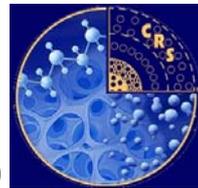
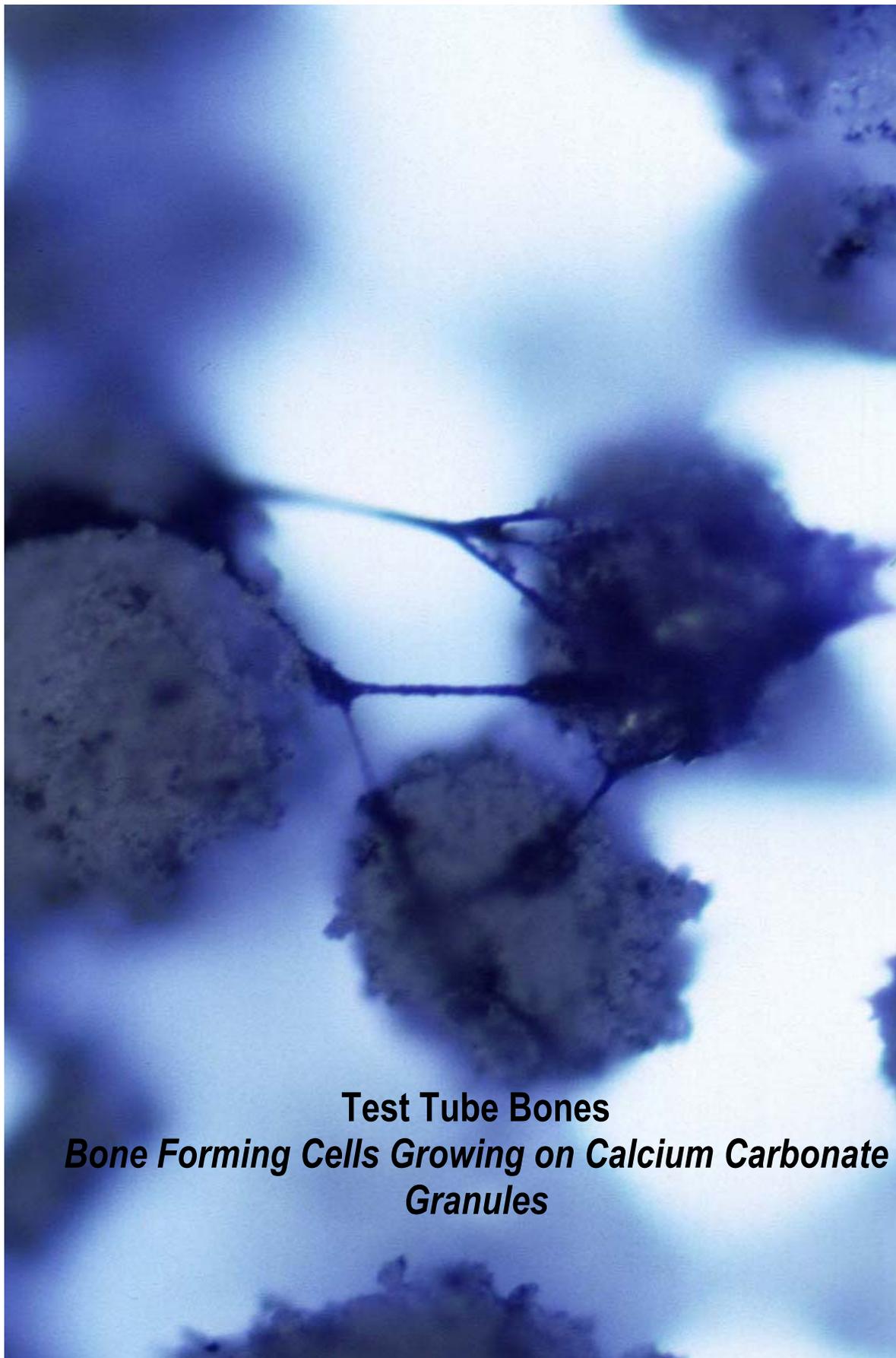


# THE UK·I·CRS NEWSLETTER

THE CONTROLLED RELEASE SOCIETY UNITED KINGDOM & IRELAND



**Volume 7 September 2001**



**Test Tube Bones**  
***Bone Forming Cells Growing on Calcium Carbonate Granules***

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Cover photograph courtesy of the BBSRC. Tissue engineering at the University of Liverpool has resulted in human bone-forming cells (stained with methylene blue) growing on granules of calcium phosphate and spanning the gaps between granules as shown above, Supplied by J A Hunt and J Gallagher, University of Liverpool and part of the Tissue Engineering Interdisciplinary Research Collaboration with the University of Manchester.

## From the Editors



Ijeoma F. Uchegbu



Neena Washington

Welcome to Volume 7 of our annual newsletter. This volume is packed with items we hope that you will enjoy. Dr Anthony D'Emmanuelle has stepped down as our chairman after seven rather hectic years on the Committee. A huge thank you goes to Tony for all his hard work. Although Tony will not be an easy act to follow, we have not been left rudderless and have a new chairman, Professor Duncan Craig of Queen's University Belfast. We are sure that Duncan will do a great job. Duncan gives his maiden Chairman's address on page 4 of this newsletter.

We have had a wonderful year and hosted yet another of our conferences in London in January this year just after Hogmanay. It was the best attended meeting we have ever had and the work on offer was truly world class. You can read all about this meeting on page 21 and more importantly read about and register for UKICRS 2002 on pages 24 and 25. Some of us were even luckier this year than most and were able to spend a few sun-filled days in San Diego under the pretext that we were attending the 28<sup>th</sup> International Symposium on Controlled Release of Bioactive Materials! A brief snapshot of this event is presented on page 19.

If you have ever wondered why you never seem to get research council grants, Beverly Parsons of the BBSRC answers all the questions you ever had but were very afraid to ask on page 9. Lets hope that after reading this interview you are convinced that your research is just what the Engineering and Biological Systems Committee needs to be funding. Thinking of saying goodbye to research council competitions and becoming rich instead? Then you must read our article on Page 7 "Cashing in on a Brilliant Idea".

The UKICRS as the name suggests is not just a UK organisation and our members in Ireland are very active controlled release researchers as David Brayden, Catriona O'Driscoll and Duncan Craig tell us on Page 5.

The glassy state? It all becomes clear on page 16!

This is your newsletter and we do sincerely hope that you read and more importantly enjoy every single article. If there are particular articles that you would like to see, email us with your suggestions. We promise not to make you write these articles!!

Till next year  
Goodbye.

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## The UKICRS in 2001 and Beyond – Chairman’s Address



Professor Duncan Q.M. Craig

The UKICRS is now established as a vibrant and imaginative organisation that has played an important role in promoting and disseminating controlled release and related technologies within the UK and Ireland. This has been achieved through a series of one day meetings, the highly successful link with the Royal Pharmaceutical Society Conference, the establishment of a comprehensive website and the publication of our newsletter. It is the full intention of the current committee to continue with these activities and indeed to build on them in the future. However, in addition we recognize the need to adapt to changes in circumstances, both in terms of the technologies available and also the organisational environment in which we find ourselves. In terms of the latter, there are a number of issues that it is perhaps useful to highlight that may impact on our activities. In the first instance, the 30<sup>th</sup> International Symposium of the Controlled Release Society annual (2003) will be held in Glasgow, organised by Professor Ruth Duncan and Professor Clive Wilson. It is the intention of all involved, emphatically including the UKICRS, to make this a highly successful meeting to maintain and hopefully enhance the high standards set by this year's outstanding meeting in San Diego. We look

forward to offering the organisers our wholehearted support over the coming two years to this effect. Furthermore, the relationship between the parent organisation and the chapters is being re-examined and clarified, to the clear benefit of our members, to whom it is hoped that we will be able to offer a very attractive package in the near future. On a more local basis, we fully intend to maintain our good relationship with the recently established Academy of Pharmaceutical Sciences and wish them every success in their endeavours.

One of the principle strengths of the UKICRS is, to my mind, the fact that this is a non-profit organisation that exists simply to serve the pharmaceutical community by representing and promoting controlled release technologies. On this basis the organisation has always been run on the basis of the goodwill of the organising committee and the various speakers who have given up their time to provide stimulating cutting-edge presentations at our various meetings. It is perhaps therefore appropriate for me to end by thanking all those who have contributed to the successful running of the UKICRS, particularly the committee members, the speakers, our various sponsors and of course the parent organisation who have made clear their support for our activities. We fully intend to maintain our high level of activity in the future and look forward to seeing you at our forthcoming meetings.

Professor Duncan Q.M. Craig  
 Chair UKICRS, The School of Pharmacy,  
 Queen's University of Belfast.

## UKICRS Committee Members

Dr David Brayden – Veterinary School,  
University College, Dublin

Dr Julie Cahill – AstraZeneca, UK

Professor Duncan Q.M. Craig – Queen's  
University, Belfast (Chairman)

Professor Martin Davies – University of  
Nottingham

Dr Jayne Lawrence – King's College,  
University of London

Dr Karen Lewis – GlaxoSmithKline, UK

Dr Catriona O'Driscoll - Trinity College, Dublin

Dr Rupri Pannu - AstraZeneca, UK (Secretary)

Dr Ali Rajabi-Siahboomi – Colorcon Ltd, UK  
(Treasurer)

Dr Snjezana Stolnik Trenkic – University of  
Nottingham

Dr Ijeoma F. Uchegbu – University of  
Strathclyde

Dr Neena Washington – AstraZeneca, UK

Professor Clive Wilson – University of  
Strathclyde

Dr Jane Worlock – JAGO Pharma AG

## The Development of the Controlled Release Society in Ireland

The CRS has had official links in Ireland dating from 1995 when a group of Irish scientists organised the successful CRS Ireland Symposium on Oral Peptide Delivery in Trinity College, Dublin. In fact, "CRS Ireland" was a bit of a misnomer then since there was no such organisation and it had no members ! It was felt however that the name might convey to prospective attendees that we were an experienced respected organisation that would not run off with their registration fees.

At that time those working in drug delivery were largely limited to researchers in Elan Biotechnology Research in Trinity College Dublin and those in Trinity College Dublin's School of Pharmacy. Trinity and Queen's University Belfast have had strong links over the years and a joint research seminar is organised every year between the two Schools of Pharmacy. At the CRS Ireland conference a number of new pharmaceutical contacts between the two islands emerged as a consequence of the influx of attendees from the UK. Following on from that as we had hoped, the then Chairman of UKCRS, Professor Clive Wilson, hit upon the idea of a merger between the UK CRS and CRS

Ireland. Clive treaded warily, no doubt weighed down by a strange combination of historical guilt about the Empire and a desire for the merger not to be seen as a hostile take-over. Since there was no actual CRS Ireland, he need not have worried himself unduly, but it was pleasant to see him grappling with his conscience.

In 1997, UKICRS was born and there has been a significant contribution from Ireland to date. Aside from the UKICRS Symposium on vaccine delivery held again at Trinity College Dublin in 2000, at least two committee members from Ireland have been on the committee at one time. In 2000, our current Chair of UKICRS, Professor Duncan Craig, was appointed to the School of Pharmacy at Queen's University Belfast, so we now have three members from Ireland contributing to the committee. Initial plans are being made to host the annual meeting for the first time in Belfast in 2003. At most of the annual meetings there has also been a senior drug delivery speaker from Ireland and this is a trend that we hope to continue.

Improving membership in Ireland continues to be a difficult process. There are about ten

members of the CRS from Elan and a smaller number from the School of Pharmacy at Trinity. Membership in Northern Ireland is fairly limited, but will hopefully increase as Duncan Craig gets established at Queen's University. However, increased membership can soon be expected in the Republic as one, or possibly two, new Schools of Pharmacy will be approved in the near future. While the location of the new School(s) has yet to be finalised potential candidates include the Royal College of Surgeons in Dublin and the University College Cork. In all probability, some of the staff likely to be appointed will have controlled release and drug delivery research interests, so this will represent an opportunity for UKICRS to expand in Ireland further. Another opportunity will be at University College Dublin's (UCD) Veterinary School. In 2001 this school is moving to a multi-million pound premises on the main UCD campus and is currently hiring research-oriented academic staff for a number of departments. This will be an opportunity for get new veterinary academic staff interested in controlled release research since CRS is the one society that caters well for these needs.

On the industrial side, Elan continues to expand its drug delivery research in Ireland and will be maintaining its links with Trinity and other colleges. In 2003 Wyeth (American Home Products) will be opening a major plant for 3000 staff in Dublin to carry out research

and to produce recombinant biotech products. It is not unlikely that staff will want to contribute to drug delivery developments such as those highlighted by this society. In Northern Ireland, Galen Pharmaceuticals is becoming a major player in drug delivery of female healthcare products and is building on its collaborations with Universities.

Over the coming years the expanding economies in Ireland, both North and South, should allow for increases in academic and industrial research though a combination of government and private funding. Recently, the Irish Government has appointed new funding bodies for academic research and priorities have been biotechnology research, the re-equipping of academic labs, and the active recruiting of internationally recognised staff from abroad. One of the growth areas of funded research will be controlled release for pharmaceuticals. Against that background, further expansion of the UKICRS in Ireland will inevitably result if we continue to make the effort. Finally, while science should always be apolitical, an organisation such as UKICRS has the power to foster scientific collaborations between individuals, groups and nations and therefore has an additional positive role to play in the ongoing development of the relationship between Britain and Ireland.

David Brayden, Catriona O'Driscoll and Duncan Craig

## Cashing in on a Brilliant Idea ....



Peter York, Co-Founder Bradford Particle Design now a wholly owned subsidiary of Inhale Therapeutics, USA.



Ian Wilding, Founder of Pharmaceutical Profiles

...well meet the people who did. What do you do when you discover that the work in your laboratory could improve healthcare and possibly improve your own financial circumstances? Well if you are Peter York, Ian Wilding, Gregory Gregoriadis or Sandy Allan you rush out, register a company and work really hard on your company product. The aforementioned scientists are selling technology and/ or expertise developed in British laboratories (Strathclyde, Nottingham, Bradford and London) to the rest of the world, thus demonstrating that despite the unfavourable funding climate for science in UK plc, new technological initiatives with direct application to pharmacy are being realised.

York founder of Bradford Particle Design (bpd) in 1995 is arguably the most successful so far and his company, which exploits supercritical fluid technology for the production of pharmaceutical particles, was recently sold to Inhale, USA for a staggering \$200m! York who also works as a Professor at Bradford University's School of Pharmacy says that it all began as a "blue sky industrially funded PhD research programme". The University of Bradford also benefited financially from the sale of Bradford Particle Design since it was a co-founder of the company.

Wilding whose company Pharmaceutical Profiles is not necessarily being developed for sale to a larger rival as "private sale is only one potential strategy" utilises medical imaging technology to evaluate drug delivery systems in man. Pharmaceutical Profiles was established in 1990 in response to the "impending introduction of more stringent quality standards" in clinical research, coupled with a recognition that an academic home was limiting commercialisation of the Company services.

Gregoriadis having worked as a liposomologist for over 30 years and amassed a mountain of intellectual property in this area decided only in 1997 to attempt



Gregory Gregoriadis, founder of Lipoxen

commercialisation and subsequently founded Lipoxen after negotiating the assignment of “two key patents”. The acquisition of rights over Gregoriadis’ own inventions represented a serious financial outlay for the embryonic Lipoxen. Lipoxen aims to launch a product based on its core DNA vaccine (Lipodine) or peptide and protein delivery (PolyXen) technology in about 2006.

Allan’s Propharma undertakes formulation of clinical trial batches and is the baby of the pack having only started to trade in February 2000. However major international contracts have been secured by Propharma already. Allan admits that on being approached to carry through the commercialisation of what started out as a University department in 1990, he felt the need to speak to “a number of contacts within the industry in order to confirm that the basis of the company made commercial sense”. It obviously did. Allan did not find the transition easy and believes that

Propharma suffered from a lack of support from its parent university in the early days. In Allan’s opinion a support structure is needed for university spin out companies. It seems that it may become necessary to set up a networking/ support organisation for University spin out company executives.

The transition from staid academia to heady commerce was never going to be easy but all scientists talk of the fascinating ride and the “roller coaster” metaphor was employed by Wilding to describe the experience. These movers are all extremely satisfied with an opportunity to make a real difference in the market place and in the lives of patients. The hardest thing about entry to the corporate world for Gregoriadis was making the non-scientist executives conversant with the technology being sold. Gregoriadis says that “I try to make sure that executives understand the significance of scientific input and that scientists are kept informed (of company developments)” thus bridging the gap between the suits and the white coats. Wilding complains that finding space to expand proved a bit of a headache and this hiccup “slowed down growth at a vital stage”. For York the most significant hurdle is identified as the fact that pharmaceutical clients often take up too much valuable time in coming to a decision. “Conservatism” in the pharmaceutical industry is also cited by York as a stumbling block in the quest for growth by pharmaceutical start-ups.

Luckily staff recruitment appears to be less of a problem and all four company executives state that existing scientific staff working on the projects were simply transferred to the new employer – the pharmaceutical start up. To the uninitiated securing finance would appear to be a particularly difficult step but not so for Bradford Particle Design who moved from a PhD studentship to profit instantly thanks to clever negotiations and sound business practice. Lipoxen also found it fairly easy to raise the initial start up costs. How much is required to get your idea from the laboratory to your own headed paper?

Well it appears that anything from £300,000 to £2,000,000 will do the initial trick, with the most expensive initial item being salary costs. Good people are indeed expensive although not necessarily difficult to find. All scientists say it is vital to research the market and all the companies mentioned above did this thoroughly and are now enjoying growth commensurate to their size. Pharmaceutical Profiles, with the launch of its intelligent capsule device Enterion has enjoyed a phenomenal 80% growth over the last year for example. In the early days the University premises are used to nurture the growth of university spin outs before expansion sees the transition to purpose built premises such as Bradford Particle Design's 15,000sq ft premises in Listerhills Science Park or Pharmaceutical Profiles 20,000sq ft premises on Ruddington Fields Business Park. At this relocation stage a major funding boost is required to allow state of the art equipment to be installed. Access to this stage of funding is sometimes difficult and financing is best left to expert negotiators at this point.

So you are working in your lab late one night and suddenly are struck by a clever idea, are surprised your hypothesis turned out to be right, feel a simple hunger for the corporate world or better still experience all three, what should you do next? First of all secure your intellectual property rights – absolutely essential, team up with a good entrepreneur (you may be hot shot scientist but the chance that you will have negligible negotiating skills are high), secure finance from the private sector, university start up finance schemes or an industrial partner. Be prepared to give up some equity at this stage. Both York and Wilding maintain that it is important to talk to professional business types. Allan suggests looking stateside, California to be exact for start up funds. There are worse places to do deals in is all I can say.

Ijeoma Uchegbu talked to Peter York, Ian Wilding, Gregory Gregoriadis and Sandy Allan

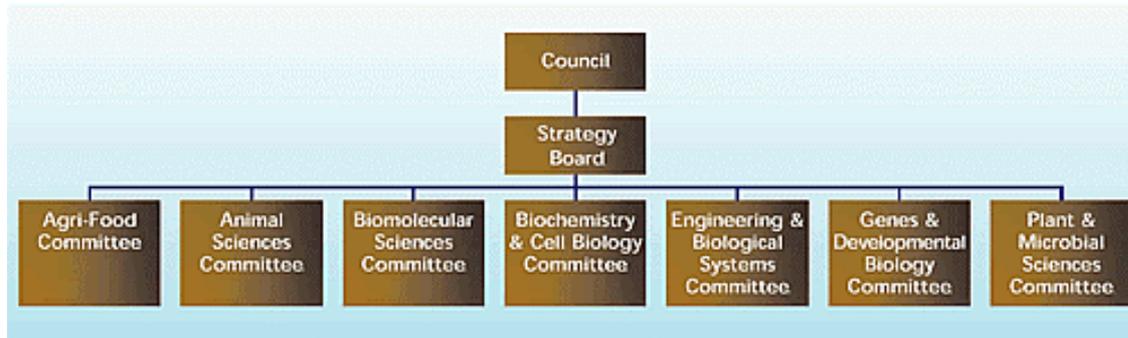
## BBSRC Research Funding

The competition for research funds has never been quite so keen as it is today. One of the avenues for funding work conducted by members of UKICRS is via the Biotechnology and Biological Sciences Research Council's Engineering and Biological Systems Committee. Here Dr Beverley Parsons, one of the programme managers of the Engineering and Biological Systems Committee tells you all the things you need to know about research priorities, the peer review process and of course the award of those precious research grants.

The United Kingdom and Ireland Controlled Release Society represents the interests of scientists working in the area of the controlled delivery of bioactive materials. In its broadest sense these scientists work in areas concerned with the delivery of drugs, agricultural compounds, reactants in industrial

processes; in the area of tissue engineering and in any scientific area which seeks to control endogenous physiological/ biochemical processes. How might the funding priorities of the Engineering and Biological Systems Committee be relevant to their work?

## 6 BBSRC Peer Review Committee and Board Structure



As you will see from the plan shown of the BBSRC peer review committee and board structure, the Engineering and Biological Systems Committee is one of seven BBSRC Research Committees. EBS supports multidisciplinary and interdisciplinary research, drawing on the skills of biologists, engineers, chemists, mathematicians and physical scientists to further our understanding of biological systems. The scientific remit of the Committee is broad and so to help the scientific and user communities to get a feel for the major areas of research that EBS supports, we have a themed description of our main activities.

The research themes of EBS (which are intended to be illustrative rather than exclusive) are:

engineering for medical applications (this includes biomaterials, drug delivery and tissue engineering), bioscience engineering, biological aspects of nanotechnology, analytical biotechnology, toolkits for functional genomics, theoretical biology, metabolic engineering, biocatalysis and environmental biotechnology.

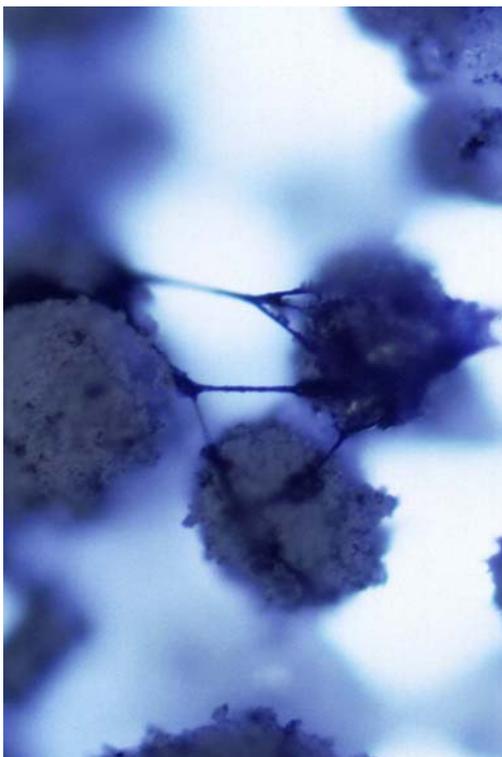
Each year, the Committee highlights priority areas of research; these are areas in which the Committee particularly wishes to encourage applications. Current research priorities for EBS are: drug delivery, tissue engineering, biological aspects of nanotechnology, toolkits for functional

genomics, clean technology and environmental biotechnology.

Training is also an important area for the Committee and each year we allocate approximately 30 studentships in priority areas (this is in addition to the standard quota allocation to University departments). The current call for Committee studentships (closing date 1 November 2001) for take up of applications in 2002/2003 includes the following areas: drug delivery, tissue engineering, nanoscale bioscience, technologies for functional genomics, environmental biotechnology and clean technology (including biocatalysis) and bioinformatics.

### How does the Committee's work benefit UK plc?

Given the breadth of the Committee, it is not surprising that the research which EBS supports underpins a range of industries, including the pharmaceutical, healthcare, bioprocessing and bioremediation industries. The Committee supports high-quality basic, strategic and applied research and offers (through the responsive mode process) a number of activities to foster innovation and promote the exchange of ideas between the science base and industry.



Tissue engineering at the University of Liverpool has resulted in human bone-forming cells (stained with methylene blue) growing on granules of calcium phosphate and spanning the gaps between granules as shown above, Supplied by J A Hunt and J Gallagher, University of Liverpool (and part of the Tissue Engineering Interdisciplinary Research Collaboration with the University of Manchester).

For example, the industrial partnership scheme aims to encourage greater exchange of knowledge between industry and universities. Both cash and in kind contributions from industry qualify for the scheme, although applications with a direct cash contribution from the industrial collaborator of 15% (or more) of the total cost requested are considered more favourably when funding decisions are made. The Committee recognises this threshold as a substantial commitment to the project by the industrial collaborator, representing added value to the Committee whilst also indicating clear strategic relevance to the user community and UK plc.

Industrial support of 50% or more to a project qualifies for LINK. Across the seven BBSRC Committees, there are a number of LINK programmes that are open to applications, including a £30M programme in Applied Genomics which aims to support the development of platform technologies that will enable UK healthcare companies to harness and exploit the output of genome sequencing projects and developments in genomics. Readers are advised to check the website for full details of the current LINK programmes, however, if there are no programmes open to applications in a particular field of interest, then applications will be considered by the Committees through responsive mode as stand-alone LINK projects.

BBSRC also seeks to encourage links between academia and industry through training to enable students to experience different research environments. CASE awards are awarded to academic institutions for doctoral studentships which provide research training in partnership with a cooperating company. Industrial CASE awards are allocated to companies who define the research topic and take the initiative in establishing a link with an eligible academic institution. In both cases, students spend part of their training period working within the company, and are jointly supervised by an academic and a company supervisor.

The BBSRC Business and Innovation Unit will be happy to provide further details of BBSRC activities for promoting knowledge transfer, innovation and exploitation of our research.

The user communities of the research base supported by the EBS Committee are well represented through membership on the EBS Committee and on the associated Network Group (a group of 20 individuals drawn from industry and academia) which further inputs into our policy making process in an industrial context.

**Roughly how many pounds of public sector funding does the EBS committee allocate per annum?**

In the last year, we have allocated approximately £7.3M (45 grants) through responsive mode in EBS, with an additional £0.75M per annum allocated to the Committee by the EPSRC Life Sciences Interface Programme to co-fund applications in bioscience engineering, biological aspects of nanotechnology and theoretical biology.

In addition to responsive mode, the Committee is also responsible for a number of other activities, including collaborations with other Research Councils. In the past year, for example, together with MRC and EPSRC, we have overseen the establishment of an Interdisciplinary Research Collaboration (IRC) in Tissue Engineering and two IRCS in Nanotechnology. The IRCS have an investment of over £9M over 6 years and are collaborations across a range of institutions and departments; BBSRC has contributed approximately £3M to the both the Tissue Engineering and Nanotechnology initiatives.

**What percentage of research proposals received by your committee actually attract private sector funding?**

For the EBS Committee, approximately 10% of grants attract private sector funding, although this excludes applications which are processed through the various LINK programmes. We would like to further encourage applicants to attract industrial support where appropriate.

**What percentage of this funding goes to areas within which members of the UKICRS are active?**

I would estimate that EBS invests approximately 30% of its responsive mode funding into the following areas: biomaterials, drug delivery, tissue engineering, bioscience engineering and biological aspects of nanotechnology. This percentage does not include the IRC investment in Tissue Engineering and Nanotechnology detailed above.

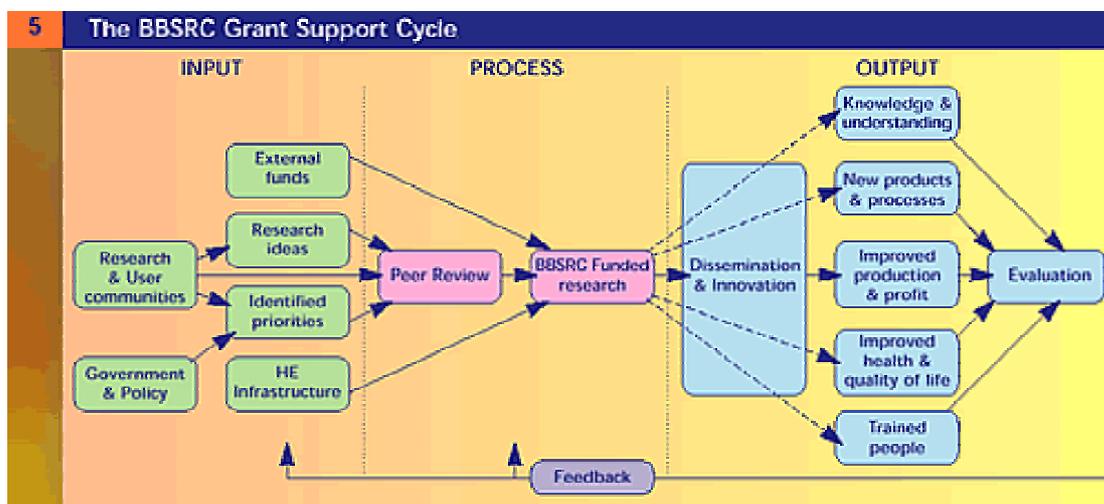
**How are the BBSRC EBS committee's priorities set and how can members of the scientific community and especially UKICRS members become involved in this process.**

Members of the Committee meet three times a year and once with the Network Group (the full membership of the Committee and Network Group are available on the web). These are the times when the Committee meet to discuss policy although there is ongoing work throughout the year by correspondence. Anyone wishing to input into the policy process is welcome to contact the office with their ideas for research priorities. Programme Managers for the Committees are out and about at workshops and meetings which also provides an opportunity for researchers to speak to us and make their views known.

**Is there any way that our members in Ireland may contribute to the EBS committee's work?**

Applicants for BBSRC funding must be resident in the UK and hold an appropriate appointment at an eligible institution for at least the duration of the award (full details of the eligibility criteria are available via the BBSRC website). However, members in Ireland would be very much encouraged to contribute through a collaboration with an eligible institution.

Please talk us through the path that a grant submitted to EBS committee would follow.



Focusing on the middle section of the BBSRC grant support cycle as pictured above. When the office receives your application, the first stage of the peer review process is to assign referees, which is done in consultation with our Committee Members. Applications are then sent out to four referees in the first instance, including to one or more of the referees nominated by the applicant. We aim to obtain a minimum of two sets of referees comments per application (we frequently receive more) and these comments are circulated back to the applicant prior to the meeting to respond to any of the issues raised by the referees.

For the meeting, members of the Committee receive all of the relevant information – the full application, together with referee’s comments and applicant’s responses. Two Committee members are assigned to speak to the application at the meeting.

The following criteria are used to assess applications: (i) scientific excellence (the extent to which the application meets the highest international standards of research in its field); (ii) strategic relevance (the extent to which the proposal meets the priorities of the Committee or the real needs of end users; applications are also given an A-C score for

this factor to highlight the strategic relevance of the application); (iii) prosperity and quality of life; (iv) timeliness and promise; and (v) cost effectiveness.

Following the discussion, a score is agreed on a 0 (low) to 9 (high) scale. When all applications have been scored, they are placed in a rank ordered list. This list is presented to Strategy Board (see above for Board and Committee structure), together with the A-C Strategic Relevance scores, and applications are funded down to a level for which funds are available.

The success rate for Committees currently average around 35-40%. Despite increasing numbers of applications, we have been able to maintain these favourable success rates due to a steady increase in the BBSRC research budget.

**While the EPSRC encourages committee members not to re-review grant proposals already assessed by experts and to rank proposals in accordance with expert opinion, the BBSRC EBS committee mentions that the opinions of expert reviewers are not the only contributory factors taken into account when funding decisions are made. What other criteria**

**are relevant to the funding decisions made by the EBS committee?**

As outlined above, the Committees Members receive the full application, referees' comments and the applicant's responses to the referees' comments. All this information is taken into account by the Committee in reaching its decision, so not only are the expert opinions of referees considered but the expertise around the table at the meeting is fully utilised. The Committees Members views are especially useful in recognising potential conflicts of interest, which may result in either strongly negative or positive assessments, and to balance these to give a fair assessment. Their views are also crucial when there are conflicting reports from the referees.

**Some scientists feel that it might be more helpful and also that it might encourage discussion and collaboration among scientists if reviewers signed their comments and the anonymity was removed. What is your view on this issue?**

An interesting question and one which the Research Councils have considered. My view is that anonymity in peer review enables reviews to be frank in the comments they provide. Without anonymity, reviewers would perhaps be too reserved (and may decline to comment at all). For example, a junior scientist may be very cautious in criticising the work of an eminent Professor which is not an issue with an anonymous system.

Bland comments do not help the Committee. It is vital that the Committee is equipped with as much information as possible to enable them to make a fair judgement on an application and I feel that the current system allows that.

Committees have on occasion suggested a collaboration with a referee, in which case the Office contacts the referee to invite them to make contact with the applicant. It would be possible for the applicant to ask the Office to

see if the referee would be willing to collaborate.

We have a range of mechanisms in place to stimulate collaboration including workshops and other such meetings, which are widely advertised. Last year we undertook a series of joint Research Council visits to 13 UK universities to stimulate collaboration at the interface between the life sciences and the physical sciences and engineering; a report of these visits is available via the web (see <http://www.bbsrc.ac.uk/tools/download/inter/univis.doc>).

**Would it be possible for reviewer's to opt for their identify to be revealed?**

The referees form comprises three parts. Sections 1 (overall assessment – strengths, weaknesses and competitiveness of the proposal) and 2 (specific comments – any specific points which the referee wishes the applicant to address) are communicated to the applicant. Section 3 (knowledge of the applicant/scientific area) is not communicated to the applicant. It is therefore possible for a reviewer to reveal their identity by writing their name in either section 1 or 2.

**How often in each year are funding decisions made and what are the grant proposal submission cut off dates?**

The bulk of BBSRC funding is through "responsive mode" where researchers can apply at any time for funding for research which is within a Committee's remit. Committees meet 3 times a year. The next administrative cut-off dates for research grant applications are 8 October 2001, 11 February 2002 and 10 June 2002, respectively for the February, June and October meetings next year. The closing date for Committee studentships is 1 November 2001.

From time to time, the Office launches initiatives in focused areas of research. Initiatives tend to have fixed closing dates and so readers are advised to check the BBSRC

website for the very latest funding opportunities.

You may be interested to note that BBSRC currently has an initiative in 'Exploiting Genomics' which incorporates the EBS initiative 'From Cell Function to Bioprocessing'. Priority topics for the 'From Cell Function to Bioprocessing' initiative include improving our understanding of aspects of cell function that limit productivity or influence the desired properties of biological products, or that influence downstream processing of biological products and changes in cell function in response to environmental change. The closing date for applications is 26 November 2001 and full details are available on the web.

**What grant writing advice would you give a new lecturer who has just been appointed?**

Firstly, we are only a phone call or e-mail away and are happy to provide advice at all times!

Take advice from helpful and friendly colleagues in your department, who have experience of applying for research grants.

Take a regular check of the BBSRC website to keep abreast of current funding opportunities. You can make this easier by registering with BBSRC News (via the website) which will send a regular email digest of BBSRC news, activities, events, announcements, new initiatives and funding opportunities.

Be aware of the types of grants that are open to you. Many people often assume that three year grants, employing one Research Assistant are the norm. However, we would actively like to encourage a diversity of applications to fit the type of research programme you may wish to carry out, including both shorter term feasibility studies and larger scale applications of multiple RAs

for up to 5 years which might cover several projects at one or more institutions, especially in multidisciplinary areas.

If you are eligible, consider applying for a responsive mode grant through the BBSRC 'New investigator' scheme which is open to new researchers, who are within three years of their first permanent appointment to apply for funding up to a maximum of £180K for 3 years (full details available on the website).

Many of EBS' interests lie at the interface between BBSRC, EPSRC, NERC and MRC and applications can be considered which cross traditional Council boundaries. If you are not clear about which Council to apply to then send in an outline (1-2 sides of A4) and we can give guidance from there.

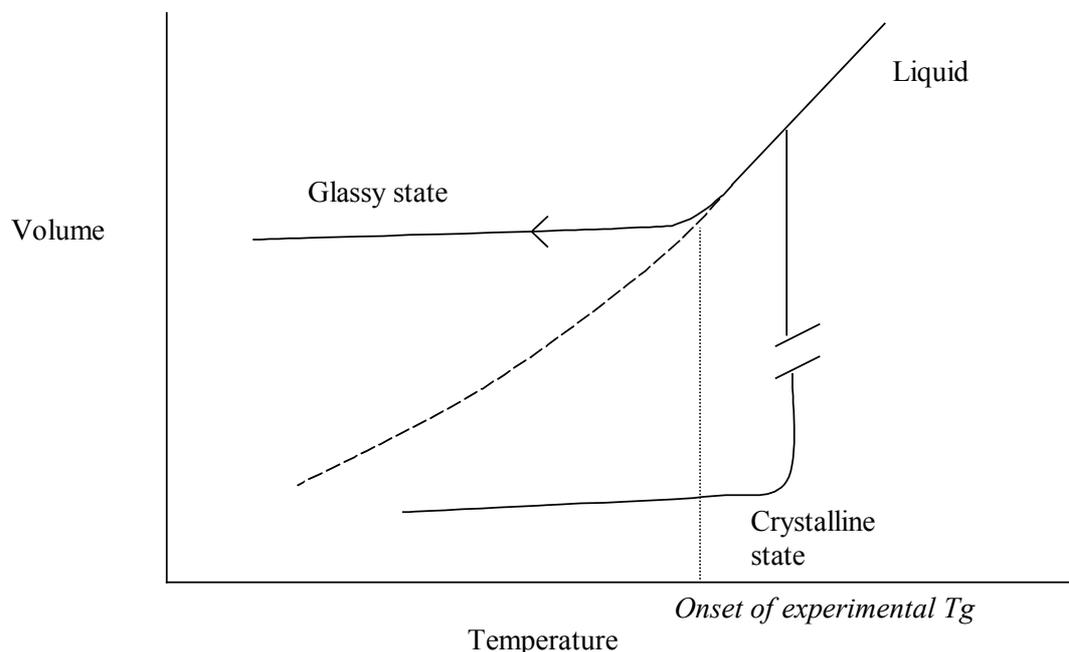
**Are there any particularly significant findings resulting directly from the EBS committee's work which you would like to highlight to our readership?**

There are many significant findings for me to highlight, crossing the breadth of the Committee. Details of all current research funded through the EBS Committee can be found by searching the Oasis database which is available on the web. Oasis contains information on all BBSRC research and can be searched for example, according to principal investigator, institution, or free text searching.

Finally, anyone who feels that BBSRC funding is relevant to their research is invited to take a look at the website at [www.bbsrc.ac.uk](http://www.bbsrc.ac.uk) which contains details of the activities of all seven BBSRC research Committees – and good luck!

Interview by Ijeoma Uchegbu

## A Beginners Guide to the Glassy State



Schematic representation of the Formation of a Glass from the Melt

Over recent years there has been a growing recognition that within the pharmaceutical sciences we need to know more about the glassy state. This recognition has arisen for several reasons. Firstly, many pharmaceutical systems (e.g. freeze dried products, spray dried products, polylactic acid microspheres) are intrinsically amorphous, hence an understanding of their behaviour is essential for effective product development. Secondly, the amorphous state may be generated accidentally by, for example, grinding a drug or excipient, with the resulting material having physical properties and stability behaviour that may be radically different to that expected for a crystalline material. Finally, the amorphous state represents an opportunity for dosage form design strategies. The classic example is the use of amorphous as opposed to crystalline drugs in order to improve dissolution and hence possibly bioavailability. A number of texts are available that have discussed amorphous pharmaceuticals in some depth (e.g. Kerc and Srcic, 1995; Hancock and Zografi, 1997; Craig et al, 1999). The present

article is intended as a very basic introduction to what can become a highly complex subject for those who would like to know more about the subject without going into depth at this stage of their interest.

The simplest means of considering glass formation is to imagine the cooling of a material from the melt (see Figure on the schematic representation of the formation of a glass from a melt above). In particular, we can consider the changes in volume that take place during this cooling process, although other parameters such as enthalpy will show the same trend. In the liquid state, the molecules will be randomly orientated and will therefore undergo random movements through the bulk. If we imagine a relatively slow cooling process in the first instance, the molten liquid will undergo some volume reduction as the molecules become less mobile but, at a specific temperature or narrow range of temperatures, will undergo a dramatic contraction as the material crystallises. Here the constituent molecules become arranged into ordered lattices, hence

both molecular mobility and the volume occupied by each molecule decrease rapidly as the material solidifies. On further cooling some contraction is again apparent but one can see from the slope of the graph below the crystallisation temperature that this effect is much smaller than was seen for the liquid, simply because of the greater conformational rigidity of the molecules in the solid state. If we now reheat this material, the substance will melt at the same temperature and the heating curve will simply superimpose on the cooling profile. This description in itself assumes that no supercooling takes place prior to crystallisation, but for the present purposes is adequate to allow comparison to glassy behaviour.

If we now assume that the material is being cooled rapidly from the melt, we can envisage a situation whereby the molecules do not have sufficient time to form ordered arrays, and instead decrease in mobility as the temperature is lowered but remain randomly orientated. In this case we can see that the material cools below the crystallisation temperature and appears to continue along the same contraction curve that was seen for the liquid. One may expect that, if cooling were sufficiently rapid, then this volume/temperature curve would simply continue and eventually cross the curve corresponding to the solid (i.e. the supercooled liquid would have a lower volume than the solid). In fact this does not happen and instead the volume curve undergoes a discontinuity, the glass transition ( $T_g$ ). At this point, the viscosity of the system undergoes a dramatic increase due to a rapid decrease in molecular mobility; this leads to the well-known effect seen for rubbers whereby below  $T_g$  the material is hard and brittle but above is soft and pliable (bread will show the same effect if placed in the fridge). This is one of the common sources of confusion within the field. The change of a material's macroscopic physical state from pliable to brittle appears to be very similar to the change from a liquid to a solid. In fact this is not the case; the molecules are randomly orientated both

above and below the  $T_g$ , hence there is no change in phase as such. It is in fact more accurate to think of the glass transition as a change between two liquid states. The potential improvements in dissolution behaviour are believed to be associated with the absence of lattice energy found in the crystalline state that would need to be overcome to allow molecular dispersion in a solvent to take place. However, there is an important catch. The glassy state is thermodynamically unstable and amorphous materials will invariably tend to recrystallise on storage. The timescales over which this process occurs may vary from seconds to years and it is the understanding of what controls this timescale that has been the focus of much attention within the pharmaceutical sciences.

One of the key issues influencing the kinetics of the recrystallisation process is the storage temperature in relation to the glass transition temperature. In brief, if one stores the material above the glass transition temperature then, for most pharmaceutical applications, one may expect recrystallisation to take place within a timescale that is unacceptably short. If one stores the sample below the  $T_g$  then the timescale is extended considerably, although whether this delay in recrystallisation is sufficient for product purposes is a more difficult question to answer. There is a general belief that if one is 50°C or more below the  $T_g$  then the system should be fairly stable (Hancock and Zografi, 1997). However, this may simply not be possible in a practical sense. For example, prednisolone has a  $T_g$  of approximately 5°C, hence the production of a viable dosage form containing amorphous prednisolone would be extremely difficult (although in fact there are ways around this). Overall, therefore, one absolutely must know the value of the  $T_g$  in order to have an idea of the storage stability of the material in question. This then leads to a very important question. Does any single material have a single  $T_g$  value, in the same way that any one crystal polymorph will have a defined melting point? The answer is no.

The value of the  $T_g$  will vary according to the cooling rate used, with faster cooling rates resulting in lower  $T_g$  values. In theory therefore, one may have an infinite number of glass transition temperatures simply by varying the preparation conditions. However, in practice the range of cooling rates that may be used is such that the  $T_g$  will not vary greatly (our own experience has been that the value may change by up to around 5°C depending on the rate used), although it should nevertheless always be appreciated that any stated value is not absolute unless preparation conditions are clearly stated. However, there are two other potential ways in which the  $T_g$  value may change that may be more profound in their implications for product development.

In the first instance, it is absolutely essential to consider plasticisation, especially by water. The presence of low molecular weight materials may cause a dramatic change in  $T_g$ , usually involving a lowering of this value. This is exploited in the polymer industry (and indeed in film coating technology) as the lowering of the  $T_g$  may result in favourable changes to the flexibility of the polymer. However, if one is considering amorphous drugs, freeze dried materials or indeed polymer microspheres the influence of water on the  $T_g$  must always be considered carefully. For example, our own experience has been that the presence of 5% w/w water in a sample of saquinavir lowered the  $T_g$  by approximately 50°C (Royall et al, 1999). Given the previous arguments regarding the relationship between  $T_g$  and storage stability it is clearly essential to have an understanding of how water may effect the glass transition. Fortunately this is reasonably simple to predict, as a range of expressions are available that allow fairly accurate estimations to be made. Indeed, we have used these expressions to develop a model whereby the storage stability may be predicted as a function of water content.

The third issue regarding the uniformity of the  $T_g$  for a single material is perhaps the least

well understood. The above description of the glassy state used the simplest method of preparing a glass, that of cooling from the melt. However, in practice glasses may be prepared in a number of ways such as solvent evaporation (e.g. polymer microspheres, spray drying), freeze drying or mechanical trauma. Is the glassy state formed by these methods equivalent? The answer to this important question remains poorly understood but evidence is mounting that they are not. Our own studies have indicated that ground salbutamol sulphate behaves in a completely different manner to spray dried material in terms of the recrystallisation profile. This issue remains one that, in our opinion, merits further exploration.

Overall, therefore, it is essential to have some understanding of the glassy state for a number of applications. This article has sought to give some very basic information regarding the current knowledge base but, as should be clear from the above, there are still a number of issues that we need to understand in more depth before we can fully exploit the opportunities and avoid the pitfalls that amorphous systems present to us.

### Suggested Reading

Craig, D.Q.M., Royall, P., Kett, V. and Hopton, M. (1999) The relevance of the amorphous state to pharmaceutical dosage forms: glassy drugs and freeze dried systems. *Int. J. Pharm.*, 179, 179-207

Hancock, B. C. and Zografi, G. (1997) Characterisation and significance of the amorphous state in pharmaceutical systems. *J. Pharm. Sci.*, 86, 1-12

Kerc, J. and Srcic, S. (1995) Thermal analysis of glassy pharmaceuticals. *Thermochim. Acta*, 248, 81-95

Royall, P.G., Craig, D.Q.M. and Doherty, C. (1999) Characterisation of the effect of moisture uptake on the glass transition of an

amorphous drug using modulated DSC Int. J. Pharm, 190, 39-46

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## 28<sup>th</sup> CRS Symposium 2001 – San Diego



Participants at the 28<sup>th</sup> CRS Symposium enjoying the Welcome reception in San Diego

San Diego in July comes highly recommended and the CRS meeting in San Diego this year was a pleasant mix of business with pleasure – a sort of pleasurable business experience. The weather was absolutely glorious, the conference venue delightful San Diego not only hosted over 2000 participants at the 28<sup>th</sup> Annual CRS meeting held at the Hyatt Regency but also played host to both a massive police presence and the conference attendees to the Biotech 2001 event! The anti-biotechnology riots failed to materialise and the closest the CRS conference delegates got to witnessing a fight was in the parrot enclosure of the San Diego Zoo. The banquet was held at this venue.

There were over 700 scientific presentations over the 3 day meeting – an excellent opportunity to learn what was cutting edge and what was considered passé, what rival laboratories were up to or simply learn something new. The award ceremony saw only one British scientist honoured, namely Saghir Akhtar a reader at the School of Pharmacy, Aston University, Birmingham who was joint winner of the Young Investigator Award.

The plenaries! George Whitesides of Harvard University presented a paper “The Biomaterials interface” demonstrating that the attachment of cells to surfaces could be

controlled by self-assembling alkanethiols and gold systems. This work is yielding valuable information on the kinetics and thermodynamics of protein attachment. James Wilson' of the University of Pennsylvania's Institute for Human Gene therapy reviewed the use of viral vectors as gene delivery systems in his paper "Gene therapy for drug delivery", presenting interesting results on gene targeting to the central nervous system. While Harvard Medical School professor - J.P. Vacenti explored the use of controlled release technology to modulate biological signals for tissue regeneration in the field of tissue engineering. These plenary lectures set the scene for the rest of the conference which saw numerous sessions on topics such as Tissue Barriers, Smart Polymers, Lipids - Liposomes and Micelles, Gene delivery, Drug Conjugates, Microfabrication, Vaccine delivery, Peptide and Protein delivery, Intracellular trafficking, Veterinary science and Oral delivery.

One of the sessions I attended was the Lipids, Liposomes and micelles session chaired by Lipoxen's Gregory Gregoriadis. Apart from my presentation on the use of polymeric vesicles possessing a surface bound enzyme for the activation of a drug load, Carl Alving presented work on the use of liposomes and emulsions as vaccine adjuvants. Alving's evidence demonstrated that liposomal antigens are accessible to antigen presenting cells, are processed by these cells resulting in

an interaction of the processed antigen with specialised T helper cells, the proliferation of Th2 or Th1 cells and finally the antigen specific proliferation of effector cells. Alving's work implied that the Golgi complex is heavily involved in the development of antibodies to liposomal antigens. Alving also presented data on a liposome-stabilised oil in water emulsion formulation which gave a prolonged uptake of antigen by antigen presenting cells and an improved antibody response.

Gregoriadis' paper also on the subject of vaccine development covered the use of liposomes as adjuvants for DNA vaccines. There are subtle differences between the host's handling of either positively charged or neutral liposomes with the neutral liposomes showing activity although to a lesser extent than the positively charged liposomes.

The University of Illinois' Carol Kirchoff presented data on the stabilisation of interleukin 2 by DSPE-PEG 500 a polyethylene glycol phospholipid providing evidence that the interaction of the fragile protein interleukin 2 with this amphiphile led to a limitation of its degradation as characterised by the alpha helical content of this peptide.

A brief snapshot I know, but I hope it whets your appetite for Seoul 2002 and more importantly Glasgow 2003.

Ijeoma Uchegbu

## 7<sup>th</sup> UKICRS Conference, January 2001 – London



Speakers and organisers at the 7<sup>th</sup> UKICRS Conference held in London in January 2001. From Left to right Jayne Lawrence (King's College, University of London), H.S. Aojula (University of Manchester), Kevin Shakesheff (University of Nottingham), Snjezana Stolnik Trenkic (University of Nottingham), Graham Buckton (School of Pharmacy, University of London), Ijeoma Uchegbu (University of Strathclyde), Richard Guy (University of Geneva and Former President of the Controlled Release Society), Anthony D'Emanuelle (University of Manchester), Robert Hider (King's College, University of London) and Barry Hirst (University of Newcastle upon Tyne).

Another successful UKICRS one day symposium was held at King's College, University of London on Thursday 4th January 2001. The event was generously sponsored by Colorcon, The Controlled Release Society, Elan, GlaxoSmithKline and Wyeth. The UKICRS gratefully acknowledges this support.

An interesting and varied program was organised by Jayne Lawrence and Ruth Duncan, which focused on key issues including tissue engineering, the role of p-glycoprotein in absorption, and gene therapy,

with an impressive panel of speakers addressing a packed auditorium.

Richard Guy, president of the Controlled Release Society opened the proceedings with a review of the events of the past year which included an expanded membership, a change to the CRS administrative staff and plans for forthcoming CRS meetings. Dr Tony D' Emanuele, formally resigned his 7 year chairmanship of the UKICRS, welcoming Professor Duncan Craig to the committee as his successor. Professor Craig, of the University of Belfast and one of the founding

members of the UK chapter of the CRS will serve the committee as chair for 4 years.

A paper entitled "The concept of Nanoparticulate Systems for the Delivery of Antisense Oligonucleotides" was presented by Patrick Couvreur, of the University Paris Sud, France. Antisense oligonucleotides (ODNs) can selectively modulate the expression of a gene, although their effectiveness is often hindered by the poor biological stability and low intracellular penetration. Experimental data on two nanoparticulate systems were presented, where the ODNs were either associated with the polymer surface or entrapped within the nanoparticle. Polyisobutylcyanoacrylate nanocapsules show great potential for ODN delivery, where the ODNs are entrapped in an aqueous core, prepared from a w/o emulsion. Entrapment into polymeric nanocapsules more efficiently protected the ODNs from degradation by serum nucleases, than adsorption on to the nanosphere surface.

The morning session continued with an overview from David Thatcher of Cobra Pharmaceuticals highlighting "Issues in the Development of Gene Therapy Products". To date non-viral delivery of genes has been difficult to achieve and has not been successful while viral gene therapy vectors have encountered safety problems. Greater biological amplification is required and therefore the delivery needs to be improved. Gene therapy aims to replace defective genes, delete genes to modify disease, deliver novel genes or DNA vaccines. For effective gene therapy the ideal vector must provide sustained and specific gene expression at an appropriate level, whilst targeting efficient gene delivery. The challenges facing gene therapy include inefficient delivery (although this can be increased by the use for a viral promoter), transient gene expression and poor pharmacokinetics. Delivery could be improved by the use of (i) viral promoter systems, which is the most common approach, (ii) non viral systems including endosomal escape and

nuclear targeting strategies, (iii) viral systems for example replicating vectors of modified tropism (modification to the viral backbone). Transient gene expression could possibly be overcome by the use of chromatin insulators and the integration into the host's genome of a persistent virus (e.g. the adeno-associated viruses). The pharmacokinetic profile of the gene product could be enhanced by both viral and non-viral methods of passive or receptor mediated targeting strategies. However, it is anticipated that gene therapy will have its maximum clinical benefit in indications where local delivery with a low level of transient expression is required.

The session continued with a presentation on "Tissue Engineering: The Link with Drug Delivery" by Kevin Shakesheff at the University of Nottingham. Developments in the field of tissue engineering have required the immobilisation of biologically active molecules onto the surface of polymer based devices. The polymer surfaces are required to present biological molecules that actively promote receptor mediated interactions with cells, or to present molecules that change the distribution of protein absorption *in vivo*. Shakesheff explained how the use of Super Critical Fluid (SCF) Technology could change crystalline polymers into a glassy state. For example poly lactic acid is a liquid at 35°C in a CO<sub>2</sub> environment and particles can be manipulated into a specific shape in the range of 10-50 micrometers. The porosity of the polymer can be altered by changing the rate of CO<sub>2</sub> venting in the systems, a low rate producing a more dense polymer as compared to a high rate of CO<sub>2</sub> venting. Therefore the polymer morphology is controllable and high loadings of guest species (e.g. enzymes or proteins) can be achieved.

The morning session concluded with a presentation by Richard Guy from the University of Geneva, on 'Optimising Iontophoretic Delivery across the Skin by Chemistry and Formulation'. The skin is negatively charged at pH 7.4, therefore when

a positively charged drug crosses the skin by iontophoresis, a corresponding negative ion e.g. Glucose is transferred in the opposite direction. Efficiency of drug transport is reduced in the presence of competing ions in a formulation, with transfer of lipophilic drugs e.g. lidocaine being less efficient than more water soluble compounds, the transport of all drugs by iontophoresis is independent of concentration.

The program continued after lunch with a presentation by Snjezana Stolnik of the University of Nottingham on the Thermodynamics of polymer-DNA interactions using techniques such as differential scanning calorimetry and atomic force microscopy. These studies are aimed at furthering the understanding of the role of carrier-DNA interactions in gene delivery and will ultimately lead to the design of more efficient carriers for gene therapy.

Ijeoma Uchegbu from the University of Strathclyde presented data on the feasibility of enzyme activated polymeric vesicular systems. Polymeric vesicles prepared from carbohydrates, polyethylenimine and amino acids have been developed for drug and gene delivery applications. Dr Uchegbu described the characterisation and feasibility of chitosan based vesicles for use in developing enzyme activated drug delivery systems. These enzyme activated polymeric vesicle systems provide a new means of controlling drug release.

H.S. Aojula continued the session with an interesting presentation on "Bioresponsively-triggered release *in vivo*". Liposomes are used as carriers in various commercial formulations, however improvements to these systems are restricted by methods to enhance targeting and to prolong the circulation time. Aojula highlighted examples of bioresponsive triggered liposomes by means of pH, thermal, photo and enzyme sensitive mechanisms, indicating that their disadvantages included a lack of plasma stability and absolute sensitivity to

control the release. Modifications are required to the amino acids to develop pH sensitivity at a physiologically relevant pH.

The role of "The P-glycoprotein barrier in the gut" was presented by Barry Hirst from the University of Newcastle upon Tyne and evidence of its exploitation for pharmaceutical means was also presented. There are various means by which this endogenous transporter evolutionary designed to limit the accumulation of toxic materials in cells may be exploited for pharmaceutical means.

Graham Buckton from the School of Pharmacy, University of London gave a very interesting and informative presentation on "New Ways of Characterising Amorphous Materials". Pharmaceutical processing, for example milling and freeze/spray drying can introduce amorphous material into crystalline products. Professor Buckton described a method of inverse phase gas chromatography and near infra red + dynamic vapour sorption (NIR-DVS) to quantify the amount of amorphous material present. The measurement of amorphous material is especially important for the characterisation of inhalation drugs and excipients.

The final presentation of the day was by Robert Hider of King's College London on "Controlled Release Goals in the Treatment of Thalassaemia". Hider explained the complex role of iron in and control of iron by the body. Iron is a reactive material which is toxic if not in the correct environment. Two proteins transferrin and ferritin control the toxic effects by limiting the absorption and distribution of iron in the healthy body, however there is no mechanism for excretion e.g. following a blood transfusion. The diverse effect of iron has resulted in many potential applications for iron chelators including: malaria therapies, reperfusion injury, neurodegeneration treatments, cancer chemotherapy, acute iron poisoning, sickle cell and thalassaemia treatments. Sickle cell anaemia patients who require regular blood transfusions require the

excess iron to be chelated, currently by an 8hr infusion of the non orally active Desferioximine five times a week. Therefore, there is a great need to develop an orally active agent to improve the method of chelation treatment. Iron chelators are rapidly metabolised, and as a result very high doses are required (1g of CP20 – to be dosed three times a day), although a further new generation iron chelators (CP502) with oral activity and a reduced rate of metabolism have been identified, a controlled release system would be advantageous.

The quality of poster submissions this year was again excellent covering the general area of controlled drug delivery, with a total of 22 posters on display. Two prizes of £500

(towards attendance at the CRS 2001 conference in San Diego) were awarded to the best postgraduate posters presented by Mr Ryan Tomlinson for work entitled "Polyacetals: degradable macromolecular components for biomedical conjugation applications" and Mr John Cleary for work entitled "Electrochemical characterisation of a thermoreversible hydrogel for the controlled release of pharmaceutically active compounds".

This was an intellectually stimulating meeting with a busy programme and an excellent networking event.

Karen Lewis

## **UKICRS 2002 - 8th United Kingdom and Ireland Controlled Release Society Annual Meeting and Symposium**

### **Oral Administration of 'Difficult' Drugs - Thursday 17th January 2002 Call for Papers**

On Thursday 17th January 2002 the 7th UKICRS meeting will be held at AstraZeneca in Loughborough. The theme of the meeting is Oral Administration of 'Difficult' Drugs. This day once again promises to be an exciting day of science. The organising committee headed by Karen Lewis and Rupi Pannu, has arranged a balanced programme of speakers covering the challenges of oral delivery, GI imaging, novel formulations, in-vitro/ in-vivo correlations and of course an industrial perspective on these issues.

To enable discussion, you are invited to submit a paper for presentation either orally or as a poster. Abstracts must be submitted on one A4 page by 16th November 2001. Notification of acceptance will be made by email before 21st December 2001. There are 2 Prizes to be won (post grad and postdoctoral researchers only) of £500 + the

registration fee, for the 29th International Symposium on Controlled Release of Bioactive Materials to be held in Seoul, South Korea from 19<sup>th</sup> – 24<sup>th</sup> July 2002.

For a registration form see page 25

For further information contact Rupi Pannu, Secretary UKICRS, AstraZeneca R&D Charnwood, Bakewell Road, Loughborough, Leicestershire LE11 5RH, UK. Tel: +44 (0) 1509 645019 Fax: +44 (0) 1509 645546  
Email: [Rupi.Pannu@AstraZeneca.com](mailto:Rupi.Pannu@AstraZeneca.com).



## Conference Calendar

Vaccines of the Future: from Rational Design to Clinic, Pasteur Institute, Paris, France  
17th October 2001 - 19th October 2001  
[www.pasteur.fr/applications/euroconf/vaccines/index.html](http://www.pasteur.fr/applications/euroconf/vaccines/index.html).

2001 AAPS Annual Meeting and Exposition, Colorado Convention Center, Denver, Colorado, USA.  
21st October 2001 - 25th October 2001  
[www.aaps.org/annualmeet.cfm](http://www.aaps.org/annualmeet.cfm)

Pharmaceutical and Biotechnology: Discovery, Development, and Delivery of Medicine  
Reno Hilton, Reno, Nevada, USA.  
4th November 2001 - 9th November 2001  
[www.aiche.org/annual/topical/pharmandbio.htm](http://www.aiche.org/annual/topical/pharmandbio.htm)

Liposome Advances 2001 Conference, School of Pharmacy, University of London, UK  
17th – 21st December 2001  
Professor Gregory Gregoriadis, School of Pharmacy, University of London, 29 – 39  
Brunswick Square, London WC1N 1AX

8th United Kingdom and Ireland Controlled Release Society Annual Meeting and Symposium, AstraZeneca, Loughborough, UK.  
17th January 2002  
[Rupi.Pannu@AstraZeneca.com](mailto:Rupi.Pannu@AstraZeneca.com)

Genes as Medicines, Royal Pharmaceutical Society Headquarters, London, UK  
14th March 2002  
[aps@associationhq.org.uk](mailto:aps@associationhq.org.uk)

11th International Cyclodextrin Symposium, Hotel Loftleidir, Reykjavik, Iceland  
12th May 2002 - 15th May 2002  
[www.cyclodextrin.is/CD2002/](http://www.cyclodextrin.is/CD2002/)

29th International Symposium on Controlled Release of Bioactive Materials, Seoul, Korea.  
19th July 2002 - 24th July 2002  
[www.controlledrelease.org](http://www.controlledrelease.org).

62nd International Congress of FIP, Nice Acropolis, Nice, France.  
31st August 2002 - 5th September 2002  
[www.congress@fip.nl](http://www.congress@fip.nl)

EUFEPS 2002: New Safe Medicines Faster  
Stockholm International Fairs, Stockholm, Sweden  
20th October 2002 - 23rd October 2002  
[www.eufeps.org](http://www.eufeps.org)