

Chapter 1

Build a mutually advantageous collaboration between the NHS and industry for patient benefit

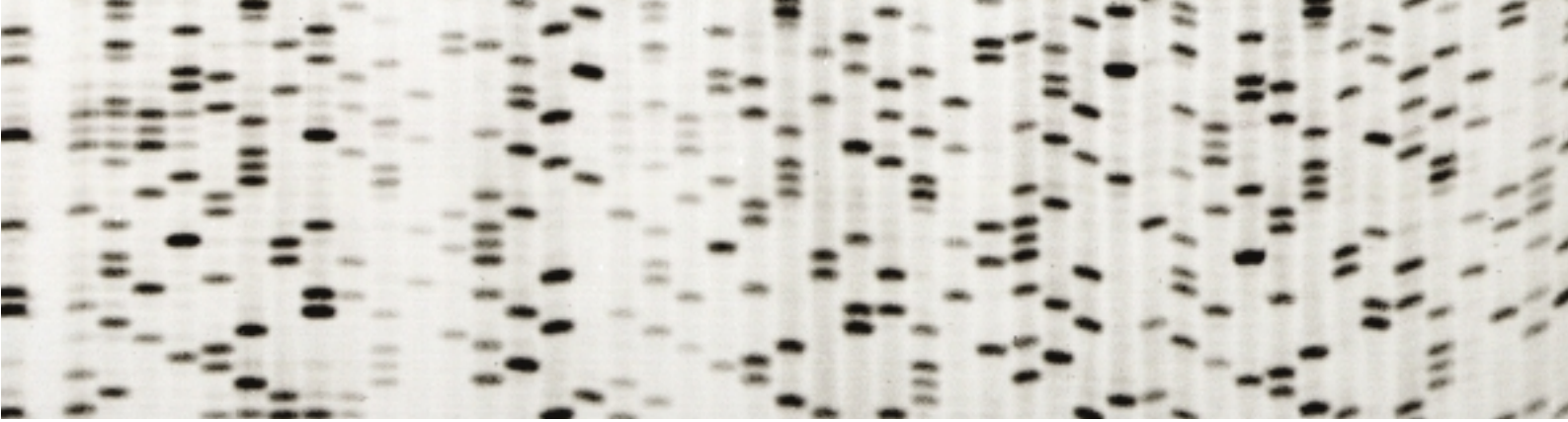
EXECUTIVE SUMMARY

The NHS should be a major source of competitive advantage for the UK bioscience sector. As the main provider of healthcare to the UK population, it acts as a gateway to the largest aggregated patient pool in the world, and can monitor that population over time. This is a major asset for conducting efficient and effective clinical trials. The NHS is also a potentially significant source of innovation and early stage products for the commercial bioscience sector. In particular, the products of NHS-derived innovation can be 'nearer to market' than that which emerges from academia.

In turn, the biopharmaceutical industry – both pharmaceutical and bioscience companies – has much to contribute. Industry can provide the NHS with expertise for commercialising its own R&D. Through clinical trials, industry offers early access to innovative therapies, and improving patient care within a protocol-driven environment. Indeed, clinical trials can support sustainable modernisation, through the high standards of care that they require, and the education of healthcare professionals that they provide. Ultimately, the BIGT wants to create a partnership between the NHS and the bioscience industry focused on *a shared commitment to improved patient care through innovation*.

There are three main barriers to achieving this vision:

- Inefficient and inadequate infrastructure to put the vision into operation.
- Insufficient cultural support for innovation and academic/industry collaboration within the NHS.
- Insufficient funding of R&D and its commercialisation in the NHS. R&D funding from the DH for the NHS has fallen from 1.2% of spend in 1997 to 0.9% in 2002, and will be 0.77% in 2005.



The BIGT addresses these barriers through the five main recommendations below. The centrepiece is the creation of a National Clinical Trials Agency (NCTA), intended to make the UK the leading location for clinical trials in the world.

Industry, Government, academia, and other key stakeholders should collaborate to:

1.1 Create a National Clinical Trials Agency (NCTA) to support excellence in clinical trials and clinical research within the NHS. The NCTA should be an arm's length body, sponsored by the DH, working in collaboration with Research Councils UK. The NCTA would require £5 million of new money in its first year to supplement £45 million from existing sources (NTRAC, NCRN, MRC and HTA).

The NCTA and funding should scale up over the initial five years to reach £200 million per year (£150 million in new money). A successful NCTA will provide benefits for patients, better quality and more effective clinical trials, and will generate further income for the NHS.

To raise the level of professionalism in the NHS surrounding clinical trials, the NCTA should focus on two main activities:

1.1.1 Develop the infrastructure required to support professional, efficient clinical trials. This would involve two types of activities.

- Create a national network that will audit available clinical trials capacity; establish 5-10 infrastructure offices to advise on clinical trial set-up, conduct and regulation, develop national costing models and provide essential training (e.g. to research nurses).
- Build business cases for, and fund further investments in critical physical and human infrastructure, e.g. the MRC clinical trials unit should form part of the NCTA. An initial pilot could include dedicated translational Phase I/II facilities and clinical research networks, along lines of the National Cancer Research Network (NCRN) and National Translational Cancer Research Network (NTRAC) for respiratory, neuroscience, cardiovascular, musculoskeletal, and paediatric areas.

1.1.2 Fund a portfolio of clinical research programmes and projects.

In the medium-term, the NCTA would fund clinical research, including hypothesis-driven, pragmatic, and long-term studies. At least some portion of this portfolio should focus on enabling NHS-academic-industry collaboration, and create vehicles for public-private partnership.

1.2 Create incentives and career structures within the NHS and academic medicine to promote clinical investigation. This will be critical to addressing current cultural barriers within the NHS. Specifically:

1.2.1 Develop an innovation scorecard for NHS Trusts.

1.2.2 Create two new cadres of clinical researchers by funding 4-5 year fellowships with programme management support: clinical investigators and clinically trained scientists.

1.2.3 Monitor and celebrate progress by upgrading the functionality of the NHS National Research Register (NRR) and developing a communications strategy for the NHS R&D programme (e.g. reporting annually to highlight major achievements), ensuring that progress of this type is highly regarded by the Research Assessment Exercise (RAE).

1.3 Increase the total funds for R&D within the NHS initially stepwise over five years, from their current level of 0.9% (~ £560 million) of total spending to 1.5%.

IMPROVING UK CLINICAL TRIAL INFRASTRUCTURE: THE BENEFITS

Patient benefits

- Improves patient outcomes by using modern protocol-based care.
- Provides earlier and easier access to drugs, including those that treat rare diseases.
- Provides treatments that improve cost of delivery and keeps patients out of hospital and in work.
- Acts as a sustainable driving force to modernise the health services in the UK and provides a source of continuous innovation in healthcare provision.
- Provides cutting edge learning for health professionals involved in conducting trials in a protocol-driven environment.

Economic benefits

- Gives the UK the opportunity to become the world's leading location for clinical trials.
- Attracts industry and academia to the UK to take advantage of the leading R&D in clinical trials.

Staff benefits

- Creates motivated and better trained staff within the NHS, both in terms of nursing and clinical scientists.

A VISION FOR NHS-INDUSTRY COLLABORATION

The NHS patient pool: a distinctive asset

The NHS could be a major source of competitive advantage to the UK bioscience industry – and indeed, to the UK economy as a whole. The NHS is:

- A potential source of bioscience innovations (e.g. drug therapies, diagnostics, tissue engineering), generated by its skilled clinicians and academic clinical researchers;
- Gives early access to NHS patients, particularly those suffering from rare or expensive-to-treat diseases, to emerging innovations. At the same time the NHS can develop and test these therapies through clinical trials in its patients;
- An end-market for licensed innovative products.

This is also true of other sole provider health service systems in countries such as Australia and Canada. But the NHS is distinctive. Although it is a decentralised organisation, the NHS provides a gateway to the largest aggregated patient pool in the world, and has the ability to monitor that patient pool over time. The UK is uniquely positioned to gather long-term data on a large patient population. The full potential of this asset remains under-exploited. However, the R&D funding from the DH for the NHS has fallen from 1.2% of spend in 1997 to 0.9% in 2002, and will be 0.77% in 2005.

The UK is already a prominent player in clinical research. The UK has long been the leading location in Europe for producing good quality clinical trial data on time – a status reconfirmed by a Centre for Medicines Research (CMR) survey¹ of pharmaceutical company Medical Directors in 1999. There is concern, however, that the UK's position is eroding.

The same Medical Directors observed that more clinical research was being placed outside the UK than in 1996. They suggested that time and cost should be the focus for improvement in the UK, as there is intensifying competition from Eastern Europe (in particular Hungary, Poland and parts of Russia) and the Nordic countries. Furthermore, the introduction of the European Clinical Trials Directive² looks likely to pose a serious threat to controlled trials. Considering there are also growing concerns about the UK market's receptiveness to innovation (discussed in *Chapter 2*), the BIGT recognises the need to ensure that the UK maintains the leading position in Europe. UK patients must not be left behind in their access to innovative treatments.

Tapping the full potential of the NHS patient pool is one way of building sustainable competitive advantage in clinical research, and in bioscience, for the future. The power of this asset will grow over the coming 10 years, as new technologies such as genetics, transcript profiling, proteomics and metabonomics start to be used more frequently in clinical development and practice.



Wellcome Photo Library/Anthea Sieveking

UK patients must not be left behind

1 "Is the UK losing its competitive edge in the area of clinical research?", CMR International, 11/12/01. www.cmr.org

2 EU Directive on Clinical Trials, 2001. www.europea.eu.int/comm/research

Pharmacogenetic and pharmacogenomic studies have the potential to improve the therapeutic efficacy and risk profile of a range of drugs. The NHS patient pool can support the large cohort studies required to gauge differential drug responses in different genetic populations. Tissue samples from that patient pool can help researchers in public and private institutions answer fundamental questions about the origins of particular diseases. Ultimately, information on the NHS patient pool can answer important questions about the long-term efficacy of therapeutic interventions, and track unwanted drug complications should they occur.

The combination of the NHS patient pool, patient data, and the UK's clinical research capability (both NHS and academic) constitutes a truly distinctive asset base. It positions the UK to become a world leader in emerging medicines and in clinical research. This position will be much enhanced by the current investment project for comprehensive IT coverage for the NHS.

NHS-industry collaboration in 2015: the largest organisation for clinical research in the world

Where does the BIGT suggest taking this distinctive asset base? To focus the recommendations, consider a picture of the world that could be created by 2015.

The BIGT envisions a world in which five key players – the NHS, academia, Research Councils, the Department of Health (DH) and industry – carry a shared commitment to improve patient care through innovation. All parties will work in partnership to position:

- The UK as a world leader in experimental medicine, with a particular emphasis on the long-term study of chronic disease;
- The NHS as the largest organisation for clinical research in the world;
- NHS and UK academic medicine working jointly as a significant source of bioscience innovation.

To achieve this leadership position, the NHS, academia, and their funders, with the bioscience industry, will need to jointly build outstanding institutions and practices. BIGT envisions by 2015:

- A well-established right of first refusal option on clinical trials for all NHS patients suffering from designated, complex diseases (e.g. colorectal cancer, breast cancer) – as has effectively been the case for acute childhood leukaemia for many years.
- Centres of Excellence for early clinical experimental medicine, bringing together key technologies (e.g. genomics, imaging) in investigator-based units, with which industry can collaborate.
- One-stop access to the NHS for companies conducting later stage clinical trials (e.g. a single point of contact where companies could organise a 1,000 patient trial).
- A network of clinical trial centres that would conduct trials for industry at competitive prices.
- NICE would be involved early on in understanding the clinical development and use of costly drugs, and in defining the type of health economic data to be gathered, rather than developing into a post-registration hurdle.
- Several early-stage companies would be spun out of NHS trusts, with support from NHS innovation hubs and university technology transfer offices.

- Integrated industry-academic-NHS sites will be used for clinical research. Collaboration and risk-sharing between the NHS and the bioscience industry will need to be central features of this 2015 vision. Industry, for example, would secure access to experimental medicine groups they could not support on their own; to patients for clinical trials; and potentially to NHS data and tissue banks to better understand treatment outcomes. The NHS would secure early access to leading edge bioscience technologies (e.g. excess industry capacity in proteomics), to industry expertise (e.g. to support commercialisation of NHS-generated innovations), and to innovative therapies for their patients.

Achieving this vision will significantly improve patient care, by enabling the NHS to develop and test innovative therapies. It should also deliver better economic outcomes for all parties. There will be better use of taxpayer money in the NHS, with a focus on, and earlier access to, the most effective therapies and improved health economics with better patient outcomes. The UK will also improve the chances of sustainable commercialisation of bioscience companies, through access to pre-clinical and clinical researchers and patients.

Why this vision is important to the bioscience industry

Some may ask how this vision will benefit the bioscience industry, as many of the changes required affect the NHS alone, rather than the NHS-industry interface. Others may argue that such a vision is more important to UK patients – particularly those suffering from rare or expensive to

treat disease, to academic medical researchers or the NHS, than industry *per se*. Alternatively, it may be suggested that this vision is as valuable to major pharmaceutical companies (who also face long clinical development time-lines) as to bioscience companies.

The BIGT expects this vision will be appreciated by many of these parties. But it is particularly valuable to the bioscience industry.

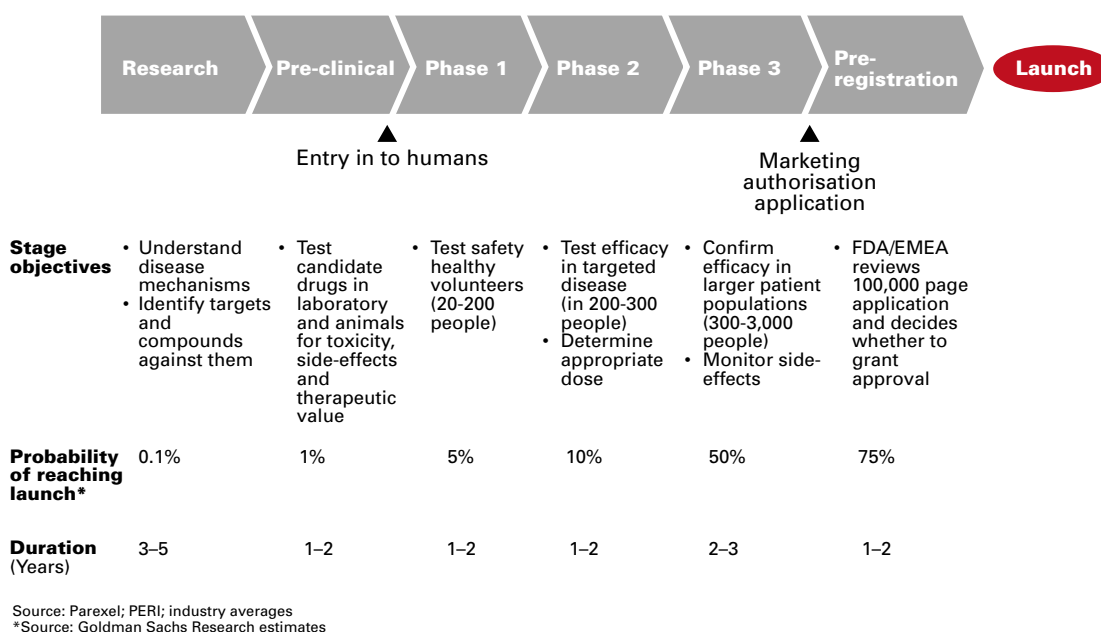
In summary: efficient, effective, swift clinical trials in the UK, and close collaboration with the main payer/provider are disproportionately important to bioscience companies due to their scale, capabilities, and geographic focus. Good clinical trial capability and infrastructure are also a major attraction to investment by global biopharmaceutical companies. Reduced investment by these companies in clinical research in the UK would also be to the detriment of the smaller bioscience firms.

1) Bioscience companies are often involved in the development of innovative drugs aimed at small populations. They depend on high quality, efficient clinical trials in appropriate patient populations to develop their treatments. They are also going to need to make significant improvements in clinical development to ensure innovative drugs continue to be developed – at affordable prices.

Developing a single prescription drug takes 10-15 years from discovery to approval (*Figure 1.1*), and usually costs £50-150 million in cash outlay, depending on the type of drug. Success is by no means certain. Taking into account the winners and the losers, the overall cost of bringing any single drug to market is in excess of £500 million.

Approximately half of that time and cost is spent in clinical development phases. Time spent in clinical development for biopharmaceuticals has doubled since the 1980s. The average total cost (including cost of failure and opportunity cost, as well as cash outlay) of developing a new prescription drug has grown 2.5 times in inflation-adjusted terms since the late 1980s³ – in part because of the increased regulatory burden. This cost rise is unsustainable and puts in jeopardy the development of innovative drugs aimed at small populations.

Figure 1.1 Drug development timeline



Fundamental changes are clearly needed in the structure and cost of drug development. Bioscience companies must use the latest scientific techniques to improve the focus and productivity of their R&D programmes. At the same time, the UK has the opportunity, through the NHS, to transform the efficiency and effectiveness of clinical trials. This will create a powerful magnet for the bioscience sector and potentially meet NHS priorities with regard to: minority patient groups, personalised medicines and new categories of treatment.

2) *Smaller bioscience companies lack the portfolio scale of large bioscience or pharmaceutical companies.* The former tend to have a small portfolio of drug candidates in development, and few (often no) products on the market. Most of the company value lies in a pipeline of products in development that carries a high level of portfolio risk. Unlocking that value hinges on advancement of compounds through clinical milestones. In this context, efficient, cost-effective clinical trials, and the opportunity to pursue risk-sharing collaborations, become disproportionately important. It is critical to remember, however, that failure of drug candidates often occurs and is expected.

3) Smaller UK bioscience companies lack the global reach of large bioscience or pharmaceutical companies. This makes them more dependent on effective collaboration with the UK domestic market to succeed: in pre-clinical development (e.g. through increased access to tissue samples); in clinical trials (e.g. through better access to patients, and agreed clinical goals with the eventual payor); and at product launch (e.g. through access to the NHS market, with favourable reimbursement/clinical guidelines). Through simple geographical convenience, the UK and neighbouring countries in Western Europe are likely to be the primary focus of clinical development for UK bioscience companies – in contrast to major pharmaceutical companies engaged in global trials and launches. If bioscience companies cannot do trials and launch products easily in the UK, they will fail to survive or they will leave.

4) Bioscience companies carry far fewer capabilities in-house than large pharmaceutical companies. Most in the UK do not have sales and marketing teams; many have only limited clinical/medical teams; few can afford best-in-class experimental medicine skills. Bioscience companies, therefore, have significantly higher incentives than large pharmaceutical companies to collaborate to access capabilities they simply cannot afford.

5) Bioscience companies have less money than large pharmaceutical companies. They cannot match the deep pockets of large pharmaceutical companies when competing for scarce resources, such as patients to enrol in clinical trials. They also lack the infrastructure to manage multiple centres of clinical development. The strong pre-clinical and clinical

contract research industry in the UK is therefore important to the success of bioscience companies. Bioscience companies cannot afford individually, nor do they have the volume of trials, to support dedicated clinical trial facilities where they are lacking in the public domain. Large pharmaceutical companies are clearly in a different position, as seen in GlaxoSmithKline's establishment of a dedicated clinical research unit at Addenbrookes Hospital in Cambridge. This means that any improvements that can be made to the speed and cost of pre-clinical and clinical development through the NHS can make a disproportionate difference to the bioscience industry. It also means that single points of contact within the NHS for clinical trials benefit bioscience companies differentially.

6) Bioscience innovations and spin-outs emerging from the NHS and academia should add to the critical mass and, therefore, bolster the bioscience sector.

Achieving the vision

Much progress has been made in recent years laying the building blocks for greater innovation within the NHS.⁴ NHS hubs have been created to support technology transfer of NHS innovations. For example, the creation of Biotechnology Exploitation Platforms (BEPs)⁵ have, in some parts of the country, formalised collaboration between academic institutions and NHS Trusts.

At the same time, a number of other new initiatives are starting to enhance and exploit the full clinical research power of the NHS, with cancer research at the forefront.

⁴ "A Framework and Guidance on the Management of Intellectual Property in the NHS" was published in September 2002, providing guidelines for trusts as they deliver on their obligation to exploit internally generated IP. www.innovations.nhs.gov
⁵ www.biotechplatform.gov.uk

The NHS and cancer research

The National Cancer Research Institute (NCRI)⁶ coordinates initiatives by the DH, MRC and cancer charities, along with industry as an equal partner represented by ABPI and AstraZeneca, and the two DH-funded related networks: the National Cancer Research Network (NCRN)⁷, and the National Translational Cancer Research Network (NTRAC)⁸, as part of the National Cancer Plan established in April 2001.

With NCRI providing strategic oversight, NCRN is creating precisely the kind of infrastructure needed to conduct large, multi-centre clinical trials, including designated clinical leads within regions and funding for key research staff (e.g. research nurses, pharmacists and data managers).

NTRAC is focused on translating research from the bench scientist to the frontline clinician, i.e. supporting the advancement of novel anti-cancer therapeutics from the laboratory into the clinic, and rapidly testing their effect in early clinical trials and diagnostics. NTRAC is creating a national network of 10 top class cancer research centres, embedded in the NHS, which integrate scientific and clinical expertise.

The NCRI is a partnership of 15 government and charitable organisations that fund cancer research, and is developing a coordinated cancer research strategy. From a clinical standpoint, the NCRI aims to increase cancer trial accrual rates from 4% to 10% through targeted funding (via NCRN), and by seeking to accredit trial units.

These cancer research institutions are creating precisely the kind of infrastructure, coordination, and clear points of contact outlined in the vision above, that industry most values. Industry is starting to get involved. GlaxoSmithKline has designated NTRAC as its preferred UK partner and has committed to placing a series of Phase I studies from its oncology portfolio with NTRAC via the NTRAC Coordinating Centre.

The BIGT supports all these initiatives and believes this approach will benefit other areas. The BIGT also recognises that the current upgrading of the NHS IT platform will be a critical enabler for this networked activity and studies of the NHS patient population, large and small.

Barriers to be addressed

The UK needs to capitalise on the building blocks already in place, and address three barriers to achieve the vision. These barriers are discussed in summary below, and more fully in the context of the recommendations that follow:

6 www.ncri.org.uk

7 www.ncrn.or.uk

8 www.ntrac.org.uk

a) Insufficient and inadequate infrastructure to put the vision into operation.

At the moment, the NHS lacks infrastructure of all types to make the vision happen, partly due to the lack of R&D funding (presently 0.9%, as highlighted earlier). This includes lack of physical facilities (such as beds for clinical research), IT systems, research staff (research nurses, pharmacists, data managers, clinical researchers), and equipment for enabling technologies.

b) Insufficient cultural support for innovation and for academic/industry collaboration within the NHS. This encompasses a web of issues. Focused on radically improving care delivery, NHS trusts do not prioritise non-target delivery related innovation. Burdened with heavy service loads, for example, clinicians do not have the time or the incentives to pursue clinical research. At the same time, there is a lack of mutual understanding and shared goals between the NHS and industry, which hinders future collaboration. One has only to look through the May 31st 2003 issue of the *BMJ*⁹, entitled “*Time to disentangle doctors from drug companies*” to understand the level of mistrust that exists. This is a critical barrier to achieving the BIGT vision.

c) Insufficient funding of R&D and its commercialisation in the NHS. The current budget for R&D within the NHS is small: ~£560 million per annum or 0.9% of the total NHS budget. All these funds are allocated, most are embedded, and would be difficult to reassign. The small amount of money that could be reassigned will not be enough to achieve the vision that BIGT outlines.

ACTION REQUIRED

Government, industry, academia, and the NHS, can collaborate to take three concrete actions to address these barriers and work towards the BIGT vision.

Infrastructure

1.1 Create a National Clinical Trials Agency (NCTA) to support excellence in clinical trials and clinical research within the NHS. The NCTA should be an arm’s length body, sponsored by the DH, working in collaboration with Research Councils UK. The NCTA will require significant start-up funding, but the industry partnership has the potential to generate income and become self-sustaining in the long-term.

The NCTA will establish a backbone of NHS infrastructure to support clinical research and facilitate industry collaboration, and fund a portfolio of programmes and projects.

Current situation: Bioscience companies find it challenging to access patients for clinical trials in the NHS. There is a lack of transparency regarding trials capacity; lack of

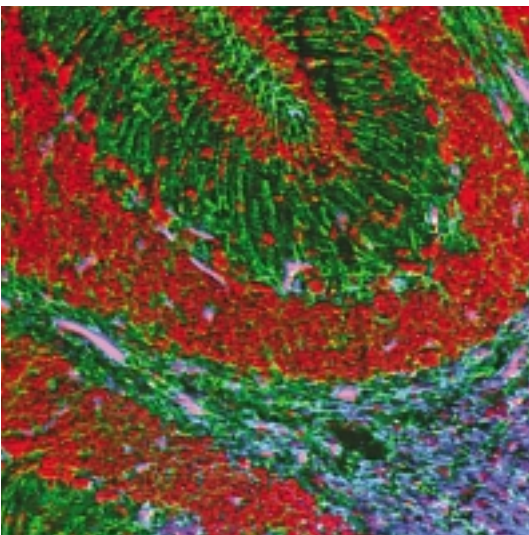


simple coordination mechanisms for dealing with multiple trusts or research centres; lack of standard practices when it comes to collaborating with industry – though progress is being made in this area¹⁰; and lack of the business mentality required to conduct these trials swiftly and to high quality standards. Medical consultants in some of the existing trials units express frustration at the need (as they see it) to solicit business personally and assist NHS Trust R&D offices handling contract negotiations. There are also clear infrastructure constraints: particularly a lack of clinical research facilities and the necessary research staff to support high quality execution.

The EU Clinical Trials Directive¹¹, which takes effect in May 2004, will substantially increase the managerial burden of conducting trials, as regulatory measures that previously applied only to late stage trials will now affect all clinical trials of investigated medical product including Phase 1 trials.

Importantly, in an increasingly decentralised NHS, there is no single organisation to champion clinical research and address the challenges above.

The recommendation: The BIGT recommends creation of a new **National Clinical Trials Agency (NCTA)** in the DH. There is currently about £45 million of existing money from NTRAC, NCRN, MRC and HTA. This would be topped up with new money each year to total £50 million in year one, £100 million in year two, £125 million in year three, £175 million in year four, £200 million in year five. Total new money over a five-year period would be £425 million. On the other hand the NCTA will also introduce new revenue into the NHS as increasing numbers of customers take advantage of the excellent services it offers.



Wellcome Photo Library/Y.C Cheng, P. Scotting

Possibly the ultimate in complex tissue – the human brain. This image shows a cross section through a lobe. Each cell type is stained a different colour.

The BIGT considers it is essential to create a new organisational entity to fund and lead clinical research in the UK. The NHS R&D Directorate is currently undergoing re-organisation, and the outcome is still unclear. The focus of the MRC trials portfolio covers late-phase clinical effectiveness and cost effectiveness studies, rather than phase I/II trials. As the MRC receives funding from the DTI, this does not provide sufficient links with the NHS to make clinical research a total success.

During the build-up phase, the NCTA would both subsume existing publicly funded networks and establish networks and infrastructure, potentially including dedicated facilities, as the MRC did in the creation of the MRC Laboratory of Molecular Biology, and the National Institute for Medical Research (NIMR) at Mill Hill. In equilibrium, the NCTA would focus, like Research Councils, on funding a portfolio of programmes and projects – focused in this case on clinical research conducted in NHS, NCTA, and academic medical facilities.

10 The lack of standard practices for collaboration has been addressed recently by the PICTF Clinical Research Group in two ways: firstly, the launch of the ABPI/NHS Partnership Agreement by Lord Hunt in March 2002 and, secondly, the launch of the Model Clinical Trial Agreement (a template for clinical trial contracts between the pharmaceutical industry and the NHS in NHS hospital trusts), launched by Lord Hunt in January 2003. www.doh.gov.uk/pictf www.abpi.org.uk

11 www.europa.eu.int/comm/research

NCTA governance should involve a wide range of stakeholders, including the bioscience industry, pharmaceutical sector, Government, patients, and research charities. At the outset a steering group should be set up.¹² Guidance would be taken from this group to flesh out the concept of the NCTA, and to run a consultation process with key stakeholders.

Funding for the NCTA will be a mix of capital and annual expenditure, totalling £425 million over a five-year period. This figure may seem large but a substantial sum will be required to make an impact on the quantity and quality of infrastructure, and of clinical research. In addition, the R&D funding from the DH for the NHS has fallen from 1.2% of spend in 1997 to 0.9% in 2002 and will be 0.77% in 2005. Like the responsibilities of the NCTA, the BIGT expects NCTA funding to develop over time.

The NCTA would ensure that its structure supported the *three* main areas that arise from clinical trials research:

- Academic-led research that can lead to company formation or other forms of communication (and may be partly industry supported).
- Commercial research that is aimed at regulatory approval. As industry would pay for the service, this would be income generating for the NHS.
- Academic/industry collaborative research that is not usually for regulatory purposes, but important to patients and the NHS. For example, NICE issues, head-to-head drug trials, and surgical protocol trials.

In order to support these three areas, the NCTA would have two responsibilities:

1.1.1 Develop the infrastructure required to support professional, efficient clinical trials. This would involve two types of activities.

i) Create a national network for clinical trials by:

- Mapping clinical trials capacity throughout the NHS.
- Identifying and learning from existing regional clinical trial practices in the UK.
- Identifying key centres and individuals who facilitate access to that capacity. As a first step, pilot centres should be established.
- Establishing 5-10 infrastructure offices in key locations to support trials and provide regulatory expertise (particularly educating researchers about the new EU Clinical Trials Directive).
- Handling contracts with CROs, biopharmaceutical companies and recruiting consultants to join trials.
- Ensuring the provision of essential training (e.g. to research nurses, clinicians and companies on regulatory issues, to small companies on good scientific practice).
- Advocating that the new NHS IT systems provide the functionality to support this network, and legitimate industry access for R&D purposes.

This network and national point of contact would enable more rapid response and better quality assurance. It would also provide a more formal, institutional interface between the bioscience industry, pharmaceutical industry, and clinical researchers, which would benefit all parties.

¹² The steering group would be chaired by the NHS Director of R&D and include as members: NHS, MRC, NICE, Medicine and Healthcare products Regulatory Agency, OST, DTI, Council for Heads of Medical Schools Academy of Medical Sciences, Association of Medical Research Charities (AMRC), key patient groups, and industry as the major sponsor of clinical research in the UK.

ii) Build business cases for, and fund further investments in critical physical and human infrastructure, which should include:

- Building on existing infrastructure from the MRC and the NHS R&D programmes.
- Developing networks along the lines of the NCRN and NTRAC, for respiratory, neuroscience, cardiovascular, paediatrics, musculoskeletal, and other disease areas. These are therapeutic areas of traditional UK strength that would benefit the most from the NCRN and NTRAC models.
- Dedicated Phase I/II facilities, as centres that bring in patients and healthy volunteers, administer drugs and monitor them for short periods.
- Research staff (including a cadre of research nurses and clinical scientists) and diagnostic equipment. Specialist research nurses in particular can make a real difference to the ease with which clinical trials can be conducted.

Industry and Government are both moving to create infrastructure for clinical research. The national cancer initiatives have already been mentioned. There are also other models, such as the Irish government initiative below:

The Irish initiative

The Irish government has partnered with BMS, Pfizer, the European Organisation for Rare Disorders, and the Genetic Interest Group to create the European Institute for Clinical Trials in Rare Diseases. This is a not-for-profit institution, based at University College Cork, which will establish a pan-European network specialising in clinical trials of products that have received orphan drug designation.¹³

Considering that different infrastructure models could be adopted, the BIGT recommends that the NCTA should build a variety of relevant business cases (or accept bids from different groups, including CROs). All will be focused on building infrastructure and capability within the NHS, which in turn could serve as a platform for establishing wider networks within Europe. Industry should be able to access these facilities for clinical trials at competitive rates, creating a revenue generating opportunity for the NHS. The possibility of creating joint public-private facilities should also be open to companies or consortia with sufficient funds to partner Government.

1.1.2 Fund a portfolio of clinical research programmes and projects. This should include hypothesis-driven, pragmatic, and long-term studies. This is what the BIGT recognises as standard Research Council work: providing 'premium status' grants to fund quality projects. These grants will go to public projects carried out by academics and/or NHS clinicians.

13 "New Institute Formed to Focus on Trials of Orphan Drugs", BioWorld International, 11/6/03. Only nine orphan drugs have been approved by the EMEA in the three years that the designation has been operating. But around 160 designated Orphan Medicinal Products have been registered. Part of the reason for the low approval rate is the small size of many of the biotech companies developing these products. About 90% of applicants come from small bioscience companies. www.Bioworld.com

In addition, at least some portion of this portfolio should focus on enabling NHS-academic-industry collaboration, and create vehicles for public-private partnership. The BIGT wants to create a solid infrastructure for conducting clinical trials in this country from public funds, but also wants to 'nucleate' collaboration between the NHS and the bioscience industry. Clearly the bioscience industry has little in the way of excess cash to invest in projects, while the pharmaceutical industry is likely to have more. The BIGT, however, wants to create the possibility of NHS-industry partnership, enabled by risk-sharing agreements, for example.

Finally, funds should be made available to work on innovative methodologies for clinical trials, such as new processes and ways of analysing data, which would help the NCTA, and therefore the UK, to maintain a leadership position.

People

1.2 Create incentives and career structures within the NHS and academic medicine to promote clinical investigation. This will be critical for addressing current cultural barriers within the NHS.

Current situation: With challenging targets for service delivery improvement, NHS Trust CEOs and clinicians prioritise patient care. Indeed, most clinicians, including many clinical academics, lack the time, motivation and incentives to pursue clinical research. Clinical research is not built into their targets, and career structures are poor. The BIGT believes that R&D-driven innovation should also be a priority, particularly in leading academic medical centres.

The recommendation: The BIGT recommends practical steps, focused on incentives and enablers.

1.2.1 Develop an innovation scorecard for NHS Trusts.

The innovation scorecard would include:

- Number of clinical trials led by and patients entered by individual clinicians;
- Number of clinical trials and patients entered by collaborators;
- Job plans/appraisals – to include clinical trials and R&D;
- Number of MD and PhD students working on patient related projects registered in the institution;
- Number of postgraduate degrees awarded to Trust employees and associates.



OSI Pharmaceuticals

1.2.2 Create two new cadres of clinical researchers by funding 4-5 year fellowships with programme management support (10 each per year, up to a rolling total of 50 each):

- Clinical investigators with access to programme management support;
- Clinically trained scientists (not on the biomedical specialist register) with consultant status, salary and related opportunities, focused on laboratory and hypothesis-generation work projects with programme management support.

Considering the strong focus on providing a service to patients, research posts are suffering. The field of clinical investigators is changing, yet basic science investigators are filling 'clinical lecturer' posts.

However, there is an increasing need for a broader physiological approach by clinical investigators. Doctors are also diverted from science and lose their science skills. The BIGT recognises the need for clinically trained scientists that are full-time scientists who understand medicine.

1.2.3 Monitor and celebrate progress by upgrading the functionality of the NHS National Research Register (NRR) and developing a communications strategy for the NHS R&D programme (e.g. reporting annually to highlight major achievements), ensuring that progress of this type is highly regarded by the Research Assessment Exercise (RAE).

The BIGT recommends the need to integrate, celebrate, and publicly promote the collective achievements of NHS R&D. Many of the current achievements of NHS R&D are only partially logged in individual Trust reports. The NHS Trusts are required to report their research projects involving patients in the NHS NRR.

This register is difficult to read, does not record outcomes and is not easily available to the public.

It is also important to encourage alignment and prevent duplication of effort among the different players involved in NHS innovation, including:

- NHS Trusts;
- Universities, medical schools, and their technology transfer offices;
- Hubs, Biotechnology Exploitation Platforms (BEPs), and technology transfer offices (TTOs);
- Regional Development Agencies (RDAs) and Special Health Authorities (SHAs);
- And at a national level, the DTI, DH, and Department for Education and Skills (DfES).

The scope for duplication is considerable, and it is important to ensure that all parties collaborate for maximum efficiency.

Funding of R&D

1.3 Increase the total funds spent on R&D within the NHS initially stepwise over five years, from their current level of 0.9% of total spending to 1.5%.

Current situation: The nominal budget for R&D today and its commercialisation within the NHS is ~£560 million per annum, or 0.9% of the total NHS budget. In practice, the majority of these funds are for infrastructure and supporting service, and as such are embedded and cannot be re-assigned. Over 80% of the innovations funded lead to service improvements, while only 20% focus on the type of product commercialisation concerned here.

Indeed, fully three quarters of this money goes directly to Trusts to fund two programmes:

- Support for Science (£330 million), funding, added service costs related to Research Council, Research Charity, and other NHS partners funded research. Research Councils do not typically fund development-related research.
- Priorities and Needs (£110 million), funding the Trusts' own, typically disease or service-related research.

Funds focused specifically on product-related innovation total about £10 million:

- Intellectual Property Management (£2.2 million): which supports patent costs.
- New and Emerging Applications of Technology Programme (NEAT) (£1 million, with plans to increase it to £1.5 million by 2005): intended to fund proof of concept/principle, in the bridge between innovation and application.
- Health Technology Devices Programme (£2 million from the DH Policy Research Programme budget): a LINK programme.
- A Seed Fund (£4 million of which £500,000 per annum will come from NHS R&D): under development, to assist with commercialisation of NHS-generated ideas.
- NHS hubs (£2 million): Hub resources remain limited. For

example, the London hubs have a budget of £1.3 million per annum (£190,000 coming from the NHS budget) to help commercialise innovations in 32 Trusts.

As new programmes in many cases, it is understandable that many of these funds remain at pilot scale. Relative to the overall opportunity, however, these remain limited resources. Importantly, little of the R&D budget is available to fund the kind of infrastructure described above (except NCRN, NTRAC, MRC networks and a few small clinical trial centres). The BIGT believes change can only be effected with new money.

The recommendation: Increase the funds available for R&D within the NHS, building a graduated rise from 0.77% until the 2006 comprehensive spending reviews taking into account the DH's 'payment by results' review. These funds should support as a priority to NCTA. The increase needs to sustain the rate of innovation in the NHS and strengthen its culture and infrastructure. Some portion of the increased funds should, in addition, be used to bolster product-based innovation and IP generating projects. An example would be the gene array research programmes:

Gene array research programmes

Increased funding would allow creation of four new national gene array research programmes. Building on the ambitions in the Genetics White Paper to ensure that the UK is involved in the discovery of the role of genes in health and disease. The four programmes should be in key therapeutic areas: cardiovascular, central nervous system (including mental health), musculoskeletal, and respiratory, complementing research already underway in cancer. This would establish a facility of prime importance to Biobank UK, for research on its tissue and data collections in addition to primary research. This will require £8 million in set-up costs and an annual operating budget of £4 million in total.