

DRUG DELIVERY MAPPING AND VALIDATION WORKSHOP
BBSRC/EPSRC/DTI
1 and 2 July 2003
DRAFT

BACKGROUND

A Royal Pharmaceutical Society Drug Delivery Report

The Royal Pharmaceutical Society produced a report in February 2001 entitled, "UK Drug Delivery Research: The way forward in the new millennium". Following the report, a workshop was organised by BBSRC, EPSRC and RPS in June 2001. Although this meeting produced few specific recommendations, it did clearly identify that Drug Delivery was an area of growing importance to the pharmaceutical industry and that important new academic research opportunities could now be identified. However, neither the Drug Delivery community nor the Research Councils were well placed to respond effectively to these opportunities at that time.

B. BBSRC/EPSRC WORKING GROUP ON DRUG DELIVERY

As a consequence BBSRC and EPSRC established a working group, which includes representation from academe, industry, MRC, ABPI, RPS and DTI.

The working group has met twice and has expressed the following views:

- The working group believed it was timely for the Research Councils to undertake a review of the area.
- Drug Delivery is an important area of research for the pharmaceutical industry but increasingly also for the biotechnology industry. The number of products coming to market has diminished and one of the main reasons for this has been poor delivery of drugs to the right targets. Historically the major pharmaceutical companies have not focussed on Drug Delivery early in the drug discovery process. This ultimately has great cost implications as compounds are put into development and ultimately fail in clinical trials due to delivery problems.
- Many of the current issues in Drug Delivery arise from problems in delivering small molecules whose solubility and other physical properties make absorption and distribution difficult and whose metabolism may be complex. The challenges are becoming much greater as new therapies under development will require delivery of proteins, peptides, fusion proteins, genes and oligonucleotides.
- As demonstrated by the portfolio analysis done by the Research Councils, there is a significant level of on-going research on Drug Delivery in the UK but it is highly fragmented and lacks co-ordination. In industry many companies support pre-competitive research in this area, but this activity is equally uncoordinated.
- Neither academe nor industry is fully aware the full range of underpinning research being carried out in Drug Delivery in the UK.

- There is a serious lack of trained people in the UK to do Drug Delivery-related work, particularly in industry that is increasingly having to recruit staff from overseas. This is compounded by the lack of senior pharmaceutical scientists in academia capable of training the next generation of industrial scientists.
- There needs to be an explicit statement by all appropriate Research Councils to clearly identify where drug delivery fits with their respective remits.

The group also recognised that the UK has traditionally been a world leading force in Drug Delivery. Current grant support from the Research Councils is of the order of £18m, which was felt to be entirely reasonable, while the ability to attract funding of this level through responsive mode is a clear statement of the quality of the research underway. However there is an urgent need to co-ordinate much more strongly the activities of the Research Councils, DTI, Industry and other interested funding agencies and to identify and respond to future needs and the potential impact of emerging technologies upon medicines. To help accomplish this the working group proposed the following:

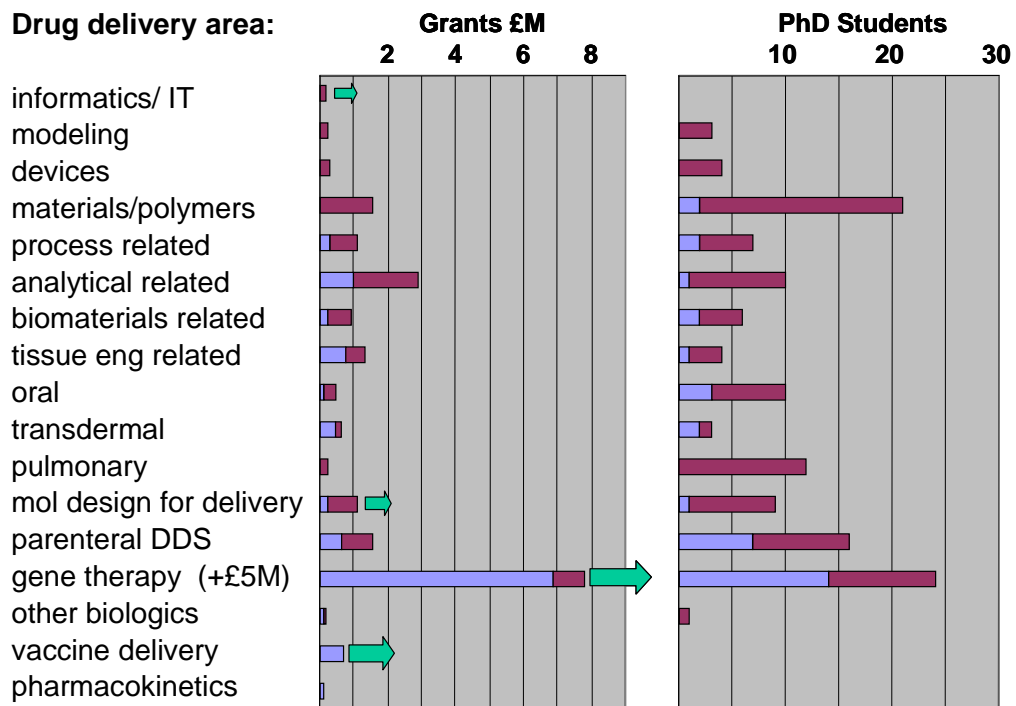
- Mapping and Validation of Drug Delivery in UK:
 - In its report “UK Drug Delivery Research: The way forward in the new millennium” the RPS defined Drug Delivery in terms of a map of activity areas. The working group would like to plot UK research activity onto this map. This will highlight the strengths and weaknesses of UK Drug Delivery research. It proposes that a workshop be organised to undertake this mapping with involvement of RCs, The Wellcome Trust, Royal Academy of Science and Academy of Pharmaceutical Science.
 - Given the breadth of activity encompassed within Drug Delivery, and the number of funding bodies with interests in that activity, that the Research Councils consider maintaining a cross-council coordinating group on an ongoing basis to ensure the continued coherence of their support activity.

In response to the first recommendation the BBSRC, EPSRC, MRC and DTI agreed to hold a mapping workshop which was arranged for 1 and 2 July 2003.

DRUG DELIVERY SUPPORT BY THE RESEARCH COUNCILS

Prof David Clarke provided a summary of the Drug Delivery portfolio. As is evident from the graph, there is an overlap between Research Councils funding. While there is strong focus in some areas, others may be poorly represented in the research and training portfolio, reflecting concerns expressed by academia, professions and industry.

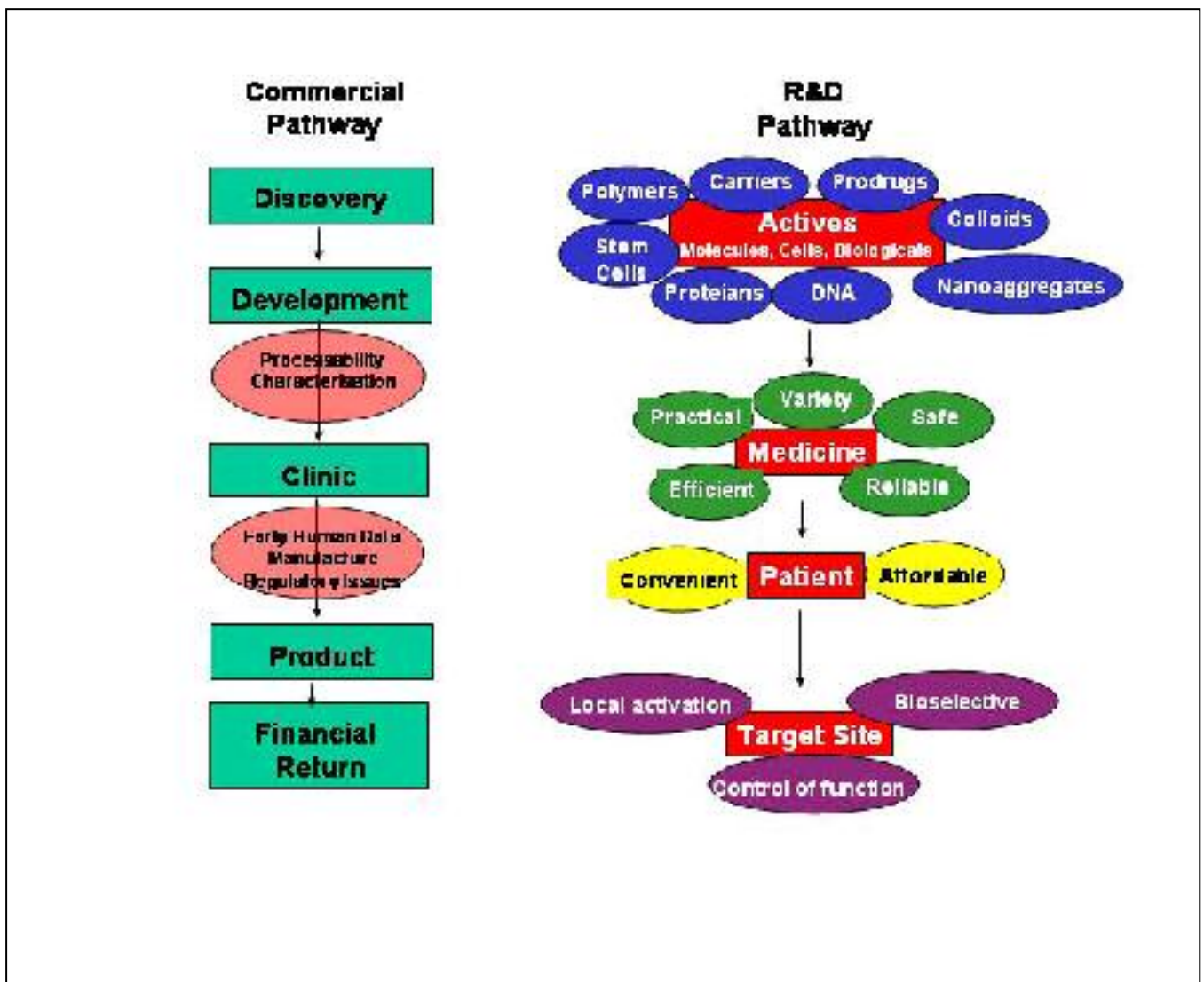
Current **BBSRC/EP SRC/MRC** grants by area



DEFINITION OF DRUG DELIVERY

All delegates were asked to produce their own written definition of what they understood drug delivery to involve. Given their broad range of backgrounds and interests it was not surprising that there was substantial variation in these definitions. The diagram below captures all the significant topics and concepts included in these definitions and provides an overall shape for what is meant by drug delivery

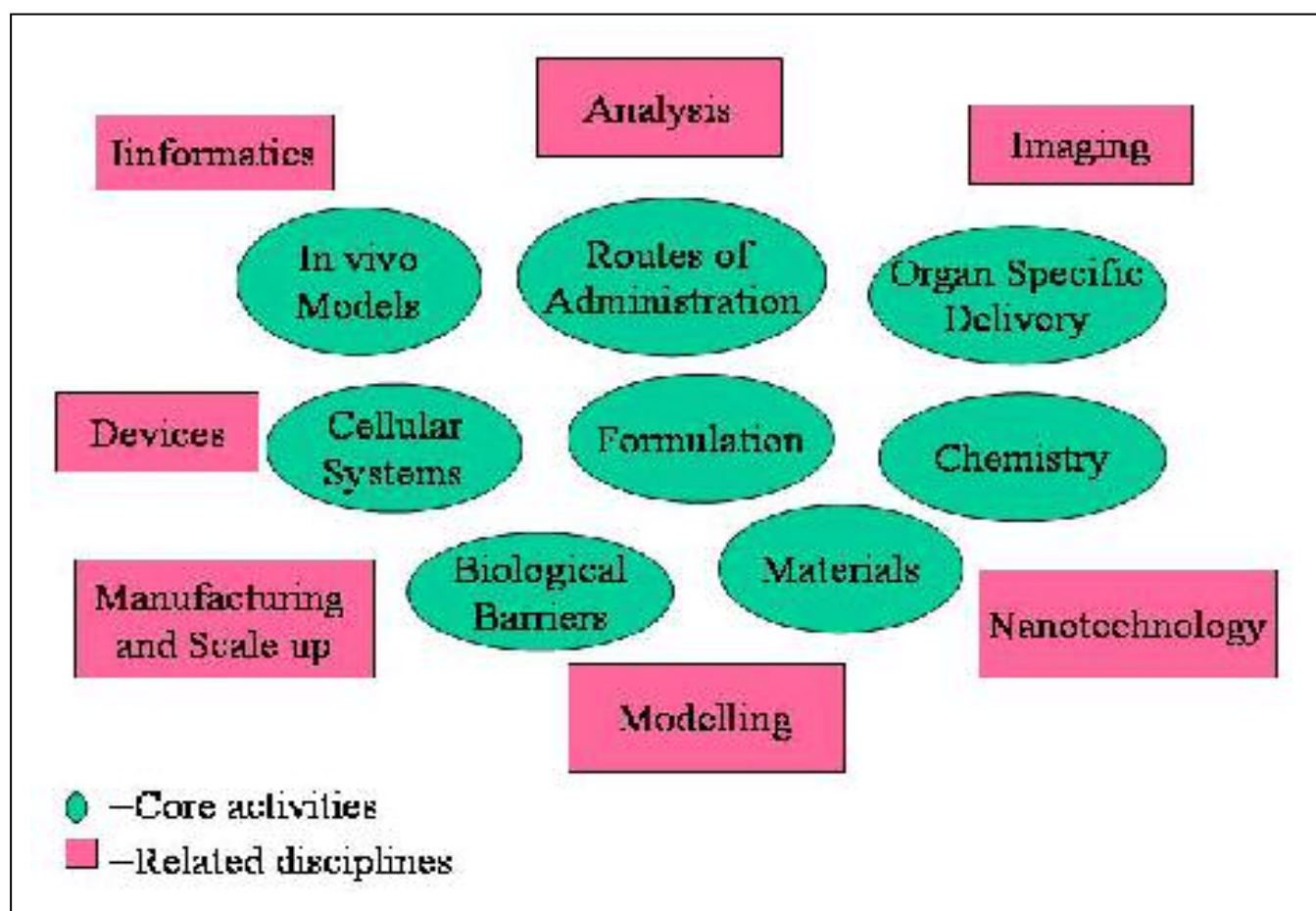
A more general definition adopted by the meeting was: “Drug Delivery encompasses those activities needed to convert a bioactive molecule into a useful medicine.”



DRUG DELIVERY EXPERTISE AND GAPS

In the first break out session, delegates were asked to map drug delivery expertise in the UK against the landscape shown below (developed by the working group), and also to identify any significant gaps. In doing this, delegates were asked to identify groups currently active in the topics shown whose primary interest was drug delivery related, but also to identify other groups from other research fields with skills appropriate to these topics but who were not currently engaged in drug delivery.

LANDSCAPE: The World of Drug Delivery



Fitting individual research groups into the landscape was neither an easy or tidy job, given, importantly in this field, the high levels of multidisciplinary displayed by many of the researchers involved. Nonetheless, it was possible to identify a critical mass of quality research activity in drug delivery in most of the core areas of the landscape, in particular in formulation and routes of administration, and in cellular systems and biological barriers. Organ specific delivery was rarely identified as a primary area of expertise, but was felt to be a pervasive attribute of much of the work identified in the other topics. The UK has large and strong research communities in

both chemistry and materials science, but engagement in drug delivery work was limited. There was a very small community currently engaged in in-vivo modelling.

Amongst the related areas there was significant UK strength in nanotechnology, modelling, tissue engineering, imaging, devices and informatics, but engagement with drug delivery was small and patchy. Manufacturing was significantly less strong in terms of numbers but there were some key groups directly engaged in drug delivery.

The map below shows the distribution of research groups and expertise identified by workshop delegates.



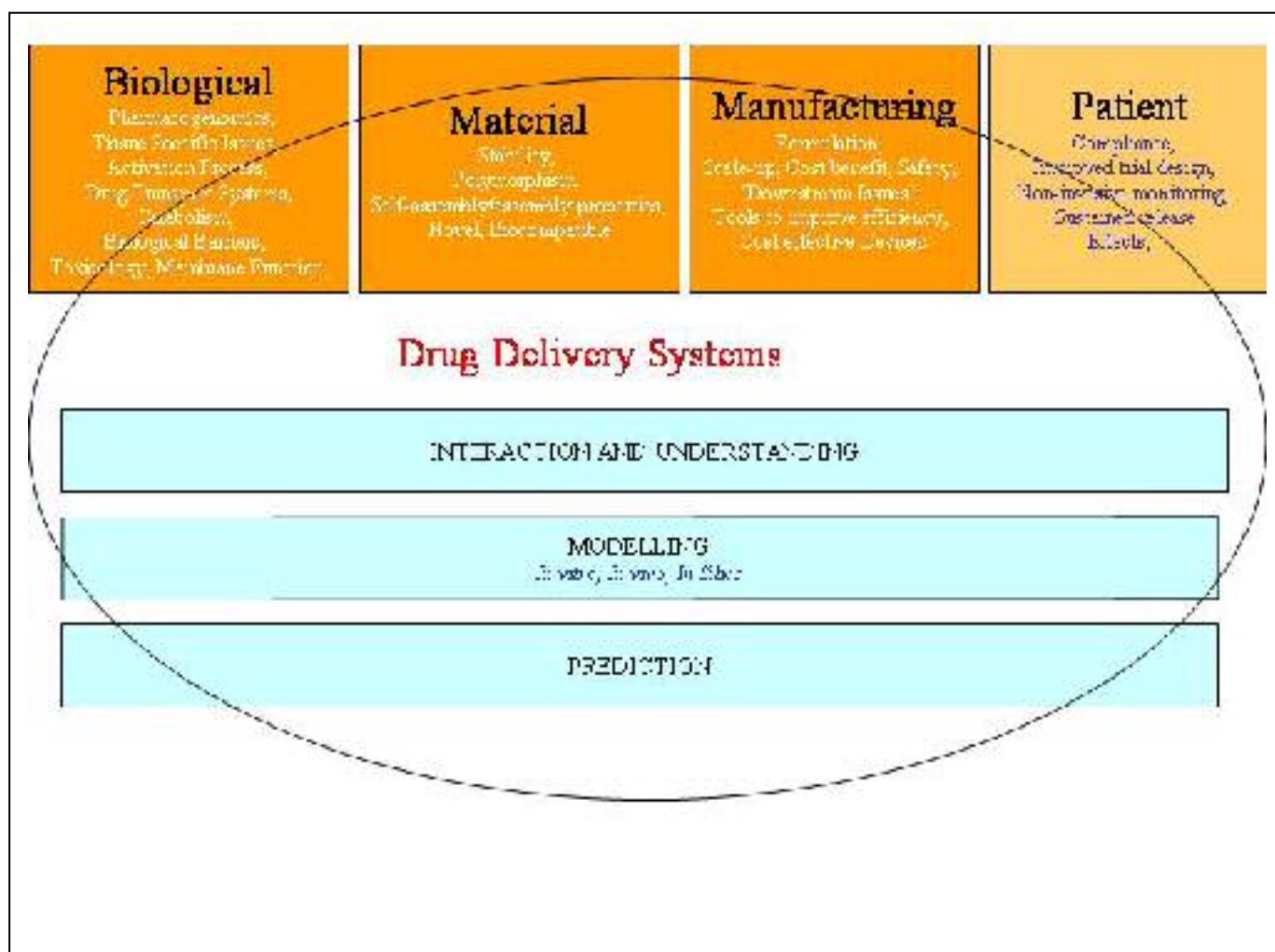
The map shows groups currently active in drug delivery specific research while and also identifies some groups with relevant expertise who might be attracted to deploy them in support of drug delivery. It should be explicitly noted that this does not purport to be a complete and accurate statement of the UK community, but simply captures the information from the workshop discussion and there may well be other workers not known to the delegates.

A number of gaps in UK activity were identified. Some, including integrated modelling, nanotechnology and colloids science, reflect areas where there is a strong wider UK community but a need to engage them in the challenges arising from drug delivery. Other areas reflect real gaps in the UK and this includes: clinical product development where there is some industrial activity but little in academe; social aspects including links with pharmacy practice and understanding patient compliance; non-standard delivery routes; manufacture and scale up.

Two other gaps were identified that warrant further comment. The first is analytical science. This area was both strongly identified as a UK expertise gap, but also had a significant number of groups identified as having analytical expertise. The explanation for this apparent contradiction appears to be that most people working in drug delivery routinely use a battery of analytical techniques as part of their research, and members of the community have become identified as particularly expert users of specific techniques. The identified gap is however a lack of specialist analytical scientists, who form a rather small community in the UK overall, able to develop new analytical methods to address problems not amenable to existing approaches. The second is the general area of pharmacogenetics. This is a new activity developing as a post-genomic science and involves both understanding the genetic basis of variation in response to drugs, and also tailoring drug delivery to meet the needs of different groups, both genetic and others (including for example tailored formulations for geriatric and paediatric medicine). This new and developing field is likely to give rise to a new research community as it develops.

KEY CHALLENGES FACED BY DRUG DELIVERY COMMUNITY

The aim of this session was to identify the major scientific challenges in Drug Delivery research. Each delegate identified challenges and they were mapped on to a 'tree'. A summary of the challenges is presented below:



Increasingly the most important drug delivery research is likely to address problems across many if not most of the boxes in the above diagram, but often with a specific focus towards a particular drug type or disease state. Some key challenges in drug delivery are:

- To be able to effectively deliver molecules which have either unfavourable physico-chemical properties, high molecular weight, or which are subject to metabolic attack;
- To understand the nature of delivery pathways and in particular to understand the physico-chemical and biological properties of the various barriers in such pathways, including membrane transport, efflux processes, intracellular trafficking and drug compartmentalisation;

- The development of integrated multi-scale models, (in-silico, in-vitro, and in-vivo) that can provide an effective predictive capability for molecule/system behaviour;
- To be able to target drug molecules to specific cells or tissues to avoid undesirable side effects;
- To understand the effects of genetic variation in terms of response to drug molecules and to be able to develop processes to overcome these (applied pharmacogenetics)
- To consider the impact and potential of new or emerging technologies upon the safe and effective use of medicines in healthcare and by the patient

KEY NEEDS OF DRUG DELIVERY COMMUNITY

The aim of the session was to identify key needs of the community to address the challenges identified in the earlier breakout group. The key needs can be broadly classified into four major headings:

People

- Attracting and retaining high calibre researchers which have appropriate breadth of knowledge
- Need for more training and increase in number of PhDs to create critical mass
- Increase in number of lecturerships and professorships in Drug Delivery
- Modelling of Complex Systems
- Interdisciplinary leadership of multidisciplinary teams
- Make Drug Delivery research attractive to outside experts
- Translational skills and community building
- Engagement with Industry
- Need to link people doing
 - Biological understanding with people doing physical delivery
 - Drug Delivery to chemistry
 - Cell biology with whole organism biology

Co-ordination

- Track progress of on-going research
- Multi-disciplinarity (science language barriers), breakdown of subject boundaries in Drug Delivery
- Avoid undue duplication
- Bring in 'outside' expertise to Drug Delivery
- Who maintains 'health of discipline'

Communication

- Drug Delivery forum/grant holder workshop
- Database open to all
- Establish Drug Delivery Network
- What does Industry want?
- Increased liaison with DoH

Funding

- Co-ordination between Research Councils, better advice and communication
- More funding for multidisciplinary activities
- Mixed funding economy
- Complement rather than compete with existing funding

RECOMMENDATIONS FOR RESEARCH COUNCILS BY THE DRUG DELIVERY COMMUNITY

In the final breakout session, participants drew on the earlier discussions and made some recommendations to the Research Councils. They are summarised below:

- There needs to be a clear statement from each of the Research Councils on where Drug Delivery fits in their respective remits.
- Existing funding should be coordinated more effectively.
- Although the research councils have made significant investments in drug delivery research there is potential for a Research Councils call possibly jointly with industry.
- Research funding priorities and gaps should be reviewed further.
- A Drug Delivery Community Network should be established.
- Discipline Hopping into Drug Delivery should be encouraged (particularly for new/young researchers).
- PhD training in Drug Delivery should be reviewed, appropriate approaches could include transitional training for PhD students (e.g. conversion year) and a Doctoral training centre for Drug Delivery
- The establishment of Drug Delivery chairs could encourage high-calibre researchers to work in the UK.
- Improved peer review mechanisms for multidisciplinary projects would help.