

**Research Report July 2008**

**DELIVERING INNOVATIVE CANCER  
DIAGNOSTICS AND TREATMENTS  
TO PATIENTS**

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newton's  **apple**



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**Foreword** by Dr Monica Darnbrough CBE, Member of the Board of Trustees, Newton's Apple, Chair of the Cancer Working Group, Newton's Apple and Former Director of Biosciences Unit at the Department of Trade and Industry

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## ■ FOREWORD

Newton's Apple's first report '*Cancer Vision 2025: The Science Pathway to Effective Treatments and Services*' made a number of recommendations about evidence-based preventive measures and most importantly about action to raise public awareness of the signs and symptoms of early cancer, which we are pleased to see have been addressed in the Government's Cancer Reform Strategy. Newton's Apple also recommended that baseline figures be established about people's knowledge of cancer in order to identify gaps and develop appropriate and effective tools.

The Government included some impressive statistics in its recent Cancer Reform Strategy. For example they state that improvements have led to: "Over 99% of patients referred immediately by their GP with suspected cancer being seen within two weeks, compared with 63% in 1997" and "More than 99% of patients receiving their first treatment for cancer within one month of diagnosis". However, too many individual patients still have stories of unacceptable delays before the symptoms they present to the GP are recognised as indicators of possible cancer. They therefore wait for long periods with symptoms, and with growing cancers, before the referral and full diagnostic process begins. Particular concerns about delays have been reported by the Teenage Cancer Trust whose young cancer patients reported that their symptoms were not recognised as indicators of cancers. We are concerned about the difficulties that GPs have in diagnosing cancers. At the same time, we are aware that researchers are discovering biochemical changes associated with cancers which could be used as diagnostic tools if only they were translated from the laboratory into tools for routine use in analysing blood and tissues taken from the patient. We want to see more support given to development of diagnostics as well as to new treatments.

At the Newton's Apple stakeholder consultation event, people with first hand experience of research, development, and of the National Health Service, Medicines and Healthcare products Regulatory Agency and National Institute for Clinical Excellence, discussed concerns about the process of turning research findings into novel diagnostics and treatments for cancers. Newton's Apple identified a number of 'bottlenecks' which are described in this report. One important issue concerns the development of innovative treatments for cancers which occur in only small numbers of patients. Some new treatments will require genetic screens or diagnostics to be developed in parallel with the treatment itself, in order to identify those patients who have specific biochemical characteristics and who will therefore benefit from the treatment. For other diseases the introduction of the so called 'orphan drug directive' has encouraged companies to develop drugs for treating diseases which affect very small numbers in the population. We would like to see incentives introduced so that companies find it financially worthwhile to invest in developing treatments targeted at small groups of patients.

We are also concerned about the take-up of innovative diagnostics and treatments and their adoption by the NHS, particularly for use by GPs.

Newton's Apple aims to involve young researchers, who are working in academia, charity and companies of all sizes, as it explores issues in science policy and Newton's Apple is running a programme called Newton's Heirs to inform and encourage their involvement. In this report we have picked up frustrations among researchers about the difficulties they experience in knowing how to satisfy bureaucracy surrounding the use of human tissues which they need to use to look at what happens as a cancer progresses. The Human Tissue Act introduced new safeguards for patients and their families and while researchers acknowledge the need for that, they have been finding it time consuming and expensive to meet the new requirements. Similarly, problems remain in getting timely ethical committee and other approvals for research projects. This report describes some excellent collaborative initiatives which should help researchers to get their 'paper work' done so that they can focus on the science. We hope that this report will help to increase awareness of these activities to support UK researchers.

**Dr Monica Darnbrough CBE**

**Member of the Board of Trustees, Newton's Apple**

**Chair of the Cancer Working Group, Newton's Apple**

## ■ CHAPTER I: INTRODUCTION

During the 1980s and 1990s, cancer had a low profile in the UK. Survival rates were among the poorest in Western Europe and there were very high death rates particularly for lung and breast cancer. In 2000 the Government published a comprehensive plan to tackle cancer, the 2000 NHS Cancer Plan. This has led to significant advances in the quality of care and treatment that cancer patients receive and has helped to revolutionise cancer services in England. In 2007 the Government released its Cancer Reform Strategy (CRS), which builds upon the 2000 Cancer Plan and sets out the agenda for the next five years for delivering cancer services in England. According to the CRS:

- Cancer mortality in patients under the age of 75 years has fallen by 17% between 1996 and 2005 – this equates to approximately 60,000 lives saved in this period.
- Survival rates for a number of cancers (such as colorectal and breast cancer) have improved each year and are coming into line with those in other European countries.
- More cancers are being detected as a result of the expansion of the NHS's screening programmes.
- Faster referral of cancer patients has resulted in more patients being rapidly diagnosed and treated.
- There has been additional financial investment in cancer services, which has helped to deliver an expanded cancer workforce with an enhanced range of equipment. This includes some 1,500 multidisciplinary teams that are now able to provide more coordinated and higher quality care for patients.

Newton's Apple commends the Government for its commitment to building on its strategy for cancer in England through the CRS. Newton's Apple also notes that the CRS promises action on a number of areas that were highlighted in the 2007 Newton's Apple report, *Cancer Vision 2025*.

Newton's Apple recommended that "A key part of any new CRS should be to spread awareness about evidence-based preventive measures and also to explore what sort of incentives might help improve the uptake of evidence based advice." To this end the CRS commits to:

- 1) A new National Awareness and Early Diagnosis Initiative to coordinate a programme of activity to support local interventions to raise public awareness of the signs and symptoms of early cancer,
- 2) The development of national surveys to collect information on awareness of and attitudes to cancer risk factors and symptoms among different groups within society and on patients' experience of treatment and care.

*Cancer Vision 2025* made the critical point that “baseline figures need to be established about people’s knowledge of cancer in order to identify gaps and develop appropriate and effective tools.” This, again, will be addressed by one of the action points put forward in the CRS; “Awareness of risk factors will be tracked and action taken to improve public awareness.”

Finally, Newton’s Apple recommended improvements to evidence-based written information for use by patients. The CRS pledges that cancer patients; “will be able to access information about the performance of their cancer services, enabling patients to make informed choices which reflect their priorities” and “action will be taken to inform and empower patients so that they can play as active a role in decisions about their care and treatment as they wish.”

Despite these positive developments, Newton’s Apple believes that more needs to be done. The primary focus of the CRS has been on the delivery of care to cancer patients. However, improvement still need to be made, especially in terms of supporting the development of promising new discoveries into innovative diagnostics and treatments for cancer patients.

Shortly before the release of the CRS, Newton’s Apple asked a range of stakeholders to identify those bottlenecks which they consider to be slowing the development and introduction of innovative cancer treatments to patients. These problems need to be addressed in order to ensure that the UK remains at the forefront of cancer research and is therefore able to deliver innovative treatments to cancer patients. These bottlenecks included issues:

- For researchers in ethical approval processes and the use of human tissues.
- In ensuring researchers understand the processes that must be undergone in order to translate their research findings into interventions for patients.
- In the development of innovative diagnostics to accompany new, more targeted, therapies for cancer.
- And in the adoption of innovative diagnostics and treatments by the NHS, particularly for use in primary care.

In the following chapter Newton’s Apple outlines some of the new initiatives being put in place to tackle such bottlenecks and makes recommendations for additional future work that will improve the delivery of new interventions to cancer patients. A key need discovered by Newton’s Apple is for Government, research funders and all those providing services to patients to work together to ensure that cancer services continue to improve and provide the highest quality of care and treatment to patients.

## ■ CHAPTER 2: REMOVING THE BARRIERS TO BASIC AND TRANSLATIONAL RESEARCH

The scientific understanding of cancer is continuously improving thanks to global research. As discoveries are made, the drug development community adapts its work to ensure that this scientific knowledge can be translated into something that will be of benefit to patients. Basic research is the lynchpin of all pharmaceutical endeavours. Much of this research is funded by charities and the Government and carried out in universities and institutes across the UK.

Many steps have to be taken before the benefits of basic research are felt at the patient level. Research, whether conducted within academia or in industry, by large pharmaceutical or by small biotech companies, provides a rich source of knowledge. An appropriate environment must be created across the UK to ensure that this research can continue. A multidisciplinary approach is needed, involving all stakeholders in the cancer community, to ensure that the outcomes of research are effectively and speedily translated into benefits for the patient. In the following chapter, Newton's Apple makes recommendations on what some of these steps should be.

### 2.1 MAKING HUMAN TISSUE RESEARCH EASIER

Human tissue samples (including solid tissue, biofluids and their derivatives) play a critical role in cancer research, by helping to build a deeper understanding of cancer and its underlying mechanisms. Studying changes at the molecular and cellular level provides the means for a fundamental understanding of a cancer and its development. This in turn increases the chances of effective new medicines and treatments being developed to treat cancers that currently are either poorly treated or lack suitable treatments altogether. The insights from this new knowledge could also lead to earlier diagnosis and so earlier and more effective treatment.

In order to move forward with the development of new cancer biomarkers (Box A), novel diagnostics and effective treatments, researchers within both academia and industry require access to tissues and data from existing patients in order to gather evidence about the effects of biologically active substances and their undesired side effects. This includes access to tumour tissue and biological profiles of patients, both living and deceased.

The Human Tissue Act 2004 regulates the removal, storage and use of human tissue – defined as “material that has come from a human body and consists of, or includes, human cells”. The Act was formulated in response to a small number of instances of what were considered to be abuse of human tissues and patient rights. The Act covers England, Wales and Northern Ireland and makes consent the fundamental principle underpinning the lawful storage and use of body parts, organs and tissue from the living and the deceased. The Act established the Human Tissue Authority (HTA)

to ensure adherence to best practice which makes it unlawful to carry out such licensable activities without a licence obtained from the HTA. The role of the HTA is not only to provide licences for tissue use, but also to devise and issue Codes of Practice and provide other practical advice and guidance surrounding the Act to the scientific community.

The regulatory framework resulting from the Act aims to assist researchers by increasing public confidence in research using human tissue. However, although they recognise the importance of the regulation, some academic and industry-based researchers feel that it is hindering their research.

There is a concern among both academic and industry-based research teams regarding the need for additional staff to handle the burden of regulation and the costs of becoming a licensed tissue bank. These costs are substantial and hence, research funding is diverted from the often fixed research budgets to meet these requirements. Both academia and industry-based research teams recognise that good research governance is crucial but feel that the bureaucracy and cost involved is absorbing too much of the time and investment in cancer research.

In order for a research facility to obtain a licence from the HTA, it must maintain detailed, accurate records of stored tissue, ensure the privacy of those records, and designate an administrator to oversee the tissue bank. They must also create standard operating protocols (SOPs) for obtaining consent. Additionally, the financial cost of a licence is £5,200 per licence, and depending on the number of research departments this can be extremely costly. One leading UK University consulted by Newton's Apple, estimates that it costs £51,000 per year to comply with the Act. A 3 year licence would therefore cost the university £153,000.

One of the primary reasons for the establishment of the Act was to tackle public concerns about the lack of regulation of human tissue use for research. In 2004/05, when the Act had been established but not yet implemented, an Ipsos MORI Science in Society survey found that 51% of those surveyed said they 'had confidence in the way science was regulated'. However, a 2007 Ipsos MORI poll conducted on behalf of the HTA (just over 1 year after implementation of the Act) found that 52% of those polled were 'confident about the way that donation, removal, storage and use of human organs and tissue are regulated'. Although these are not precisely the same measure of confidence, they are similar enough to suggest that the benefits of the regulation in terms of increasing public confidence could be minimal, whereas the costs and burden to cancer research alone could be substantial. However, there is not yet sufficient evidence available to create a balanced analysis of the impact of human tissue regulation. The evidence still needs to be gathered.

In 2007 an influential paper by the Cancer Campaigning Group called for the HTA to carefully monitor the impact of the legislation, but as yet, no publicly available impact assessment appears to have been produced. **Newton's Apple therefore recommends that the Government sponsor an independent review of the regulatory framework resulting from the HT Act**

and its impact on the practise of research in the UK. Such a review should be conducted in cooperation with the HTA and should examine whether the regulatory system in place is contributing positively to the Government's ambition that the UK should be the best place in the world to carry out research. If such a review were to find the regulation to be detrimental in any area it should make recommendations on how the regulation could be refined in order to ease the problem.

## **BOX A**

### **Biomarkers**

The U.S. National Institutes of Health define a biomarker as: A distinctive biological or biologically derived indicator (as a biochemical metabolite in the body) of a process, event, or condition.

Biomarkers can be useful across the whole spectrum of translational and clinical research, from basic biomedical research through to pharmaceutical discovery and preclinical development, clinical trials, and patient care. Clinical applications include: disease screening, diagnosis and prognosis/prediction, treatment planning and monitoring, and post-treatment observation. For drug development, biomarkers may be used to assess candidate drugs for evidence of safety and efficacy at each step of the drug development process. Biomarkers should improve patient outcomes by ensuring that each patient receives the drugs that are most likely to be effective for his or her particular tumour, thereby enhancing the effectiveness of the drug and limiting toxicity. In addition to improving the effectiveness of therapy, biomarkers have the potential to improve the cost-effectiveness of treatment, both by avoiding the use of costly therapies to which a cancer will not respond and by avoiding the need to manage the associated side effects of such treatments.

### **Diagnostic Biomarkers**

It has been a long-standing ambition in cancer research to identify the molecular mechanisms by which cancers develop, and then to detect the molecular markers or biomarkers of those cancers early so as to target the mechanisms of the developing cancers with drugs specifically designed to attack them. In recent decades, knowledge about the biology of cancers has increased greatly and some strides have been made towards reaching this ambition. For example, the over-expression of HER2 (a growth factor receptor) in breast cancer serves as a biomarker for prognosis and for treatment with Herceptin (a drug that targets the function of that receptor).

However, for most cancers, the molecular characteristics have not been fully classified and there are no known or validated markers for early detection or targeted therapy. Diagnosis of cancers is still largely based upon morphological examination of tumour biopsy specimens and sometimes with the use of body scanning technologies. This approach has significant limitations for predicting a given tumour's potential for progression and response to treatment. In addition, most cancer drugs are toxic agents that affect cell growth, so they often have significant side effects due to their activity against normal tissues in the body – in particular those with high cell turnover rates such as the bone marrow and intestinal mucosa. The availability of accurate and relevant biomarkers could considerably improve the ability to identify targeted drug therapies.

## The Confederation of Cancer Biobanks

To identify new means of preventing, diagnosing or treating cancer, tissue samples from cancer patients need to be collected for use by researchers. A wide variety of tissue samples exist. Some are within banks, and others are gathered for specific research projects or for the use of an individual laboratory. However, samples belong to the research institutions where they were collected and therefore the decision to allow or deny other researchers access to the tissues is based on the discretion of the tissue bank administrator. Recognising that this could be detrimental to cancer research, the Confederation of Cancer Biobanks (CCB) was established by Glasgow Biobank, onCore UK, Tayside Tissue Bank and the Wales Cancer Bank, with the support of the National Cancer Research Institute (NCRI). Their aim is to allow human tissues for cancer studies to be widely available to all researchers by facilitating their collection and distribution. The CCB is currently a consortium of nine cancer biobanks (Box B), but is still growing to bring more of the other existing or new cancer biobanks into the cooperative group. The CCB supports the development of a standard operating protocol for all of the biobanks therefore making the processes involved in the collection, preservation, and storage of samples universal. It is also constructing a database which incorporates information from all of the cancer biobanks, in order to provide researchers with a single portal for accessing human tissue.

The CCB is an excellent example of how the burden of regulation on researchers can be effectively reduced by collaboration within the cancer community and should go a long way towards addressing issues encountered by researchers in working with the HT Act. **Newton's Apple supports the NCRI in urging new banks planning to collect and distribute human tissue to join at the earliest stage possible.**

## **BOX B**

### **The Confederation of Cancer Biobanks**

The Confederation of Cancer Biobanks (CCB) is currently made up of nine biobanks:

- CamUro-Onc Biorespository
- Candis Cancer Tissue Bank Research Centre
- Glasgow Biobank
- Leukaemia Research Fund
- Northern Ireland Tumour Bank
- OnCore UK
- Tayside Tissue Bank
- UK DNA Banking Network
- Wales Cancer Bank

## **2.2 FROM DISCOVERY TO DEVELOPMENT**

Most researchers in higher education establishments and charities are aware of the potential that their work might have for the development of new drugs to fight cancer. Many research organisations already have technology transfer offices that can provide guidance for academic researchers to support them in identifying options and opportunities for translating their research into diagnostics or treatments. However, there are many researchers who do not have access to such support or do not avail themselves of it.

Providing information to academic researchers about the steps which have to be taken in drug development will allow them to take such factors into consideration when planning their research. It should also enable them to collect the 'right' data to support their 'proof of concept' and to establish safety profiles. This could make their discoveries more attractive to investors and avoid the need for developers to repeat early, preclinical, laboratory studies. This should speed up the transition of potential treatments from the laboratory to Phase I trials – the first step in delivering treatments to patients.

The formulation of a drug development training course would provide an easy means of encouraging academic researchers to take into account aspects such as regulatory licensing of a drug and clinical development/commercial scale supply, during the research process. Such a course would not only encourage younger researchers to think ahead, but it would help established researchers to think about the different aspects they should consider when developing new agents.

**Newton's Apple suggests that such a course might cover the following points:**

- *The standards required by regulators such as compliance with Good Laboratory Practice (GLP), Good Clinical Practice (GCP) and Good Manufacturing Practice (GMP).*
- *The requirements of GMP – (Box C).*
  - *The need to think about the quality and quantity of manufacturing of the agent if it is to be used later in clinical trials, and hence the need to think early on about involving manufacturing or bio-manufacturing expertise.*
  - *Where the agent will be manufactured and whether the site meets international current GMP standards.*
- *The biological, chemical and animal studies required for preclinical regulatory submission encompassing information regarding:*
  - *Pharmacokinetics, Pharmacodynamics (Box C), Safety studies – toxicology.*
  - *The formulations and delivery systems to be utilised.*
- *What intellectual property protection needs to be obtained and when and how it should be done.*

Such a course would provide a bridge to ensure the smooth transition between the discovery, development and eventual commercialisation of novel entities. **Newton's Apple recommends that academia, industry and regulatory bodies collaborate, via an organisation such as the UK Clinical Research Collaboration (UKCRC), to develop a training course for anyone working in the discovery and development of medicinal and diagnostic compounds.** If such a course were a success in the cancer field it could then be rolled out to other clinical areas and incorporated into researchers' training.

## **BOX C**

### **Definitions**

#### ***Pharmacodynamics:***

A branch of pharmacology dealing with the reactions between drugs and living systems.

#### ***Pharmacokinetics:***

The characteristic interactions of a drug and the body in terms of its Absorption, Distribution, Metabolism and Excretion (ADME).

#### ***Good Manufacturing Practice (GMP):***

Refers to good manufacturing practice regulation, which is used to control and manage the manufacture and quality control testing of drugs, medical devices and some food. The regulation ensures that products are safe, pure and effective for the consumers.

Definitions from:

Medline Plus (a service of the U.S. National Library of Medicine and National Institutes of Health) [www.nlm.nih.gov/medlineplus/medlineplusdictionary](http://www.nlm.nih.gov/medlineplus/medlineplusdictionary)

The GMP Institute [www.gmp1st.com](http://www.gmp1st.com)

## **Collaborations Aiding Transition**

There are a number of excellent collaborative initiatives that are already underway, which have been designed to speed up the transition of ideas from the laboratory to Phase I studies.

The Medical Research Council has recently announced a new funding stream to support the translation of basic research into clinical benefit. The Developmental Pathway Funding Scheme (DPFS) will support the development of new therapies, interventions and diagnostic tools, and will strongly encourage partnership applications between academics and charities and industry. This new fund could go some way to enable “proof of concept” and so help close the funding gap between discovery and development.

Two other helpful collaborative initiatives are a system that allows a single ethics application for translational and clinical research (Box D) and the “off-the-shelf” Model Clinical Trials Agreement (mCTA).

## **BOX D**

### **A Single Ethics Application for Translational and Clinical Research**

An integrated system for research applications was introduced across the UK in January 2008. The system was designed in order to streamline the permissions and approvals application processes, which have often been criticised by researchers for being cumbersome and time consuming. Rather than having to complete a number of separate application forms for each review body, researchers can now enter their information once into a single, Integrated Research Application System (IRAS). Using filters, the system ensures that data is collected and collated appropriately to the type of study, approvals and permissions required.

IRAS is especially noteworthy because of the extent of the collaboration involved. Led by the National Research Ethics Service and run under the UK Clinical Research Collaboration, the system is designed for UK-wide use. The initiative is supported by the NHS R&D Forum, the major regulatory and governance bodies, the UK Health Departments, the UK Clinical Research Network (UKCRN), the Forum of NHS Wales for R&D Management in Health & Social Care (FORWARD) and various funders of research.

The IRAS captures information needed from researchers when submitting for the relevant approvals from a range of review bodies:

- Administration of Radioactive Substances Advisory Committee (ARSAC)
- Gene Therapy Advisory Committee (GTAC)
- Medicines and Healthcare products Regulatory Agency (MHRA) – Medicines and Devices
- National Health Service (NHS) and Health and Safety Commission (HSC) research offices
- National Research Ethics Service (NRES)/NHS/HSC Research Ethics Committees
- Patient Information Advisory Group (PIAG)

The mCTA was published by the Department of Health and Association of the British Pharmaceutical Industry (ABPI) in February 2003 and aimed to produce a model agreement that all trial sponsors, and trial-running NHS hospitals, would regard as acceptable for use without any modification. This would have the benefit of speeding up the contracting process and initiating research at the earliest opportunity. It would also save money for the NHS and pharmaceutical and biotech companies by removing the need for bespoke drafting and legal review of trial specific agreements.

In November 2005, the Clinical Research Working Group of the Pharmaceutical Industry Competitiveness Task Force (PICTF) commissioned a thorough review and revision of the mCTA, in order to update the agreement in light of a number of recent developments. Consultations with pharmaceutical and biopharmaceutical companies, Foundation Trusts and Research and Development offices in research-active NHS Trusts were also conducted. Detailed discussions were also held with representatives of medical schools to make sure that universities, who employ many investigators involved in clinical trials, were fully informed about projects which their staff are involved in. Following this consultation process, a new agreement – the “NHS-ABPI-BioIndustry Association (BIA) mCTA 2006” was issued. The updated mCTA covers all the issues that sponsor companies and NHS bodies believe are essential to represent the legal relationship between them. It is proposed that the mCTA be used routinely without modification by all pharmaceutical and biopharmaceutical sponsors of clinical trials and the NHS hospitals in which patients are recruited. The documents are endorsed for use without modification by Health Departments throughout the UK, the trade bodies (ABPI and BIA), the NHS Confederation, the NHS Research and Development Forum, the UKCRC, the Foundation Trust regulator (Monitor), and the Council of Heads of Medical Schools. Versions have also been adapted to take into account the special governance and legal arrangements of Scotland, Northern Ireland and Wales. The mCTA is designed to simplify and therefore speed up the process for signing off and initiating trials involving NHS patients in NHS hospitals. It removes any need for either sponsors or hospitals to undertake further legal review of contracts in response to another party proposing modifications and clearly highlights the progress that can be made through Government, industry and academia collaboration.

There are still many barriers between basic and clinical research that need to be overcome, if new knowledge is to be translated to the clinic most effectively – and lessons taken back again to the bench. For example some clinical trial sponsors have been unwilling to accept the mCTA without revisions being made, which has led to some clinical trials being stopped. These challenges could be having adverse effects on the development of diagnostics and treatments for cancer patients at a time when innovation should be thriving. **Newton’s Apple acknowledges and welcomes the collaborative initiatives above and would like to see the dialogue between Government, industry, academia, and regulatory bodies through collaborations grow further, in order to speed up the transition of research findings into interventions for patients.**

## 2.3 ENCOURAGING PERSONALISED MEDICINES

Development of innovative new drugs is driven by the pharmaceutical and biotech industry. The associated costs are very high for a candidate drug that makes it through successful registration and commercialisation and can routinely run in the order of five hundred million pounds (according to figures from the Centre for Medicines Research International). Further evaluation of the clinical usefulness of a drug also adds significant additional costs. The number of candidate drug compounds which fail far outweigh those that get to market to provide financial return on the investment. For those that do make it the reward can be high but is ultimately limited by the period of market exclusivity. Development can therefore be viewed as a high risk and high reward model. The degree of risk and potential reward varies between candidate drug development projects. The resources and scientific and technological abilities of the pharmaceutical industry are considerable but not unlimited. Thus careful selection of research and development projects to invest in, and prioritise, must be made and is a complex assessment that must balance risk, investment requirements and opportunities (known as portfolio assessment).

In addition to this, patients, healthcare professionals and government officials are calling for better targeted drugs so that the right medicines are administered to the right patients (often termed personalised medicines) to achieve effective treatment and better utilisation of health care budgets. Through greater understanding of the disease processes and evolution at a molecular level, translational science approaches offer the possibility of developing better and more cancer-cell selective medicines. In the field of oncology it is recognised that some tumours can be better characterised to enable a rational selection of a drug therapy based on the genetic mutation driving the tumour. From a development perspective this requires that a candidate drug and accompanying diagnostic for detecting the mutation or biomarker (Box A) be developed concurrently. Once the drug is registered there must be access to the diagnostic and the results from the diagnostic tests need to be reliable and readily available, either through a laboratory service provider or a diagnostic kit that can be run within the hospital setting. This increased complexity involves greater upfront investment and increased technical and commercial risk, resulting ultimately in the selection of a smaller population to treat.

There are currently very limited numbers of drugs which are targeted to particular cancer patient subtypes (e.g. Herceptin), but as the disease is better understood at the molecular level and candidates are identified to target these patient subpopulations, such approaches become more technically feasible. However, personalised medicine approaches are often deprioritised within the portfolio assessment by pharmaceutical companies because of the increased complexity and costs involved in their development. Additionally, the time taken to develop such approaches can be longer and further limit the patent exclusivity of a drug.

In recognition of this increased complexity and to support development of personalised medicine approaches, additional incentives should be developed. The application of such incentives will act to encourage the pharmaceutical industry to invest more heavily in personalised medicines. **Newton's Apple recommends the introduction of incentives such as those listed below to encourage industry to work towards the development of agents (and supporting diagnostic tests).**

Possible incentives for personalised medicines and their accompanying diagnostic tests:

- *Shorter review periods by the medicines regulatory authorities. A quicker turn around from filing to approval and to the granting of a licence.*
- *Favourable reimbursement (drug and diagnostic) such that reimbursement is more rapidly given and is coordinated to ensure that both drugs and accompanying diagnostics are covered. Also, that higher prices are given for innovative drugs to reward and encourage personalised medicine approaches, where the drugs are shown to significantly improve patient outcomes.*
- *Extensions of market exclusivity for personalised medicines (e.g. through the use of Supplementary Protection Certificates) would provide a greater reward for the industry to invest in personalised medicines and would be a positive signal that such approaches are valued.*

## 2.4 THE INNOVATIVE DIAGNOSTICS PIPELINE

A patient whose cancer is identified at an early stage, and who has it treated quickly, has a better chance of long term survival than someone whose cancer is not treated until it has grown for considerable time. For example, a study in 2002 showed that 5 year survival rates for colorectal cancer ranged from 83% for patients whose tumour is limited to the bowel wall to only 3% for patients with disseminated disease. In an earlier Newton's Apple report "*Cancer Vision 2025*" a number of recommendations were made that would improve rates of early diagnosis. Laboratory researchers are finding biochemical changes which occur at the early stages of different cancers, and if those biomarkers are developed into diagnostic tests they could be used routinely to enable cancers to be accurately diagnosed at an early stage. This needs to be reflected in the Government's health research strategy.

Diagnostic methods are derived from research findings which identify biological changes associated with different phases of development of different cancers. These biomarkers (Box A) can be very useful indicators of the progress of disease. However, it is difficult to get diagnostic methods developed into techniques that can be used routinely in hospital laboratories. Development of diagnostic kits is often done by small research based companies who cannot afford to develop and support widespread use of the techniques. The NHS National Technology Adoption Hub has been established to help to pull through emerging technologies, including diagnostics into the NHS by

setting up demonstration sites and then encouraging widespread uptake by working with the National Institute for Health and Clinical Excellence (NICE) and the MHRA, where appropriate. **Newton's Apple strongly supports this initiative and wants to see diagnostics for cancers given a high priority in the work of the NHS Technology Adoption Hub.**

Although statistics show that cancer patients are getting treated more quickly, there are still problems and delays at the stage of diagnosis. Patients present their early symptoms to their GPs and too frequently GPs fail to identify the cancer straight away – partly because each GP sees very few examples of the rarer cancers and initial symptoms can vary widely.

The Cancer Prediction in Exeter (CAPER) score demonstrates an example of a decision making tool which has the potential to be utilised by GPs (Box E). The scoring system enables primary care professionals to evaluate patients presenting with possible colorectal cancer symptoms and to make appropriate investigations or refer them to hospital without delay. Newton's Apple welcomes the development of tools like the CAPER scoring system and recommends that further funding be provided so that more decision making tools can be developed.

Use of tools such as CAPER would ensure that more common cancers are detected earlier, thus giving patients a greater chance of survival. At the time of publication, the New and Emerging Applications of Technology (NEAT) programme, administered by the National Institute for Health Research (NIHR), listed 68 projects, feasibility studies and 'pump priming' initiatives receiving funding. Newton's Apple was informed that the list did not cover all NEAT activities, but that it would provide a close approximation. Of the 68 listed, 10 studies were for developing innovative diagnostics and treatments. Of those, three were treatments and seven were diagnostic tools. However, none of the diagnostic tools appeared to be algorithms or decision-making tools for use by GPs and other primary healthcare professionals. **Newton's Apple therefore recommends that funding bodies make it a priority to allocate funding for the development of decision-making tools and to ensure that these tools are properly validated for use within GP surgeries.**

## **BOX E**

### **The CAPER score**

The CAPER (**CA**n**C**er **P**rediction in **ExeteR**) score is a scoring system that is aimed at selecting which patients with low-risk symptoms of colorectal system cancer would benefit from an urgent referral. This system can be used by GPs.

The score was developed following a population-based study. Symptoms were analysed in terms of the risk of colorectal cancer attached and examined to see what symptoms carried a significant risk when presented alone rather than in combination with other risks. The data from this analysis was used to create the CAPER score. This score was calculated in patients who had these low-risk symptoms, and aimed to select out the patients most at risk.

A feasibility study followed, in which the logistics of using the CAPER score were tested in GP practices throughout the UK. This study focused on the number of patients attending the clinics, the various scores, the usability of a patient-held scoring sheet and whether the practices could manage with this system.

This study was followed by a validation study in which the CAPER score was applied to data from the Health Improvement Network database. The CAPER score was found to perform much better than the official guidance sent to GPs.

## ■ CHAPTER 3: CONCLUSIONS

Although excellent progress in providing cancer treatments and services have been made since the 2000 NHS Cancer Plan, more work needs to be done to ensure that the trend continues, especially in the development and delivery of innovative treatments for cancer patients.

Newton's Apple welcomes the promises made in the recent Cancer Reform Strategy, some of which deal with issues highlighted in *Cancer Vision 2025: The Science Pathway to Effective Treatments and Services*. Newton's Apple also commends the excellent collaborative initiatives, such as the Confederation of Cancer Biobanks and Integrated Research Application System, which have now been established.

Despite all this progress, it still takes decades to translate promising new discoveries into benefits for the patient. The purpose of this report is to make recommendations that will help to streamline the delivery of innovative cancer diagnostics and treatments from the lab bench to the patient. The key recommendations are that:

- The Government sponsor an independent review of regulation resulting from the Human Tissue Act (2004) and its impact on the practice of research in the UK.
- That an organisation such as the UKCRC develop a training course for anyone working in the discovery and development of medicinal and diagnostic compounds, in order to accelerate the transition of research findings into interventions for patients.
- The dialogue between Government, industry and academia is continued through collaborations, so that the UK remains at the forefront of delivering innovative cancer diagnostics and treatments to patients.
- Incentives should be devised to encourage the pharmaceutical industry to work towards the development of personalised medicines and supporting diagnostic tests.
- The Department of Health and its Agencies make it a priority to allocate funding towards the creation and validation of decision making tools for use in Primary Care in order to increase the chances of early detection of cancers.

Newton's Apple wishes to continue working in this area and will continue to engage with stakeholders, to identify how as a neutral, inclusive organisation it can continue to contribute to the debate and identify the science which can inform it.

## ■ APPENDIX I: WHO'S WHO AT NEWTON'S APPLE

**Patron:** Baroness Kennedy

### **Trustees (also Founding Members):**

Aisling Burnand MBE

Rt Hon David Curry MP

Dr Monica Darnbrough CBE

Professor Michael Depledge

Dr Michael Elves (**Chairman**)

Branwen Hide

Dr Ian Gibson MP (**Honorary President**)

Dr Brian Iddon MP

Professor John Masters

Dame Bridget Ogilvie

Willie Rennie MP

Dr Caroline Wallace

**Director:** Gillian Pepper

### **Founding Members:**

Wendy Barnaby

Sarah Beyrath

Professor Derek Burke CBE

Professor Susan Jocelyn Bell Burnell

Professor Ann Dowling

Sarah Doyle

Dr Emma East

Richard Foxton

Dr Ben Goldacre

Michael Gove MP

Dr Frances MacGuire

Vivienne Parry

Dr Alun Roberts

Sir Richard Sykes

Dr Desmond Turner MP

Scott Fleming

Lord Winston

## ■ APPENDIX II: WORKING GROUP MEMBERS:

**Chair:** Dr Monica Darnbrough CBE – Member of Board of Trustees, Newton's Apple and formerly Director of Bioscience Unit, Department of Trade and Industry

Fran Balkwill – Centre Lead Translational Oncology, Queen Mary, University of London and Director, The Centre of the Cell

Charlotte Bevan – Senior Lecturer and Head of the Androgen Signaling Group, Department of Oncology, Imperial College

Melanie Burfitt – Lymphoma Association

Aisling Burnand MBE – Member of Board of Trustees, Newton's Apple and CEO of the BioIndustry Association

David Cameron – Director, National Cancer Research Network

Dr Jane Cope – Administrative Director, National Cancer Research Institute

Dr Michael Elves – Chairman of the Board of Trustees, Newton's Apple

Louise Hendry – Senior Product Manager, Pfizer

Hilary Jackson – Policy Manager, Cancer Research UK

Professor John Masters – Member of the Board of Trustees, Newton's Apple, and Professor of Experimental Pathology, University College London

John Ramsey – Vice President Global Product Development, AstraZeneca

Dr Tim Sparey – Director of Scientific Liaison, Merck, Sharp and Dohme

Dr Richard Tiner – Medical Director, Association of the British Pharmaceutical Industry

Sally-Anne Tsangarides – Head Oncologist, Merck, Sharp and Dohme

Alastair Whittington – Network Director, South East London Cancer Network

## ■ APPENDIX III:

### A NEWTON'S APPLE STAKEHOLDER CONSULTATION EVENT

*in association with*

**Cancer Research UK, Lymphoma Association, AstraZeneca, MSD, Pfizer,  
BIA & the ABPI**

***Delivering Innovative Cancer Diagnostics & Treatments to Patients***

6th November 2007 held at the King's Fund

#### AGENDA

- 8.30** Registration
- 9.00** Welcome: *Mia Nybrant*, Director, Newton's Apple
- 9.05** Keynote Speech 'Looking at Cancer NICELY': Professor Sir Michael Rawlins, Chair, NICE
- 9.20** Keynote Speech 'Earlier Access to Medicines': Professor Sir Alasdair Breckenridge, Chair, MHRA
- 9.35** The Journalist's Inquiry: Alok Jha, Science Correspondent, The Guardian, interviews experts on the 'bottlenecks':
- Professor Herbie Newell, Cancer Research UK;
  - John Ramsey, Vice President Global Product Development, AstraZeneca;
  - Dr Ian Gibson MP, Member of Joint Committee on the Draft Human Tissue and Embryos Bill 2007 and Honorary President, Newton's Apple;
  - Margaret Parton, NHS National Technology Adoption Hub;
  - Ros Redding, Head of Patient Services, The Lymphoma Association
- 10.55** Breakout Group Session: five groups each examining a 'bottleneck':
1. In the process of moving innovative diagnostics and treatments from the laboratory to Phase I trials – especially difficulties facing academic labs and smaller companies.
  2. In the development and use of Personalised Medicines – particularly issues concerned with pre-screening of subgroups who could benefit from novel treatments.
  3. Resulting from ethical issues – including delays associated with deliberations of ethical committees (especially for multi-site and international trials); ethical issues arising from the use of human tissues; patients' concerns etc.
  4. In post-licensing uptake of innovative diagnostics and treatments in the NHS – including problems of demonstrating cost effectiveness of cancer treatments initially used in late stage disease.
  5. Unmet needs in the development of innovative diagnostics and treatments of rarer cancers.
- 12.10** Plenary Session: Chaired by Alok Jha, Moderators of each Breakout Group report back followed by Open Discussion
- 12.55 – 13.00** Closing Remarks: Dr Michael Elves, Chairman, Newton's Apple

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**Human Tissue Authority** – [www.hta.gov.uk](http://www.hta.gov.uk)

**Integrated Research Application System (IRAS)** – [www.ukcrc.org/activities/regulationandgovernance/iras-streamliningapplications.aspx](http://www.ukcrc.org/activities/regulationandgovernance/iras-streamliningapplications.aspx)

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**National Institute of Health and Clinical Excellence (NICE)** – [www.nice.org.uk](http://www.nice.org.uk)

**National Institute for Health Research (NIHR)** – [www.nihr.ac.uk](http://www.nihr.ac.uk)

**National Institutes of Health (NIH)** – [www.nih.gov](http://www.nih.gov)

**Newton's Apple** – [www.newtons-apple.org.uk](http://www.newtons-apple.org.uk)

**NHS Technology Adoption Hub** – [www.technologyadoptionhub.nhs.uk](http://www.technologyadoptionhub.nhs.uk)

**New and Emerging Applications of Technology** – [www.nihr-ccf.org.uk/site/programmes/neat](http://www.nihr-ccf.org.uk/site/programmes/neat)

**Office of Public Sector Information** – [www.opsi.gov.uk](http://www.opsi.gov.uk)

**Teenage Cancer Trust** – [www.teenagecancertrust.org](http://www.teenagecancertrust.org)

**The Confederation of Cancer Biobanks** – [www.ncri.org.uk/ccb](http://www.ncri.org.uk/ccb)

**UK Clinical Research Collaboration** – [www.ukcrc.org](http://www.ukcrc.org)

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