thomas Gelbrich moved to the Comb-e-Chem grant, to develop work on crystallographic data mining, resulting in the program XPac,[7] which is now receiving much attention, and we appointed Dr Peter Horton to the vacancy. Peter had completed his PhD in the Department, with Dr Martin Grossel and had trained extensively with us, developing excellent skills in handling difficult crystals. In 2004, Mark Light was appointed to a full-time Departmental position, as Manager of Diffraction Services, and Thomas Gelbrich returned to work on the Service at the end of the Comb-e-Chem funding. These movements, and different levels of appointment resulted in the availability of some staffing funds, and these were used to support David Hughes for two periods. David had completed a PhD with us, and stayed on as a visitor in the Group, whilst he was looking for a more permanent position. Some of the available funds were also used to support a Southampton MChem placement student, Ms Brenda Farrow, for six months, during which she contributed to our Service data collecting activities, whilst also completing a small project in structural systematics, and Ms Sarah Fisher, one of two vacation students (the other funded by CCDC) who worked on "de-archiving" old, unpublished Service structures from the 1980's and 90's for submission to the CCDC as private communications. Some 350 structures have been released to the public domain via this method. The help of these co-workers has been particularly valuable, since it enabled us to manage staff holidays, with little interruption to Service output.

The funds awarded for the SRS Service have been used essentially as proposed, except that increases in salaries and studentship maintenance payments over the five-year period (in which we have tied studentship maintenance to the EPSRC-recommended levels) have led to a 5.5% greater expenditure on personnel than proposed. This has automatically generated the same small proportion of over-expenditure on overheads. To balance this, consumables and travel have been a little lower than budgeted, and studentship fees were slightly lower, a proportion of these being met from other sources. The consumables costs have been mainly for computing and related equipment and materials (including large amounts of data storage media) used for the Service and the costs of chemicals, minor equipment and other materials for the students' PhD projects. Travel, as proposed, has been for conferences, courses and workshops, and for meetings of the MAP, Service directors and managers.

The entire costs of synchrotron beam-time, including travel to Daresbury for experiments, has been met by EPSRC (through tickets initially awarded for five years and actually used for the first two) and CCLRC (through PMA approval and subsequent six-monthly allocations). Improvements in the equipment at SRS during the grant, particularly the new detectors and the availability of a helium-based cooling device on one visit, have been at no direct cost to the Service grant, though we have benefited enormously from them and were involved in discussions and decisions regarding these improvements.

10. Highlights

A few projects are selected here to illustrate the range of samples studied through access to the NCS, both the Southampton and the new SRS components, and some of their impact in the wider context of UK chemistry research. These projects feature in the majority of publications so far from the SRS Service, showing how successful is the seamless link between the two facilities. Relevant publications from the full list available on the SRS Service web site at http://www.ncl.ac.uk/xraycry/srs_service.htm, are given in brackets.

It is not surprising that the burgeoning area of supramolecular coordination chemistry represents a significant proportion of the work of the Service, since polymeric coordination networks frequently generate only very small crystals and disorder, particularly of counter-ions and solvent, is a common feature of the structures. The major users in this area are in Nottingham (Schöder, Champness, Hubberstey) and Sheffield (Ward), together with some of our own samples from Newcastle. The main ligands are amines, carboxylates, and mixed species, and metals are drawn from main groups, transition series and lanthanides. [2003: 1,3,5; 2004: 2; 2005: 11,12; 2006: 27, 29, 30]

Anion recognition and binding has provided numerous samples from Southampton (Gale). One of the ingredients here is hydrogen bonding, which features in a number of studies, including the investigation of extended hydrogen-bond network motifs (Low, Glidewell *et al.*in Aberdeen and St Andrews). [2004: 7; 2005: 3,14; 2006: 1,4,7,8,9,15,16,23,26]

The structural chemistry of s-block metals has been explored in our own work in Newcastle, together with Mulvey (Strathclyde) as part of a long-standing collaboration exploring new key reaction intermediates in metallation reactions, and with Izod (Newcastle) alongside related work in unusual coordination complexes of lanthanides and group 14 elements, for which the s-block complexes are starting materials. [2003: 2; 2005: 7; 2006: 5,10,17,18,28]

A series of closely related high-symmetry chromium and iron jarosite samples from UCL (Wills) have been studied at room temperature and at temperatures around 85 K to investigate subtle structural changes associated with magnetic properties. For some of these samples, where magnetic phase transitions seem to occur at lower temperatures, we have been able to collect data in the range 15–65 K. The large body of data obtained is currently being processed and the results interpreted, but there are certainly some important changes in orientation of coordination octahedra. [No publications yet]

Polynucleating ligands have been exploited in the creation of approximately planar grids of metal ions (Matthews and others, Nottingham Trent); these contain as many as 20 metal ions, and common grid patterns are 2×2 and 4×4. Work continues on some of these structures, as they display a very high degree of disorder, but the structure of a circular array with one of the ligands has already been published. [2004: 3]

Organometallic chemistry, with particular reference to catalysis, has been a common theme of samples from East Anglia (Lancaster), Cardiff (Aldridge), Bangor (Butler) and Newcastle (Doherty and Knight). [2005: 1,4; 2006: 13,14,25]

11. Conclusions

It only remains for the authors to acknowledge the unstinting support of all the Service staff, and their commitment both to the Service and its users, and the developments and major new extensions we have been able to make to its operation in these fruitful five years.

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