



A report by the All Party  
Parliamentary Group on  
Stem Cell Transplantation

# Cord blood transplantation: meeting the unmet demand

Supported by  
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# Foreword by the APPG on Stem Cell Transplantation

Stem cell transplantation already transforms many lives, curing otherwise untreatable blood diseases. Yet finding a match is a painstaking process and – tragically – matches are not available for all patients. We urgently need to both increase the pool of potential, adult bone marrow donors, and also to investigate new ways of transplanting stem cells.

Donation from cord blood – where umbilical cord blood is collected and stored for future use – has the potential to transform our ability to meet the needs of patients who require a lifesaving stem cell transplant. Cord blood enables more matches to be found, particularly for groups in society where suitable donors are particularly hard to find. Yet the process of collecting and storing sufficient samples of cord blood to translate this vision in to reality is not a simple one. This report builds on the work of the UK Stem Cell Strategic Forum and identifies a practical, high quality, affordable and cost effective way forward.

If the recommendations made in this report are acted upon, we firmly believe that the UK can become the world leader in cord blood donation and transplantation, treating more patients, saving more lives, tackling inequalities and stimulating world class research. Crucially, reducing our reliance on imported cells has the capacity to reduce costs to the NHS by £6 million a year for the foreseeable future; and as such represents the kind of invest-to-save model necessary to secure the future of the NHS.

Although cord blood donation and transplantation is a highly technical subject, we must not forget the lives that can be transformed by getting this right. Too many

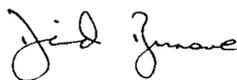
health problems have no obvious answers, but this is an issue which we can address right now. It is an investment for today's patients as well as those in the future. We urge the Department of Health, the NHS, charities and healthcare professionals to act on our recommendations, and we look forward to working in partnership to deliver radical growth in cord blood collection and transplantation, saving many hundreds of lives for years to come.

Seven hundred thousand women give birth each year in the UK and, according to a ComRes poll for this report, 85% of those women would willingly donate their umbilical cord blood to help a stranger. This is a huge well of altruism that could save the lives of two hundred people each year and the tapping of this well must be a priority. For those patients, who would otherwise face death, there is no other choice.



**Mark Tami MP**

Chair, All Party Parliamentary Group on Stem Cell Transplantation



**David Burrowes MP**

Vice Chair, All Party Parliamentary Group on Stem Cell Transplantation

# The history of transplantation: Introduction by Professor Sir Mike Richards



In March 2011, I was extremely privileged to hear a Blackburn father, Robert France, speak about his six year-old son Jackson's battle against leukaemia. Jackson's life was saved by a transplant of stem cells from umbilical cord blood, brought to Manchester from Australia. Rob spoke powerfully and eloquently of the need to increase cord blood collection in the UK, not from a medical or financial perspective, but on the most fundamentally human level – the need to save the life of his precious little boy. Many in the room were moved to tears.

I have been working in the field of cancer for 30 years and when I began my career cord blood transplants were unheard of. Indeed, bone marrow transplantation in general was a relatively new area. The first transplant from an unrelated donor took place in 1973 to an infant, Simon Bostic, here in the UK. I'm pleased to say that Mr Bostic recently celebrated his 40th birthday. A year later the indomitable Shirley Nolan set up the world's first donor register, the Anthony Nolan register, named after her son who tragically died before a matching donor could be found.

Meanwhile, work to understand and unlock the potential of umbilical cord blood was just beginning. It wasn't until the 1980s that cord blood was shown to have similar attributes to bone marrow and proposed as an alternative for use in transplantation. The first cord blood transplant took place in Paris in 1988, to treat a young boy with Fanconi's Anaemia, using cells from the cord blood of his sibling, and the first unrelated transplant took place in 1993. Seeing the potential for using cord blood to treat numerous conditions, the first public cord blood bank was set up by Prof. Pablo Rubinstein in New York, followed by others around the world, including the NHS and Anthony Nolan cord blood banks in the UK.

Since then, the development of cord blood banking has been an area of rapid

development and intense international cooperation; more than 20,000 cord blood transplants have been reported worldwide and more than 400,000 cord blood units have been stored in over 100 banks. Cord blood is now being used to treat more than 70 life-threatening illnesses, and research is showing it also has huge promise for regenerative medicine, including therapies to treat spinal cord conditions and Parkinsons disease.

However, despite pioneering stem cell transplantation in the 1970s, the UK is now lagging behind in taking advantage of the remarkable opportunities offered by cord blood.

The UK Stem Cell Strategic Forum, which published recommendations in December 2010 has already identified a clear target: if we had a UK cord blood inventory of 50,000 units, we would be able to meet 85% of currently unmet transplant requests for UK patients. This equates to saving 200 lives a year, lives of people like Jackson France. This report sets out further actions we can take to move closer to that goal.

I believe we now have a major opportunity, and a responsibility, to make this happen.



'In March 2011, I was extremely privileged to hear a Blackburn father, Robert France, speak about his six year-old son Jackson's battle against leukaemia.'

A handwritten signature in black ink, appearing to read "Mike Palmer". The signature is fluid and cursive, written on a light-colored background.

# Summary of recommendations

The APPG endorses the findings of the UK Stem Cell Strategic Forum (December 2010) and supports their road-map for increasing the availability of stem cells for transplantation. On the elements of the plan relating to umbilical cord blood, we make the following recommendations:

**Recommendation 1:** The Strategic Forum Oversight Committee should undertake a progress review of implementation of the Stem Cell Strategic Forum recommendations by the end of 2012, and the findings should be used to inform the next spending review.

**Recommendation 2:** The Strategic Forum Oversight Committee should review on an on-going basis the scientific developments that have impact on the aims of the Stem Cell Strategic Forum recommendations, including the accepted cord unit Total Nucleated Cell counts and CD34 counts.

**Recommendation 3:** The Strategic Forum Oversight Committee should review the unmet demand for stem cell transplants on an annual basis to ensure that the figure is current and to monitor progress.

**Recommendation 4:** The Strategic Forum Oversight Committee should work with the British Society of Blood and Marrow Transplantation to maintain an observatory of indications, publishing trends in the use of stem cell transplantation for different diseases and by cell source.

**Recommendation 5:** The Strategic Forum Oversight Committee should determine the optimum locations of the 13 cord blood collection hospitals outlined in the Stem Cell Strategic Forum report.

**Recommendation 6:** The All Party Parliamentary Group on Stem Cell Transplantation should ensure further research and assessment is carried out into the savings that can be achieved through extending the cord blood bank inventory.

**Recommendation 7:** The Stem Cell Strategic Forum agreed that cord blood is a proven, potentially curative therapy for both paediatric and adult patients and in recognition of this, Commissioners should ensure that all patients have access to this therapy.

**Recommendation 8:** Commissioners should investigate the possible impact of a best practice tariff to reimburse designated centres for securing high quality cord blood donations.

**Recommendation 9:** The All Party Parliamentary Group on Stem Cell Transplantation should invite submissions from interested parties on the future regulation of stem cell transplantation and respond to the forthcoming Government consultation on regulation.

**Recommendation 10:** The All Party Parliamentary Group on Stem Cell Transplantation should invite submissions on how the EU Tissue and Cells Directive could better service patients through international joint working and make relevant recommendations.

**Recommendation 11:** The Strategic Forum Oversight Committee should investigate the standard training and education that should be required for cord collectors and others present at childbirths where cord collection is taking place.

**Recommendation 12:** The All Party Parliamentary Group on Stem Cell Transplantation should invite submissions on the advantages and disadvantages of private banking, the potential for

collaboration between the two sectors and the standards of information that should be available to mothers when deciding whether to bank cord blood and whether to do so privately or publicly.

**Recommendation 13:** The Departments for Health and Business, Innovation and Skills should jointly review the available funding for research into haematopoietic stem cell transplantation in the UK and report on the adequacy of funding of this field to support their priorities within regenerative medicine overall.

**Recommendation 14:** As part of its core purpose in promoting research, the NHS should declare an aspiration for Britain to be a world-leader in research into the understanding of cord blood, its collection, its use in treatments; and for all stem cell transplant patients to have the opportunity to take part in a clinical trial.

**Recommendation 15:** The Strategic Forum Oversight Committee should engage relevant stakeholders to create a clinical trials network for stem cell transplantation.

# Background

Transplantation of stem cells from unrelated donors can extend or save the lives of people suffering from potentially fatal conditions, including leukaemia and lymphoma. Stem cells from unrelated donors come from two sources – adults who have volunteered to donate and the collection of cord blood units.

Cord blood is the blood that remains in the placenta and umbilical cord after a baby is born. It is rich in stem cells, which can help to cure a range of life threatening diseases. The first cord blood transplant was performed in 1988 by Dr Eliane Gluckman<sup>1</sup>.

The UK Stem Cell Strategic Forum was set up at the request of the Minister of State for Public Health in January 2010 to advise on future options for the provision and use of stem cells derived from unrelated adult volunteer donors and cord blood. The group, comprising of over forty leading scientists, clinicians, economists, patient representatives and international experts, who report in October 2010, made a number of recommendations aimed at increasing the number of stem cell transplants in the UK, meeting unmet demand and reducing inequalities in treatment. The report resulted in a commitment to additional funding from Government of £4 million for stem cell transplantation, including cord blood.

With the support of Government, progress is now underway to achieve a central recommendation of the Strategic Forum, that the cord blood bank should be increased to 50,000 units. This report sets out the case for increasing the collection of cord blood and for building upon the recommendations of the Strategic Forum.

<sup>1</sup> Gluckman, *New England Journal of Medicine* (1989)

Of those recommendations, a number of them have direct impact on Britain's performance in the collection and supply of cord blood and on our ability to research therapies using cord blood to improve patient outcomes<sup>2</sup>. The APPG endorses these recommendations in full as the keystone in a plan to save two hundred additional lives each year. Furthermore, the APPG commends the Government for its support for those recommendations and for funding progress along that plan.

The Department for Health should be congratulated for reforming the UK Stem Cell Strategic Forum (SCSF) as the "Oversight Committee" for the implementation of the SCSF recommendations, however, it is crucial that this body provides focus and drive for the community seeking to deliver them.

In 2011, the Nuffield Council on Bioethics published an important report on tissue and cell donation, "*Human bodies: donation for medicine and research*"<sup>3</sup>, which endorsed the recommendations of the SCSF and the work of NHS Blood & Transplant and Anthony Nolan as part of that. Nuffield singled out the 50,000 cord target for its importance.

**Recommendation 1:  
The Strategic Forum Oversight Committee should undertake a progress review of implementation of the Stem Cell Strategic Forum recommendations by the end of 2012, and the findings should be used to inform the next spending review.**

**Recommendation 2:  
The Strategic Forum Oversight Committee should review on an on-going basis the scientific developments that have impact on the aims of the Stem Cell Strategic Forum recommendations, including the accepted cord unit Total Nucleated Cell counts and CD34 counts.**

**Recommendation 3:  
The Strategic Forum Oversight Committee should review the unmet demand for stem cell transplants on an annual, or more regular, basis to ensure that progress has been made.**

<sup>2</sup> Annex 1, Recommendations of the UK Stem Cell Strategic Forum. Numbers 1, 6, 7, 8, 9, 12, 16 and 17.

<sup>3</sup> [http://www.nuffieldbioethics.org/sites/default/files/Donation\\_full\\_report.pdf](http://www.nuffieldbioethics.org/sites/default/files/Donation_full_report.pdf)

# The benefits of cord blood transplantation

The blood in the umbilical cord and placenta is rich in stem cells. These stem cells can be used for lifesaving transplants for patients suffering from leukaemia and other serious blood disorders.

Professor Pablo Rubinstein, who set up the first public cord blood bank, has done a great deal of research into the outcomes and benefits of the procedure. He sets out a number of reasons for increasing the use of cord blood transplantation<sup>4</sup>, for example:

- the logistic advantage of assured availability of the sample, avoiding the uncertainties and delays that affect bone marrow or peripheral blood stem cell donations
- better long-term prognosis for well-matched cord blood graft recipients compared with recipients of equally well-matched bone marrow
- more ethnically diverse inventories, allowing more patients to receive grafts with no more than one mismatch and improving the overall prognosis as the average match level gets better

Querol et al. also emphasise the benefit of a reduced requirement for matching, compared with adult stem cell donations, allowing transplants between incompletely matched donors and recipients<sup>5</sup>.

<sup>4</sup> Pablo Rubenstein, Why Cord Blood?, *Human Immunology* 67, 398–404 (2006)

<sup>5</sup> Querol et al, Cord blood banking: 'providing cord blood banking for a nation', *British Journal of Haematology*, 147 (2): 227-35

## Patient case study: Sorrel, 7, Suffolk

Sorrel is seven years old and lives in Suffolk with her parents, Samantha and Robert, and her younger sister, Daisy. Her father runs a gardening centre.

As a toddler, five-year-old Sorrel was very active. Although her mother Samantha was concerned that the bruises she picked up took a long time to heal, most other parents brushed it off as being normal. Then at her sister Daisy's christening, her father noticed she looked very pale. A routine check-up at the GP the following day would change everything.

After further tests at Addenbrooke's Hospital in Cambridge, they were told the devastating news that Sorrel had a rare strain of acute myeloid leukaemia. Samantha says: "I remember the first time I saw her hooked up to all those machines. It broke my heart."

Yet Sorrel refused to give in to hospital life, running down the corridors, playing puzzles and doing jigsaws.

Her first dose of chemotherapy didn't reduce the leukaemia much. After trying another kind of chemotherapy, the infected cells

were reduced to eight per cent, which meant she could be considered for a bone marrow transplant.

Samantha and Robert had never heard of cord blood donation before Sorrel was diagnosed, or how it was becoming a vital source for stem cell transplants. She says: "It's quite hard in this country to donate your umbilical cord. Hopefully as time goes by there'll be more places that offer this lifesaving opportunity."

These days, life for the family is great. Sorrel started school last September and is leading a full and active life. Samantha says: "Thank God she's a really healthy, happy child. She's got lots of friends at school and she's so normal you wouldn't think anything had happened."



### **Donor search to transplant time**

Analysis carried out by the Stem Cell Strategic Forum demonstrated that the shorter search time to identify a cord blood transplant, as compared with bone marrow donations, means that cord blood units stored in situ are more readily accessible for testing and shipping when a transplant centre makes a request. This has a significant impact on the success of treatment. A study of 3,857 transplants between 1998 and 2003 found that, compared to patients transplanted at an early stage of their disease, the mortality risk for immediate-stage patients was 38% higher. For advanced-stage patients the risk was roughly double<sup>6</sup>.

### **Reducing inequalities in stem cell transplantation**

There are millions of different tissue types but the best match is likely to come from someone in the same ethnic group as the person needing a transplant. It can be much harder for people from Black, Asian, mixed race or other ethnic backgrounds to find a match because there are fewer people from these groups both on the UK registers and stem cell registers abroad. Furthermore, ancient and historic patterns of population movement mean that non-Caucasoid patients are likely to have more complex and consequently harder to match tissue types.<sup>7</sup>

<sup>6</sup> Lee et al, High-resolution donor-recipient HLA matching contributes to the success of unrelated donor marrow transplantation, *Blood*, (2007).

<sup>7</sup> Prof. Steven Marsh, Race and genetics in stem cell transplantation, *BioNews* (2011) [http://www.bionews.org.uk/page\\_109729.asp](http://www.bionews.org.uk/page_109729.asp)

As set out by Anne Milton MP, Parliamentary Under secretary of State for Health, “an important aim of the NHS Cord Blood Bank is to help redress the current inequality experienced by sections of the population, mainly from Black or mixed parentage backgrounds, when looking for a suitable adult donor on bone marrow registries”. At present, it is far less likely that a person from a Black or minority ethnic background will be able to secure a match than a Caucasoid person - on average, about 90% of Caucasoids can find a suitably matched donor, compared with only 30% to 40% of those from other ethnic backgrounds.

### **Research into new treatments**

Not all cord blood collected has sufficient cell volumes to be suitable for clinical transplant purposes. In these cases, it can be supplied to accredited research centres. Research using umbilical cord blood is essential if medical progress, potentially affecting millions of people, is to be made in the fields of cellular and regenerative medicine. Research is being carried out using cord blood to improve the success of transplants in fighting leukaemia and serious blood disorders.

Research programmes are also being established to explore how cord blood stem cells might help treat a wide range of degenerative conditions such as heart disease<sup>8</sup>, spinal injuries, stroke and multiple sclerosis.

Professor Colin McGuckin, formerly of the Newcastle Centre for Cord Blood, is now president and director of the Cell Therapy Institute in Lyon. He has published substantially on the use of cord blood for regenerative medicine and especially on the potential of cord blood stem cells to regenerate and repair neurones. In Lyon, his work still focuses on cord blood regenerative medicine. However, he has become more ambitious and his aim is to be able to create any type of cells from cord blood to be able to repair any organ of the body.

<sup>8</sup> Martin-Rendon E, Brunskill SJ, Hyde CJ et al. Autologous bone marrow stem cells to treat acute myocardial infarction: a systematic review, *European Heart Journal* 29: 1807-18, (2008).

# The current situation and the need to grow the cord blood bank

Cord blood is currently collected for public use by a number of organisations in the UK, including NHS Blood and Transplant, Anthony Nolan, the Scottish National Blood Transfusion Unit and the Northern Ireland Blood Transfusion Service.

Although the number of cord blood units banked has increased in recent years (Figure 1: Annual number of high dose cord blood units banked ), unmet demand is a real issue. The UK does not currently collect and store enough cord blood suitable for use in transplants – it collects less than other countries and nowhere near enough to provide for the number of people who desperately need stem cell transplants. This is despite the fact that the vast majority of women (85%) would be happy for their umbilical cord blood to be donated as long as there were no impact on them or their baby.<sup>9</sup>

The Human Tissue Authority (HTA) collects information from those procuring cord blood to be made available for allogeneic use through registries. There are three principle centres, which are managed by NHS Blood and Transplant, the charity Anthony Nolan and the Northern Ireland Blood and Transfusion Service.

The Scottish cord bank has been licensed since July 2011 so there are no annual figures available. Approximate numbers for procurements in these three registers have risen in the three calendar years for which

the HTA has collected information. In 2008, 568 units were collected, rising to 1,337 in 2009 and 3,204 units in 2010. These figures refer to the total number of cord units collected in each year, a small proportion of which are deemed to be suitable for transplant. (Figure 1 on the next page shows the banked cord units by financial year).

From January 2012 HTA will be collecting additional information including the number of units available for use that are in storage in each centre.

The British Society of Blood and Marrow Transplantation (BSBMT) maintains a patient registry, which serves as a valuable resource for research into treatments and as a tool for commissioners. As well as recording the outcomes of treatment, BSBMT also records the disease afflicting the patient (known as the “indication”) and other relevant information. Depending on how diseases are classified, there are up to 40 of such indications for which a blood stem cell transplant may be a potential treatment, many of which occur very rarely.

The data collected by BSBMT could be used to maintain an observatory of indications, plotting trends in the quantity of treatments by indication. Published regularly, perhaps even quarterly, this could become a live resource for transplanting clinicians to see how their peers in the UK are using therapies in this fast developing field of treatment.

<sup>9</sup> ComRes poll of over 1,000 women for Anthony Nolan.

Figure 1: Annual number of high dose cord blood units banked

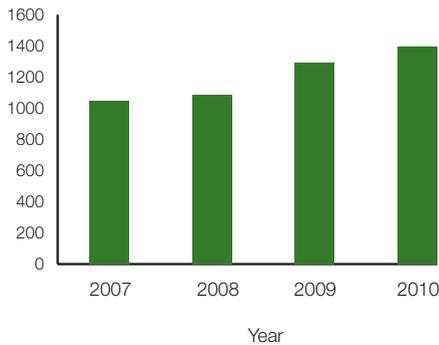
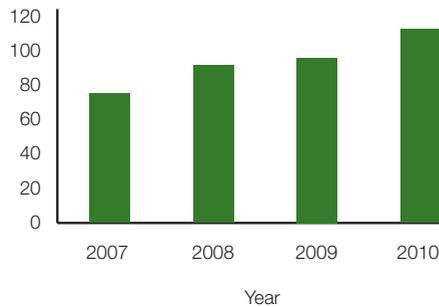


Figure 2: Number of umbilical cord blood units used for transplants in England



Such an observatory would allow regular comparison with practice in other countries, readily illustrating where the UK may be under or over using certain forms of cell therapy.

Figure 2, left, shows that in 2010, 112 cord blood units were used in transplants carried out in England. This is an increase from previous years; however, the Stem Cell Strategic Forum estimated that unmet need for donor stem cells is at least 440 patients per annum.<sup>10</sup>

**Recommendation 4: The Strategic Forum Oversight Committee should work with the British Society of Blood and Marrow Transplantation to maintain an observatory of indications, publishing trends in the use of stem cell transplantation for different diseases and by cell source.**

<sup>10</sup> UK Stem Cell Strategic Forum, *The Future of Unrelated Donor Stem Cell Transplantation in the UK*, (2010).

### Stem cell transplants imported from abroad

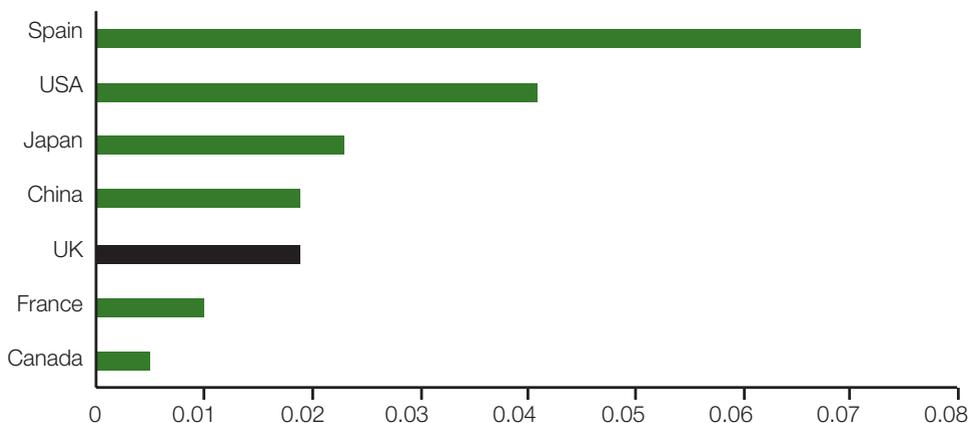
In the last year, the UK imported over 80% of the cord blood units used by UK transplant centres from cord banks overseas because there was no matching donor or cord available in the UK. Anthony Nolan manages all such transfers and has imported nearly 300 cord blood units for UK patients over the last four years. However, if more patients are to benefit from cord blood transplantation in the most efficient way possible, it will be necessary to create a system for collecting more cord blood units in the UK.

### Expanding collection to meet the demand

The case for increasing cord blood donation in the UK is clear. If the UK is to maintain a leading place in this fast developing field of medical science, it needs to be level with Spain, Japan, the USA and others where there are government-supported national collection programmes. As Figure 3 demonstrates, the UK falls behind Spain, the USA and Japan in the proportion of cord blood units stored.

Furthermore, as science has developed, cords collected under previously-accepted Total Nucleated Cell count (TNC) thresholds are no longer acceptable where they fall behind more recent standards.

Figure 3: Cord blood units stored as a percentage of population<sup>11</sup>



<sup>11</sup> Department of Health, *Cord blood banking in the UK, An international comparison of policy and practice*, (2009).

<sup>12</sup> UK Stem Cell Strategic Forum, *The Future of Unrelated Donor Stem Cell Transplantation in the UK*, (2010).

<sup>13</sup> Querol et al, Cord blood stem cells for haematopoietic stem cell transplantation in the UK: how big should the bank be? *Haematologica*, (2009).

The UK Stem Cell Strategic Forum recommended expanding the UK inventory to 50,000 cords. It has been estimated that a UK inventory of 50,000 cord blood units would be able to meet:

- 85% of the unmet need from Caucasoid patients
- 50% of the unmet need from ethnic minority patients
- 90% of the unmet need from patients whose conditions deteriorate while waiting for an adult donor<sup>12</sup>

The Strategic Forum report, which was welcomed by the Government, estimated that expanding the inventory to 50,000 units means that 200 lives would be saved annually.<sup>13</sup>

### **The number and location of collection centres**

As cord blood donation increases it is likely that the number of women wishing to donate will also increase. The box below sets out the views of some mothers on MumsNet who were disappointed at the relatively low number of hospitals where collection is possible. However, this desire needs to be balanced against the need to collect cord blood units as cost effectively as possible. The Stem Cell Strategic Forum report sets out that maternity units collecting cord blood are best managed in clusters, so that quality can be managed consistently and so staff can move from hospital to hospital and ensure 24/7 coverage.

### **Expanding the number of collection centres – mums' views<sup>14</sup>**

“I was really disappointed to learn that my nearest hospital collecting cord blood is a 2.5 hour drive. If I could do it locally I definitely would but I'm not really up for driving to the south of England whilst in labour...”

“Why don't more hospitals offer public donation? ... I am storing my baby's stem cells privately. I would have liked to donate but as I'm sure you know its not an option at my hospital. What can people do if they would prefer to donate than store privately?”

The Strategic Forum argues that an inventory of 50,000 units could be achieved from around 13 hospitals. It is important that work done to determine the location of these centres takes into account the desire of women to donate as well as the ethnic minority breakdown of certain areas to ensure that genetic diversity of banked cord blood units can be achieved.

Identifying the 13 optimum hospitals may mean taking into account factors including the available funding sources and whether the centre is already licensed for cord collection by the HTA.

**Recommendation 5:  
The Strategic Forum Oversight Committee should determine the optimum locations of the 13 cord blood collection hospitals outlined in the Stem Cell Strategic Forum report.**

<sup>14</sup> Mumsnet comments forum

# The economic case and making funding structures work

The Stem Cell Strategic Forum set out the economic case for expanding the cord blood inventory to 50,000 units. The analysis considered the likely costs and benefits associated with the improved provision, including collecting, storing, transplantation and the survival and quality of life improvements.

As well as the clinical benefits outlined, financial savings from increasing collection were identified, for example:

- Reducing cost through domestic supply
- Some costs will be recovered through exporting cord blood
- Costs will also be recovered through samples supplied for research and development

**Recommendation 6:  
The All Party Parliamentary Group on Stem Cell Transplantation should ensure further research and assessment is carried out in to the savings that can be achieved through extending the cord blood bank inventory.**

The cost effectiveness of a treatment is always going to be important in a system with limited resources. This has long been recognised, and the National Institute for Health and Clinical Excellence uses the

Quality-Adjusted Life Years measurement (QALY) to assess the economic case for introducing medicines in the NHS.

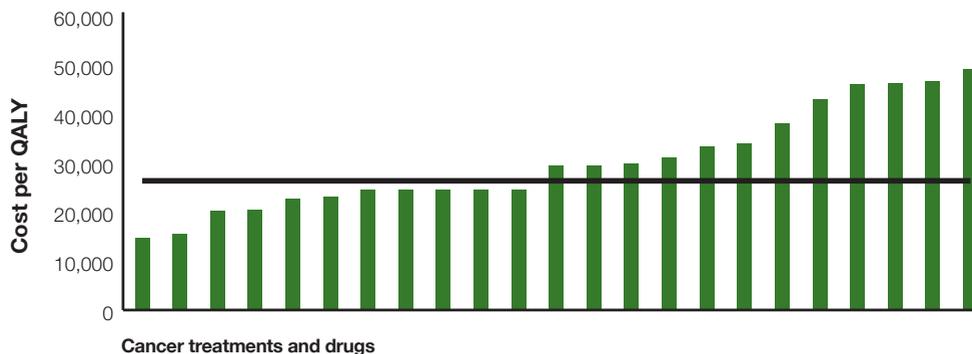
A QALY gives an idea of how many extra months or years of life of a reasonable quality a person might gain as a result of treatment. Cost effectiveness is expressed as '£ per QALY'. Generally, if a treatment costs less than £20,000-30,000 per QALY, then NICE would consider it to be cost-effective<sup>15</sup> and recommend it for use in the NHS.

The NICE assessment process has, however, been focused on drug treatments and is rarely used to analyse other forms of treatment such as surgery, radiotherapy or transplant. Despite this the Stem Cell Strategic Forum used the QALY methodology and estimated that the costs associated with increasing the size of the cord blood bank are in the region of £27,000 per QALY.

Figure 4 shows how this cost of £27,000 per QALY compared with cancer treatments that have been approved by NICE. The QALY for cord blood transplantation not only falls below the limit of £30,000 set by NICE, but is also considerably lower than a number of treatments that have been approved for funding by the NHS.

<sup>15</sup> NICE, *Measuring effectiveness and cost-effectiveness: the QALY*, available at: [www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenessstheqaly.jsp](http://www.nice.org.uk/newsroom/features/measuringeffectivenessandcosteffectivenessstheqaly.jsp)

Figure 4: Cancer treatments approved by NICE, 2007–2011, by QALY compared to £27,000 cost of cord



**Recommendation 7:**  
**The Stem Cell Strategic Forum agreed that cord blood is a proven, potentially curative therapy for both paediatric and adult patients and in recognition of this, Commissioners should ensure that all patients have access to this therapy.**

#### Funding cord blood

Although cord blood donation and transplants are both clinically and cost effective, it will nonetheless be important to develop sustainable funding mechanisms to support NHS providers of care.

As the collection and use of cord blood becomes more common, the funding for the service should become more mainstream. Unless providers are reimbursed for facilitating cord blood donations, there will be a perverse incentive not to collect blood.

As a principle, we believe that funding should be provided on the basis of quality and outcomes, rather than simply the existence of the service. To this end, tariffs could be developed as a mechanism for reimbursing the costs associated

with donation. A review group should be established to consider the case for tariffs, as well as the best mechanism for implementation. A starting point could be a best practice tariff for cord blood donation.

This would have a number of benefits, including:

- Providers would be reimbursed for the additional costs associated with the process
- Providers would be rewarded for securing high numbers of donors, according to strict quality criteria, creating economies of scale
- An incentive would be created to ensure high quality, safe donations
- A proportion of the provider costs would be recouped at collection stage rather than when those cells are subsequently provided to a patient, which can be a number of years later.

**Recommendation 8:**  
**Commissioners should investigate the possible impact of a best practice tariff to reimburse designated centres for securing high quality cord blood donations.**

# Delivering high quality donations and transplants

Despite the clear clinical, equality and financial arguments for extending the collection of cord blood it remains a contentious issue. In this section we will set out some of the key issues that lead to debate.

It is important that there are processes and standards in place to guarantee that the mother and baby remain the key priority during the birth process and that the collection of cord blood does not take precedence.

## **Safety and quality**

Some mothers and midwives have expressed concerns about the potential risks to mother and baby from cord blood banking, particularly that the welfare of the mother and baby will suffer if attention is focused on cord blood collection rather than their care.

However, since 2007, the collection of cord blood has been strictly regulated by the Human Tissue Authority (HTA) and there are stringent rules in place to ensure that nobody is put at risk by the procedure.

The European Union Tissue and Cells Directives (EUTCD) set out to establish a harmonised approach to the regulation of tissues and cells across Europe. The Directives set a benchmark for the standards that must be met when carrying out any activity involving tissues and cells for human application (patient treatment). The Directives also require that systems are put in place to ensure that all tissues and cells used in human application are traceable from donor to recipient.

The EUTCD is made up of three Directives, the parent Directive (2004/23/EC) which provides the framework legislation and two technical directives (2006/17/EC and 2006/86/EC), which provide the detailed requirements of the EUTCD.

The HTA as one of the Competent Authorities in the UK under the EUTCD, has responsibility for regulating tissues and cells (other than gametes and embryos) for human application. The Human Fertilisation and Embryology Authority (HFEA) is the other Competent Authority in the UK and is responsible for the regulation of gametes and embryos for human application.

[www.hta.gov.uk/legislationpoliciesandcodesofpractice/legislation/eutissueandcellsdirectives.cfm](http://www.hta.gov.uk/legislationpoliciesandcodesofpractice/legislation/eutissueandcellsdirectives.cfm)

To be authorised to collect cord blood, organisations have to be licensed by the HTA. The licensing regulations state that:

- All staff collecting cord blood need to be trained to ensure the best quality sample is taken
- Medical attention must not draw away from mother or child during collection
- The risk of contamination is minimised during collection and storage
- Cord blood cells are traceable from collection to their use in treatment<sup>16</sup>

In addition to clinician-led organisations such as the European Group for Blood and Marrow Transplantation, the major statutory regulator in the field is the HTA, which sets the minimum standards for quality and safety of cord blood<sup>17</sup> under the terms of the EU Tissue and Cells Directive.

While the Government plans to consult on the new regulatory responsibilities of the HTA, the Human Fertilisation and Embryology Authority and the Care Quality Commission early in 2012<sup>18</sup>, it should be recognised that these changes have the potential to create barriers for agencies involved in stem cell supply and transplantation.

The Government's recent streamlining of the medical research regulatory framework has been widely received as a positive advance and the benefits of this approach should be considered when reviewing the framework for the regulation of medical care. Given the rapidly advancing science surrounding stem cell transplantation, in particular using cord blood, the Government should be mindful that many of the institutions involved in treating

patients and providing stem cells are engaged, directly or indirectly in research activities and therefore caught within both regulatory regimes.

## **Recommendation 9: The All Party Parliamentary Group on Stem Cell Transplantation should invite submissions from interested parties on the future regulation of stem cell transplantation and respond to the forthcoming Government consultation on regulation.**

Organisations responsible for collecting cord blood for public use only collect cord blood in maternity units where there are specifically assigned collection teams and specialised facilities in addition to the midwives attending the birth. The collection procedures are designed to have no impact on the care of the mother and baby and to ensure the aseptic collection of the cells; collection teams are highly trained to ensure the procedures are carried out correctly.

The Royal College of Obstetricians and Gynaecologists (RCOG) and the Royal College of Midwives (RCM) support medically directed and altruistic cord blood collection for public banking and endorse the HTA licensing rules.<sup>19</sup>

The All Party Parliamentary Group has heard from representatives of the Royal College of Midwives and from midwives working in cord collection centres and it is clear that they are crucial partners in the expansion of cord blood transplantation in the UK.

<sup>16</sup> Human Tissue Authority, *Position statement on cord blood collection*, March 2010 [www.hta.gov.uk/legislation/policiesand-codesofpractice/positionstatementoncordbloodcollection.cfm](http://www.hta.gov.uk/legislation/policiesand-codesofpractice/positionstatementoncordbloodcollection.cfm)

<sup>17</sup> [www.hta.gov.uk/\\_db/\\_documents/Annex\\_-\\_Guide\\_to\\_Quality\\_and\\_Safety\\_Assurance\\_for\\_Tissues\\_and\\_Cells\\_for\\_Patient\\_Treatment.pdf](http://www.hta.gov.uk/_db/_documents/Annex_-_Guide_to_Quality_and_Safety_Assurance_for_Tissues_and_Cells_for_Patient_Treatment.pdf)

<sup>18</sup> HTA E-newsletter #32 [www.hta.gov.uk/newsandevents/e-newsletter/e-newsletterissue32december2011.cfm](http://www.hta.gov.uk/newsandevents/e-newsletter/e-newsletterissue32december2011.cfm)

<sup>19</sup> RCOG/RCM statement on umbilical cord blood collection and banking.

## European regulation

The key directive governing the regulation of the supply of cells for transplantation is the EU Tissue and Cells Directive.

The Tissue and Cells Directive sets out to establish a harmonised approach to the regulation of tissue and cells around Europe. The APPG believes that this directive does help facilitate the movement of cells for transplant around the continent. However, each member state has assigned regulation of the directive to its own competent authority, whose remit can include expanding on the directive over time. Many competent authorities do this, resulting in a complex regulatory environment and distinct standards within the EU. This creates barriers to the distribution of tissues and cells within the European Economic Area. Nevertheless, the HTA has not extended the requirements beyond those set out in the European Directive, therefore any cord blood lawfully collected within the EEA will meet the UK requirements and can be distributed to UK transplant centres without additional regulatory burdens.

The Alliance for Harmonization in Cellular Therapy Accreditation (a group made up of international and region-specific authorities in stem cell transplantation and research) has been conducting a survey in to the different tests required by various competent authorities, both European and worldwide, to certify the importation of donor tissue. European establishments must ensure that the mother's blood has been tested for the presence of infectious diseases, including HIV, Hepatitis B, Hepatitis C and syphilis. Imported cord blood from countries outside the EEA may

require further testing before they can be accepted for use in UK transplant centres. This incurs delay and additional cost, however, the tests are necessary as they help to assure the safety of the cord blood, and lower the risk of viral transmission to the transplant recipient.

**Recommendation 10: The All Party Parliamentary Group on Stem Cell Transplantation should invite submissions on how the EU Tissue and Cells Directive could better service patients through international joint working and make relevant recommendations.**

## Late clamping

In the collection of cord blood, what matters most is the health of the mother and the child. The successful collection is always secondary and there should never be a conflict between these priorities.

There are discussions about whether the speed at which a newborn's umbilical cord is clamped and cut (ending the blood supply from the placenta) could make a difference to the baby's health. When collecting cord blood, delayed clamping can reduce the chances of collecting a sufficient quantity of blood for clinical use.

## Cord blood collection – mums’ concerns<sup>20</sup>

“We decided against cord blood collection. To my mind it was a choice between a possible benefit to my child at some point in the future vs a very definite benefit to my newborn baby.”

“I think it is very important to think about the fact that you will be depriving your own baby of its own first stem cell transplant. Babies are supposed to get this blood themselves. Lots of information about it in the news this past week too.”

The evidence on this issue is mixed, though a recent study in the British Medical Journal of 400 births in Sweden suggests there may be benefits to a child whose cord was clamped late<sup>21</sup>. There is a consensus of agreement that late clamping has measurable benefits to children in under-resourced families where access to good nutrition is limited during childhood and where anaemia is more prevalent<sup>22 23</sup>.

We support an informed decision by a mother that might result in either early or late clamping in the context of cord blood collection. This informed decision should be taken in the normal mother-clinician relationship without any external interference and that information should take advantage of the latest evidence base.

The APPG recognises the excellent practices of NHSBT and Anthony Nolan in their cord blood collection work in ensuring that the mother’s choice is always paramount and that the function of cord collection never interferes with the care of the mother and child. If late clamping were to become a standard practice, this may well have an impact on the cost of tissues for transplant.

**Recommendation 11:**  
**The Oversight Committee should investigate the standard training and education that should be required for cord collectors and others present at childbirths where cord collection is taking place.**

### Private banking

Some families choose to bank their baby’s cord blood privately, rather than donate it to a public bank, for use in the event that the cells can be of benefit to their own child in the future.

The HTA regulates this arena to ensure that mothers have adequate information to make an informed decision about cord collection. Information is available from the HTA<sup>24</sup> and the Genetic Alliance<sup>25</sup> as well as from the private and public banks engaged in cord collection.

There has been a steady increase in the practice in recent years and some healthcare professionals have expressed their concerns about this trend.

<sup>20</sup> Mumsnet comments forum

<sup>21</sup> [www.bmj.com/content/343/bmj.d7157](http://www.bmj.com/content/343/bmj.d7157)

<sup>22</sup> [http://apps.who.int/ihl/pregnancy\\_childbirth/childbirth/3rd\\_stage/cd004074\\_abalose\\_com/en/index.html](http://apps.who.int/ihl/pregnancy_childbirth/childbirth/3rd_stage/cd004074_abalose_com/en/index.html)

<sup>23</sup> [www.nice.org.uk/nicemedia/live/11837/36275/36275.pdf](http://www.nice.org.uk/nicemedia/live/11837/36275/36275.pdf)

<sup>24</sup> [www.hta.gov.uk/licensingandinspections/sectorspecificinformation/tissueandcellsforpatienttreatment/cordbloodcollection/faqs-forparents.cfm](http://www.hta.gov.uk/licensingandinspections/sectorspecificinformation/tissueandcellsforpatienttreatment/cordbloodcollection/faqs-forparents.cfm)

<sup>25</sup> [www.geneticalliance.org.uk/docs/cordbloodbanking.pdf](http://www.geneticalliance.org.uk/docs/cordbloodbanking.pdf)

<sup>26</sup> [www.rcog.org.uk/news/rcogrcm-statement-cord-blood-collection-and-banking](http://www.rcog.org.uk/news/rcogrcm-statement-cord-blood-collection-and-banking)

## Private collection – mums’ views<sup>27</sup>

“I read somewhere that if stem cells are needed there is a much greater chance of cells from the NHS bank being a match than your own privately stored ones, which put me off storing privately.”

“My hubby and I are trying to decide whether we bank the cord blood of our baby when he is born in case he develops a disease where he needs it in the future. This is expensive (about £1,200 give or take £200) and the odds of needing to use it have been quoted as between 1/1,000 and 1/20,000 but a part of me feels that I would find it very hard to cope knowing I didn’t do it if he DID need it. Then I get angry that these companies are playing on my paranoia!!! We really don’t know what to do – does anyone have any experience of this?”

The RCOG and RCM believe that there is not enough evidence at present to recommend routine private cord blood collection and banking unless there is a medically-indicated reason.<sup>26</sup> The likelihood of a given person needing a stem cell transplant is very small, and in the event that they do, a patient’s own cells may not always be the ideal source for a transplant. Tissues from an unrelated donor can stimulate a “graft versus leukaemia” effect that can impede subsequent cancerous relapse. In fact, public banks have systems in place to ensure that patients are not

accidentally given their own cord blood cells because of the possible negative effects.

There is an alternative body of opinion that private banking creates jobs for relevant technicians and has the potential to support and enhance the capacity for public banking and research into treatments. Recent research also suggests that more conditions may in future be treatable with privately collected cells, indicating that cell usage levels from private banks could be expected to increase in future.

In 2011 the APPG held a session where representatives from private banks, public banks, the Royal college of Midwives and the Human Tissue Authority explored some of the issues and challenges in this field. It is clear that a range of approaches have been taken in comparable countries that should be looked into further.

Given the potential for private and public banks to co-operate or conflict with each other, and the lack of a settled opinion on the benefits and disbenefits of private banking, the APPG should consider investigating this arena in more depth.

**Recommendation 12:**  
**The All Party Parliamentary Group on Stem Cell Transplantation should invite submissions on the advantages and disadvantages of private banking, the potential for collaboration between the two sectors and the standards of information that should be available to mothers when deciding whether to bank cord blood and whether to do so privately or publicly.**

<sup>27</sup> Mumsnet comments forum

# Making it work

The report from the UK Stem Cell Strategic Forum represents an essential starting point in efforts to improve donation and transplantation of cord blood. A summary of the Forum's recommendations is included in Annex 1.

A radical change is now required, increasing the bank of cord blood units to 50,000. In delivering this increase, it will be important to ensure that services are developed sustainably and according to consistent quality standards. Examples of international good practice should also be built upon.

The examples on page 27 demonstrate the approaches that have been taken in Spain and the USA respectively, where state funding has contributed to increasing the number of units collected, and therefore the number of patients able to benefit from cord blood transplant.

## Cord blood collection in Spain

The Organización Nacional de Trasplantes published the National Umbilical Cord Blood Plan in March 2008, setting out how to organise a National Cord Blood Network, and providing guidelines for the collection, storage and use of cord blood, as well as for the communication between different stakeholders (parents, obstetricians, midwives, cord blood banks).

In June 2008, there were about 30,000 units stored in its cord blood

banks; this represented 10% of the world's stored cord blood. There are seven public cord blood banks and, like the UK, they have to adhere to the European Union Tissue and Cells Directive. Cord blood stored in private banks must be made available for any patient searching for a matched unit on REDMO (Spanish Bone Marrow Registry).

Several government ministries are involved in implementing the plan.

## Cord blood collection in the USA

The Stem Cell Therapeutic and Research Act of 2005 authorised \$79 million over a 5-year period to be provided for the collection of cord blood stem cells with the goal of building the nation's public umbilical cord blood supply by adding 150,000 new cord blood units. The Act also created a national registry to match cord

blood to those in need – the Center for Cord Blood (run by the National Marrow Donor Programme).

In 2008, 123,012 cord blood units were stored in its public cord blood banks; this represented 43,75% of the world's total and a significant increase from when the Act was introduced.

The UK Stem Cell Strategic Forum creates an opportunity to ensure that a similarly strategic, planned approach is adopted. The challenge now will be ensuring that the vision and ambition of the Stem Cell Strategic Forum is realised, and that the recommendations are incorporated into the reformed NHS structures.

However, implementation of these recommendations cannot take place in isolation and must reflect the spirit and direction of reforms to health and social care. A number of the processes set out in Equity and Excellence: Liberating the NHS can and should be applied to cord blood donation and transplantation.

### **Supporting research**

Research has and will continue to be critical to unlocking the potential of cord blood to save and transform lives. Although significant progress has been made in relation to cord blood research, much remains unknown and it is imperative that progress on research is maintained.

Research into cord blood therapies benefits from the ongoing interest in and focus on the Government on lifesciences and on regenerative medicine in particular. 2011 saw the implementation of a streamlining of regulation in research and the announcement of a lifesciences strategy, including the commitment of up to £10 million per year for five years to support a Cellular Therapy Catapult.

In maintaining progress, it will be necessary to plan future investment in research and ensure that funding is used to maximum effect. At present, it is difficult to determine the extent of public research funds that are used to explore the donation and transplantation of cord blood. Of particular concern is the difficulty of funding research where it leads to a treatment improvement that carries with it no intellectual property that can be commercialised. In contrast to innovations in drugs and devices, stem

cell transplantation research also has a focus on novel tissue typing techniques, the use of alternative donors and adjustments to patient conditioning regimes and post transplant care.

Despite an admirable record of academic publications in the cellular therapy field, Britain cannot maintain world leadership in this area while the focus is so heavily weighted to commercial research and to work with embryonic cells. Furthermore, this imbalance prevents patients benefiting from the very best possible survival rates that could be achieved as the scientific understanding advances.

**Recommendation 13: The Departments for Health and Business, Innovation and Skills should jointly review the available funding for research into haematopoietic stem cell transplantation in the UK and report on the adequacy of funding of this field to support their priorities within regenerative medicine overall.**

**Recommendation 14: As part of its core purpose in promoting research, the NHS should declare an aspiration for Britain to be a world-leader in research into the understanding of cord blood, its collection, its use in treatments; and for all stem cell transplant patients to have the opportunity to take part in a clinical trial.**

The Strategic Forum set out that the Stem Cell Advisory Forum should work with key stakeholders to define research opportunities, facilitate the translation of basic research into the clinical practice, and maximise income through the commercialisation of intellectual property. It is important that this opportunity to stimulate research is not lost, and that structures are established to ensure that the benefits of research into cord blood are fully realised.

Of crucial need is a strategic approach to translational research to enable the speedy availability to patients of improvements in treatments. The APPG endorses the recommendations of the Strategic Forum that relate to research, in particular the need to develop a clinical trials network to support translational research.

**Recommendation 15: The Strategic Forum Oversight Committee should engage relevant stakeholders to create a clinical trials network for stem cell transplantation.**

# Annex 1: Recommendations of the UK Stem Cell Strategic Forum

- 1.** In collaboration with third sector organisations, there should be greater engagement with Black and minority ethnic donors to increase their representation on donor registries and cord blood banks
- 2.** Selected donors should be retrospectively and prospectively HLA typed to high resolution to obviate the need for this test as part of the donor selection process
- 3.** The UK should create or purchase predictive search technologies (such as those used by German and US registries) to increase the chance that selected donors are a match for the patient
- 4.** A 'graft identification advisory service' should be established to ensure optimal donor selection for each patient
- 5.** Registries should increase contact with donors, updating information on their contact details, health status and willingness to donate
- 6.** The UK should increase its inventory of cord blood to 50,000 units over eight years. This time period represents a cost-effective approach to achieving the required inventory
- 7.** The inventory should contain 30% to 50% of donations from Black and ethnic minority women
- 8.** Newly banked units should have a high total nucleated count threshold (over  $9 \times 10^8$  TNC from ethnic minority donors, over  $12 \times 10^8$  TNC from Caucasian donors)
- 9.** High resolution HLA typing should be performed on all of newly stored units and selected existing units
- 10.** Educational tools and platforms should be developed to improve understanding among commissioning bodies. With the support of physicians, commissioners should align their strategies with the latest clinical guidance and patient outcome data
- 11.** Commissioning bodies should operate within a standardised funding framework, using a baseline figure adjusted to reflect market forces factors. This should detail the necessary costs for each stage of the patient's treatment to provide clarity and certainty to all service providers. This framework should cover the entire patient pathway, including pre- and post-transplant treatment
- 12.** Resources and expertise for cord blood transplantation should be concentrated into designated Regional Centres of Excellence, promoting high quality care and the best use of resources. Regional Centres of Excellence should undertake a minimum of 5, preferably 10, cord blood transplants per annum and serve a minimum population of 4-5 million
- 13.** All centres performing unrelated donor stem cell transplantation should be accredited by the Joint Accreditation Committee of ISCT and EBMT (JACIE)

**14.** Local networks should be linked into designated centres and make appropriate referrals when necessary

**15.** Standardised data collection and outcome monitoring should be integrated into every stage of the patient pathway so that reliable outcome data can be used to benchmark individual performance and promote best practice. Funding streams should be identified to support the collection and analysis of outcome data from Regional Centres of Excellence

**16.** Designated transplant centres should work together to support an alternative donor clinical trials network. The commissioning process should encourage the development of registration studies and early and late phase clinical trials in alternative donor transplantation. Funding streams should be identified to develop what would be a uniquely important translational initiative worldwide

**17.** Acknowledging differences in policy and process between the four countries of the UK, a commissioning framework should be developed and supported by a UK Stem Cell Advisory Forum to performance manage the provision of:

- A UK stem cell registry;
- A UK cord blood inventory;
- A database of patient outcomes following transplantation

**18.** Each element of the framework should be contracted; the Advisory Forum should advise on the specification of each contract. Provider organisations should report on key performance indicators annually

**19.** The Stem Cell Advisory Forum should build on the work and membership of the UK Stem Cell Strategic Forum. It should develop standards and specify the service levels required of supplier organisations

**20.** In addition to advising on the provision and use of stem cells for transplantation, the Stem Cell Advisory Forum should work with key stakeholders such as UK Blood Services, the ANT, research organisations and charities to define research opportunities, to facilitate the translation of basic research into the clinical practice, and to maximise income through the commercialisation of intellectual property

## Further Information

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