Chemistry Programme Instrumentation - National Mass Spectrometry Service Centre

EPSRC research grant report on GR/M13992 *"To Continue the Special Research Grant to the EPSRC National Mass Spectrometry Centre until April 2002"*

PREFACE

This grant financed a National Service Centre and not a standard research project. This support document thus particularly covers aspects not included in the IGR form. As a national centre, the role of the National Mass Spectrometry Service Centre (NMSSC) at Swansea is to support high quality research rather than to do its own, and the criteria against which its work should be measured are not those normally used to judge research, but rather those set by EPSRC for national services.

INTRODUCTION

This grant provided funds for continuation of the EPSRC National Mass Spectrometry Centre at Swansea. Our major objective was to underpin high-quality chemical research in the UK by provision of state-of-the-art mass spectrometry for EPSRC supported research groups. The success of the service ensured that UK chemists could be assisted to compete at international level without disproportionate costs for analysis. The facility is particularly important to synthetic chemists for the full characterisation of compounds and compares favourably with similar centres internationally [1].

Key advances made during the funding period were:

- introduction of a high-volume routine ESI† and APCI accurate mass-measurement service
- introduction of a Summer School and Users' Forum
- significant increase in the number of samples run
- significant improvement in turnaround statistics

The work of the Centre has been carefully monitored through the return of Annual Reports to EPSRC (copies are attached in Appendix 1), which include numerous statistical performance indicators.

The recent successful grant renewal (GR/R70088/01), for the period 2002 to 2007, (£2,107,399) has guaranteed the continuation of an EPSRC National Mass Spectrometry Service Centre (NMSSC) at Swansea. Peer review underpins the competitiveness of the UK science base; the renewal of the NMSSC was made in open competition, thereby underlining the chemistry community's confidence that an excellent service is provided at reasonable cost by the Centre. Recent reviews of National Service facilities emphasize the need for such an expert mass spectrometry service.

Demand for the MS service has almost doubled from 14,826 analyses in 1997-8 to 28,423 in 2001-2. (Appendix 2). In this time productivity has struggled to keep pace but also increased significantly from 10,636 analyses in 1997-8 to 17,771 in 2000-1. The NMSSC has served the mass spectrometry requirements of more than 230 research groups supporting the work of more than 800 research personnel on over 270 projects each year. A list of the major service users and their usage of the service may be seen in Appendix 3. More than 70,000 analyses from EPSRC supported research groups have been done during this period, with more than 1400 papers published in which the Centre's analysis had been used and acknowledged. (A small selection of these emanating from the major service users is given on the IGR form). Staffing levels have grown only modestly during this period, increasing by half of one full-time technician, while the number of instruments has remained constant.

† See page 5 for a glossary of terms and common abbreviations

MAJOR ACHIEVEMENTS AND EVOLUTION OF THE SERVICE CENTRE

Major achievements were:

- keeping within budgetary targets, with close matching of predicted and actual expenditure in all categories;
- significant increase in the number of samples run, in both low resolution and high-resolution mode;
- improved sample turnaround time;
- improved accurate mass service through introduction of accurate mass ESI and APcI services;
- reduction of an inefficient accurate mass FAB technique by substitution with more efficient methods;
- continuation of accurate mass service during instrument changeover;
- introduction of a Summer School and Users' Forum in September 1999 (repeated in July 2001);
- continued integration of the management advisory panel (MAP) in the administration of the Centre.

Reports for 1st October to 30th September periods for each year of the grant were sent to the EPSRC (Appendix 1). It should also be noted that the successful grant application "*Continuation of the EPSRC National Mass spectrometry Service Centre at Swansea to the 31st of March 2007*" has assured the Centre will continue to provide a high quality MS service to the UK chemistry research community, as well as provide new facilities, such as MALDI.

During the grant period Professor D.E. Games succeeded Dr J.A. Ballantine as Director, Mrs B.K. Stein was promoted to Service Manager, Dr A.P. Hunter replaced Dr C.J. Reid as Research Officer and Mr G. Llewellyn joined as a part-time and eventually full-time technician. Since its start the Centre has grown and thrived despite significant changes in both personnel and equipment. No initial staff or equipment presently remains in the Centre and, during the last grant period, several new services were brought seamlessly on-line. In 2001, Prof. A.G. Brenton joined the Centre management team, with the approval of the MAP, to shadow the Director's position to which he will succeed when Professor Games retires at the end of 2002.

The other major event was the introduction of the ThermoFinnigan MAT900-XLT high-resolution mass spectrometer to replace the obsolete ZAB-E for accurate mass measurement. The MAT900 continued to provide the EI and CI services performed by the ZAB, but improved on them by addition of the intrinsically more efficient API techniques. Accurate mass FAB was initially continued on the Autospec mass spectrometer, but during the grant period this work was also taken over by the MAT900 when the aging Autospec could no longer achieve sufficient mass stability, and the MAT900 method was found to be faster.

RESEARCH QUALITY

Every effort has been made to provide a high calibre service. Additional value was provided to service users by commentary on results where these were ambiguous, and analysing samples by alternative techniques, if initial analysis failed. A flexible application of quotas is applied to promote a customer- orientated rather than quota-based service.

The high quality of the work carried out by the Centre is reflected in the very positive feedback from users of the service (Appendix 4). Additionally, the Centre has developed a reputation for achieving good mass spectral results where other laboratories have failed.

The quality of research underpinned by the Centre is assured by the regulation and allocation of quotas in proportion to the level of EPSRC and other research council funding already held by the projects seeking support (Appendix 5).

Manual processing of data is made for all analyses to ensure good quality output.

RESEARCH PLANNING AND PRACTICE

A variety of statistics have been taken over the grant period (and many years before this) to give a meaningful indication of the performance of the Centre, and the outcome of these measurements vouch for good management and practice. Careful planning allowed the maintenance of a good accurate mass service through instrument changeover when the ZAB was replaced by the MAT900, and new techniques have been developed and new projects successfully undertaken whilst maintaining an excellent quality of service. Examples of this include the introduction of the summer schools and development of new accurate mass methods simultaneously to increasing throughput and improving turnaround time.

Since 1998 more flexible staffing arrangements have been deployed in the laboratory, which have allowed better cover during vacations and illness and thus reduced service fluctuations. Staff attitude has been positive throughout the many changes over the past four years, promoting high standards and creativity in their work, as well as a responsive attitude to each other and their customers' queries and problems.

The actual expenditure on this grant matched the predicted figures very well, with all categories of expenditure within a few percent of their expected values; the project was within budget throughout its life.

POTENTIAL SCIENTIFIC IMPACT

More than the requisite 80% of service time was dedicated to EPSRC-approved projects from more than 50 UK institutions (Appendix 5). More than 60% of this time was used by projects directly funded by EPSRC grants, and more than 2.4% by projects funded by other research councils (Appendix 6). The quality of supported work is thus amongst the top rated in the UK with concomitant major scientific impact and economic benefit. Coincidentally, more than 50% of time in 2001 was spent on work for researchers from institutions with RAE rating 4 and above (using the 1996 RAE; this percentage is 85% if 2001 RAE ratings are applied, with more than 52% of work from institutions with RAE 5 and 5*).

OUTPUT OF RESEARCH STAFF

Rigorous application of performance indicators over the grant period (and preceding years) has allowed a meaningful measure of staff output, which can be seen to have increased dramatically over the grant period. Good examples of this are the increased throughput and improved turnaround, which can be observed in Appendices 3 and 7, respectively. From these data, it can be seen that throughput increased by 2/3 in 3 years, with 10,636 analyses completed in 1997-8, and 17,771 carried out in 2000-1. This incredible increase in volume of work was accompanied by an improvement in turnaround rates, with 90% of samples completed within 7 working days, and more than 50% of results returned within 3 working days in 2000-1, as opposed to this taking 10 and 4 working days, respectively, at the start of the grant. Sample turnaround and throughput both peaked in 2000-1. 2001-2 was not as efficient due to the absence of a key staff member (Dr Hunter) on maternity leave for 6 months coinciding with the additional administrative load on the service manager in the preparation of the recent grant application. A key objective of the current management team is to bring the service quickly back to its optimum performance; this will be realised once the new instrumentation has been installed and bedded in.

Apart from this rapid throughput of more routine samples, the staff also took time to comment on ambiguous results, respond to customer queries by telephone, post or email and repeat analysis of samples where submitted mass spectral data (obtained in users home laboratory) is poor. They also collaborated with “customers” on projects requiring attention beyond the scope of the standard

service. Examples of the latter are listed in Appendix 8 and led to the publications by Centre staff listed in the publications list.

For most electrospray analyses, data was obtained using both polarities with soft and hard ionisation (by varying the cone voltage) to give researchers more comprehensive information about their sample. Although this may seem excessive diligence, this method has been found to actually increase efficiency by reducing the number of repeat analyses required if initial attempts fail to yield a result, as many conditions have already been applied on the first attempt.

COMMUNICATION OF RESEARCH OUTPUTS

Data obtained is returned to customers as rapidly as possible, with 50% of samples returned within 3 working days in 2000-1 (Appendix 7). As part of an expert specialised service, mass spectral results are processed by qualified and experienced analysts rather than automated processes. This ensures that data is clearly displayed, and that less intense but significant ions are clearly visible and labelled. It also allows productive use of regional graphical expansions and theoretical isotope pattern matching to allow clear comparison of the expected data with observed results.

On average, more than 350 publications have appeared in the Literature each year using data obtained by the NMSSC, many of which are in first class journals. (A small sample of these publications is listed on the IGR form, together with patents and Centre publications).

POTENTIAL BENEFITS TO SOCIETY

Because of the high calibre and wide variety of research supported by the NMSSC (Appendix 9), the potential benefits to society of the Centre's work is very far reaching indeed.

As well as supporting highly rated projects, the Centre also provides time for young researchers and those with minimal local facilities. Additionally the Centre assists departments whose local facilities experience temporary failure or difficulty, so that their research disruption is minimised. This included Exeter and Leeds in 2000 and Nottingham and Warwick in 2001.

The Centre provides a free consultancy for universities seeking expert advice on mass spectrometry matters. These include instrument problems, instrument purchasing, analytical techniques and provision of reference tables or materials. In a more formal manner, the Centre also educates researchers, postgraduate students and technical personal through the Summer Schools and other training programs. Summer School attendance averaged 40 PhD students, researchers and technical personnel on both occasions, while one-to-one teaching has been achieved with visits to the Centre from a Cambridge PhD student (Ze-Yi Lim) for a few days in 2000, and a technician from Cardiff (Rob Jenkins) for 2 weeks in 2001. Visits by students requiring special analyses also fell into an educational role, as did telephone time spent assisting researchers and technical staff who requested advice from time to time on a variety of topics. Experience suggests this facility could be expanded with much benefit to the technical expertise within the community.

COST EFFECTIVENESS

The national centres offer an economy of scale and centralisation of resources and expertise that give them tremendous advantage over isolated facilities. The mass spectrometry service is an excellent example of this. Throughput is relatively rapid because instruments and analysts can be dedicated to a small range of related tasks; fast turnaround is maintained even through staff vacations and illness by provision of a flexible staffing backup system; instrument downtime is minimised by limiting switch-over operations and having experienced staff. (Downtime was logged at <5% for all instruments except those reaching the end of their life, *viz*. the ZAB was down 50% or the time for the last 3 months before its replacement in 1998, and the Autospec downtime has been approximately 10% since 1999.)

The NMSSC makes a conscious effort to continuously improve efficiency and thus increase cost effectiveness. Thus, for example, the development of a method of accurate mass measurement in API has replaced the intrinsically slower probe techniques, and, in particular, replacement of LSIMS ("FAB") accurate mass by API has significantly decreased the number of repeat analyses required, thus increasing efficiency more than 4-fold! (typically 20 analyses per day by LSIMS against >80 per day by ESI).

The average cost per analysis in the Centre of <£25 compares favourably with laboratories worldwide.

FUTURE DEVELOPMENTS

Future developments planned for the NMSSC are detailed in the recent grant application that secured continued funding for the next 5 years. These include the institution of a MALDI service; further exploration and exploitation of TOF with both MALDI and API; further development of the training and educational functions of the service; continuation of a "FAB" service (which is becoming less available within local department services but which is still a necessity for many, in particular inorganic chemists); development of a WEB based interface for easier and faster exchange of sample information and results with customers. It is anticipated that these will contribute to improving both the quality and cost-effectiveness of the service so that developments over the next grant term may emulate the achievements of this one.

ANY OTHER ASPECTS

There are other several aspects of our work we can cite. For example, there has been much interest shown by other MS laboratories in some of our methods and standard operating procedures developed such as API accurate mass measurement. Collaboration with the Laboratory of the Government Chemist (LGC) on accurate mass methodology has been on going. In 2001 an exchange student (Ms Stephanie Bennett, an American student) worked in the Centre for 100 hours and has subsequently proceeded to do research in MS.

REFERENCES

[1] K.V. Wood and D.L. Hachey, *Journal of Mass Spectrom*., **35** (2000) 1157-1164.
"Organization, management and operation of contemporary academic mass spectrometry service facilities"

GLOSSARY OF TERMS and COMMON ABBREVIATIONS

Terms used in text

APcI	Atmospheric Pressure Chemical Ionisation
API	Atmospheric Pressure Ionisation (ApCI, ESI)
ESI	Electrospray Ionisation
FAB	"Fast-atom Bombardment" (actually generally LSIMS)
GC-MS	Gas Chromatography Coupled to Mass Spectrometry
LC-MS	Liquid Chromatography Coupled to Mass Spectrometry
LSIMS	Liquid Secondary Ion Mass Spectrometry
MALDI	Matrix-assisted Laser Desorption/Ionisation
MAP	Management Advisory Panel (of the NMSSC)
MSRU	Mass Spectrometry Research Unit (in the Chemistry Department at UWS)
NMSSC	National Mass Spectrometry Service Centre (at Swansea)
RAE	Research Assessment Exercise
TOF	Time-of-flight Analyser
UWS	University of Wales Swansea

No. **List of appendices**