NHS CYMRU WALES

WALES CANCER BANK
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Wales Cancer Bank

Annual Report
April 2008 - March 2009

Funded By:

Llywodraeth Cynulliad Cymru
Welsh Assembly Government

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VELINDRE NHS TRUST

CANCER RESEARCH WALES

Contents

Abbreviations

AJAX	Asynchronous JavaScript and XML (Extensible Markup Language)
ASP	Active Server Pages
CanISC	Cancer Information Service Cymru
CASE	Cancer support South East Wales
CCB	Confederation of Cancer Biobanks
CRW	Cancer Research Wales
DI	Designated Individual
DNA	Deoxyribonucleic acid
ECMC	Experimental Cancer Medicine Centre
EDTA	Ethylenediamine tetraacetic acid
EGFR	Epidermal Growth Factor
H&E	Haematoxylin and Eosin
HTA	Human Tissue Authority
ISBER	International Society for Biological and Environmental Repositories
IT	Information Technology
LLEG	Lay Liaison and Ethics group
MRC	Medical Research Council
MREC	Multi-centre Research Ethics Committee
NCRI	National Cancer Research Institute
NHS	National Health Service
NRES	National Research Ethics Service
PD	Person Designated
QA	Quality Assurance
RCN	Royal College of Nursing
RNA	Ribonucleic acid
SOP	Standard Operating Procedure
SLA	Service Level Agreement
SRE	Skeletal-related event
TMA	Tissue MicroArray
UAT	User Acceptance test
UHW	University Hospital of Wales
WCB	Wales Cancer Bank
WCTN	Wales Cancer Trials Network
WCTU	Wales Cancer Trials Unit
WORD	Wales Office of Research and Development for Health and Social Care

Figures

Aim

To provide a population based resource of tissue and blood samples from all patients in Wales, who are undergoing an operation to remove tissue where cancer is a possible diagnosis, for future research into cancer

The printed version of this year's Annual Report is an edited version to reduce printing and related costs. A link to the full version of the Annual Report can be found on the WCB website **www.walescancerbank.com**

Directors Report

5 Years and 3,000 patients later….

This year marks the 5th anniversary of the establishment of the Wales Cancer Bank (WCB). In that time, nearly 3,000 patients have consented to donate tissue and blood samples for future research, with no expectation of direct benefit to themselves, in an act of generosity which will resonate down the years. When we started, there were many doubts - both inside and outside the bank. Would patients be prepared to donate samples in such an open-ended way? The furore around Bristol and Alder Hey were fresh in the memory at that time. Would scientists themselves want such samples? At the time, laboratory research using cell lines and animal models was the cornerstone of cancer research, and the use of human samples was seen as somehow "messy", or, at best, difficult. Was the Wales Cancer Bank needed at all? After all others in the UK and elsewhere were seeking to establish human tissue collections that, we were assured, would fully meet the needs of the scientific community. Five years later, it is clear that patients and their relatives not only agreed to donate their samples, but positively wanted to do so. However, WCB can only approach patients where their own doctors have agreed that we may do so. It is now for the minority of doctors, who refuse to allow us to approach their patients, to justify their actions to the people of Wales. What of the scientists - do they need our samples? To date, more than 40 research projects have applied to the WCB, and 25 such projects have already been issued with samples. As our sample collection grows, others elsewhere in the world have had less success. However, the need is a growing one. Human tissue studies to date have suffered from two major problems. The first is that studies have been published without any information about the quality of the samples, which, at worst, might completely invalidate the scientific results. The second, still a pressing problem, is that human tissue studies are far too small (in statistical terms, they are undepowered, in many cases, hopelessly so). The WCB joins the clarion call issued by the National Cancer Institute of America, for more human tissue studies that reflect the reality of the human disease, for a proper measure of sample quality to underpin the scientific claims that are made by such studies, and for adequately large studies to give real statistical power to the results. We strongly support the efforts to add value to clinical trials, by collecting samples from the patients in those trials for allied research. However, we believe that the need for population-based sample collections, such as the WCB, will continue to grow, as a resource for studying the causes of cancer in a population, as a resource to supply very large numbers of samples where they are needed, and as the pivotal resource to validate any hypothesis that is generated by smaller-scale, or clinical trial studies.

Five years on from our establishment, the WCB is going from strength to strength. I would like to thank our funders, the Wales Assembly Government, Cancer Research Wales, and Velindre NHS Trust for their unfailing support, but mostly, our thanks go to the cancer patients of Wales, who by supporting this project have given us a precious resource, the full benefits of which we can only imagine.

Professor Malcolm Mason
Director, Wales Cancer Bank

Targets for 2008/09

TARGETS for 2008/09	Achieved
Accrue 3100 patients in total	Target July 09
Supply six projects with biosamples	January 09
Develop a web accessible version of database	ongoing
Collate clinical data for patients consented to end 2007	March 09
Continue to raise awareness and promote WCB	ongoing

Central Administration

Director	Professor Malcolm Mason
Director of Scientific Services	Professor Gerry Thomas
Manager	Dr Alison Parry-Jones
IT Manager	Mr Daniel Naeh
Project Officer	Miss Sarah Phillips
Web Developer	Dr Yasmin Friedmann
Database Manager	Mr Matthew Shaw
Clerical Officer	Mrs Debbie Way
Information Assistant	Miss Claire Alford

Office Move

The central administration office for WCB relocated in August 2008. The office is now based half a mile away from the main University Hospital of Wales Heath Park site in a self contained building. Email addresses remain the same but the new address and contact numbers are:

Grove Mews
1 Coronation Rd
Birchgrove
Cardiff, CF14 4QY
Tel: 02920 529226
Fax: 02920 621937

Team Building Day

Twenty members of WCB staff from around Wales took part in a team building day in June 2008 and demonstrated their prowess in archery, team challenges and showed their competitive edge in laser tag. The day gave the team the opportunity to come together and work in different surroundings to help cement a pan Wales team spirit across all sites.

Recruitment

656 patients were recruited between April 2008 and March 2009 across all collecting sites to take the total number of patients consented since the beginning of the project to 2845. The gender split of patients recruited since inception remains the same as last year at 57% female and 43% male. The majority of donors (69%) are aged 60 or over and 88% of consents are obtained pre-operatively. Breast, colorectal and prostate remain the three largest collections in the bank although consent rates in four out of the five geographic locations have dipped slightly on the previous year.

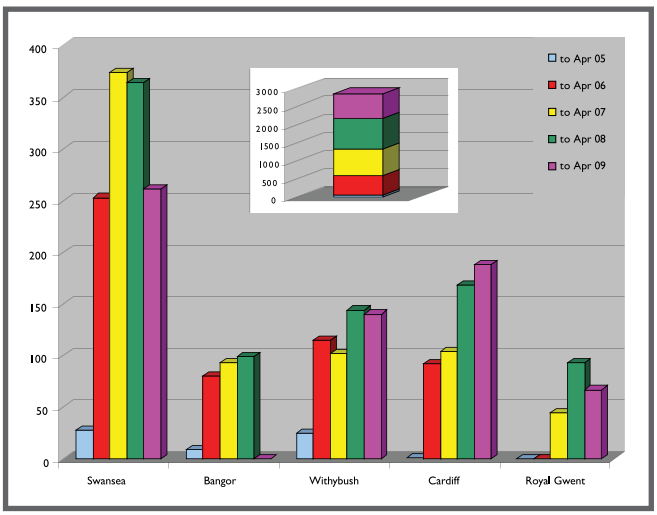

Figure 1 – Annual recruitment by centre

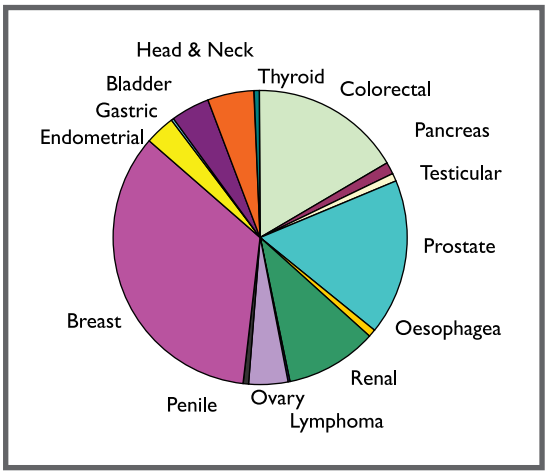

Figure 2 – Collection by tumour type

Bangor Site

Due to the vacant nursing post in Bangor, no patients have been consented during the reporting period. All biosamples were moved from Bangor to Cardiff. The laboratory post was filled early in 2009 and interviews for the nurse post are scheduled for May 2009. It is hoped that collection can resume in Bangor over the summer of 2009.

Cardiff Site

One full time nurse covers the clinics and wards to consent at Llandough from gynaecology and colorectal patients. A bespoke ascitic fluid collection was initiated during the year from gynae patients. 91 patients were recruited in Llandough Hospital during the reporting period, 77 from gynae and 14 from colorectal. After discussions with the pre assessment nurse and consultants in the colorectal team, a new system has been set up for the WCB to see the patients in the pre assessment clinics. Consultants, theatre staff and clerical staff from both specialities have fully supported the collection in Llandough.

Collection for breast tissue will commence later in the year following discussions with the breast team. It was agreed the breast specialist nurse will consent the patient and the patient would be followed up by the WCB nurse to collect bloods and control bloods when they came into hospital.

Ally Davies presenting her poster

The WCB nurse from Cardiff successfully submitted a poster abstract to the Royal College of Nursing Annual Research Conference at Cardiff City Hall in March 09. The poster updated attendees on WCB progress and gave the opportunity to talk to a WCB nurse regarding consent issues or general tissue collection.

The urology collection continues to flourish in UHW and staff are involved in procuring fresh prostate tissue for culture for one research project as well as collecting routine frozen and paraffin tissue and blood samples.

Royal Gwent Site

The urology collection continues to function well in the Royal Gwent. The WCB nurse in Newport also facilitates on the Communication in Randomised controlled Trials course held at the Cancer Care Cymru Centre, Cardiff Gate.

Additional funding will allow an increase in nurse hours from 1 April and a contribution will also be made to the histology department in recognition of their continued support. Two new specialities,

head/neck and colorectal will be targeted for new collections and initial responses from both of these Consultants (Mr Duncan Ingrams and Mr Gethin Williams) have been very supportive. The Royal Gwent site looks forward to the changes/challenges the following year will bring.

Swansea Site

The Swansea site, split over Singleton and Morriston hospitals, consented 261 patients over the twelve month reporting period. One nurse was on maternity leave for over half of the year which reduced potential recruitment. Suzanne Williams, lead WCB nurse, participated in an RCN run 'Personal Leadership Development' Study Day in March 2009 to complement her increased role in co-ordinating and leading all the WCB nurses in Wales. Two members of laboratory staff travelled to London to undergo a two week training programme for DNA/RNA extraction and are now fully trained.

Colleen Lloyd and Suzanne Williams with Leila Couto (r) from the tumour bank in the National Cancer Institute of Brazil (INCA BNT), located in Rio de Janeiro.

In November 2008 WCB hosted Leila Couto, a paediatric nurse from the Tumour Bank in the National Cancer Institute of Brazil (INCA BNT), located in Rio de Janeiro. The exchange was facilitated through membership of the Marble Arch group of International Biobank leaders in which Dr Parry-Jones from the WCB and Dr José Cláudio Casali da Rocha from the National Cancer Institute of Brazil Tumour Bank, are both involved. Leila spent time with the WCB nurses in Swansea to see how WCB operates and discover the differences and similarities between collecting tumour and blood samples in Brazil compared to Wales. She shadowed the nurses taking consent and saw the interaction between WCB, theatre staff and pathology staff and tracked the samples through to storage with the biomedical scientist staff in the labs. The INCA BNT and WCB operate in a similar fashion. The BNT is the first tissue bank in Brazil and aims to establish a network for collection and storage of samples in Brazil to facilitate studies focusing on diagnostic and therapeutic markers. Suzanne Williams will be completing the exchange when she visits Rio in June 2009.

The Singleton site hosted the first WCB open day in January and all Swansea members of staff participated in the day.

Withybush Site

Dr Sally Williams has stepped down from her position as the local WCB lead and, in January, Dr Martin Sevenoakes took up the position just in time for the Human Tissue Authority inspection. Sadly Dr Gareth Melville Jones passed away peacefully in December. He will be missed by all who had the good fortune to know him and work with him. Two new pathologists, Dr Laura Pineyro from Argentina and Dr Iwona Kaminska from Poland have now taken up posts in Withybush and are enthusiastic about the WCB role and research.

Catherine Macphee, the Withybush lead nurse also went to pastures new in March with the Wales Clinical Trials Network. WCB and the WCTN are now trialling a more co-ordinated approach to working together, which so far has been successfully implemented. The recruitment process for her replacement is underway. Staff continue to update and expand their personal skills and knowledge by attending study days, workshops and conferences.

Funding

Funding has been secured from Cancer Research Wales to expand the collection to two new hospital sites in 2009/2010 and increase the collection in two of the current centres. The new funding will also facilitate some research work to produce tissue microarrays of the breast and colorectal collections and fund a scientist post to carry out this work. The initial grant from CRW continues to fund processing work in both Swansea and Cardiff to ensure the maximum use of samples and ensure the quality of samples issued to researchers, as well as funding the ongoing support of the expanded IT department.
Core funding from the Welsh Assembly Government is due for renewal over the coming months as the current contract expires on 31 March 2010. It is hoped that contractual discussions and continued funding can be confirmed as soon as possible to ensure a smooth transition period.

Samples And Scientific Report

WCB continued to collect frozen and paraffin blocks of matched tumour and normal tissue as well as EDTA and serum samples from the patient and EDTA samples from a partner, spouse or friend as a control. An amendment was successfully sought from MREC to include fluid, such as ascites, in the consent procedure and a small collection of ascitic fluid from ovarian and endometrial patients commenced in September as a bespoke collection for a research group. The ascitic fluid is being frozen and stored at -80°C prior to issue to the group. Following another application for ascitic fluid, WCB has decided to investigate the feasibility of routine fluid collection and will be validating a protocol for isolating epithelial cells from ascites at the beginning of the next reporting period.

A semi-automated tissue microarrayer was trialled and then purchased at the beginning of 2009 and microarray construction will commence during 2009. Vicki Woods will be setting up a WCB laboratory in Velindre hospital, Cardiff to concentrate on quality assurance, TMA production and clinical trial hosting arrangements. She will also start a PhD in molecular biology with Professor Gerry Thomas in Imperial College during 2009.

Scientific Report

The Wales Cancer Bank consents its patients for material to be used in cancer research. It is therefore extremely important that not only do we collect and store samples correctly, but that we also distribute these to researchers for use in scientific projects that aim to provide new insights into cancer biology, and ultimately to provide better treatment for cancer patients of the future. Scientists use material in different formats. For some projects using a piece of intact tissue is important – for example if the project wishes to study whether a particular protein is expressed on the cell membrane, making it a potential target for antibody therapies, or inside the cell, making it a better target for drugs that can cross the cell membrane to bind to their target. Other studies concentrate on studying many different proteins, or mRNAs, the precursors of proteins, or factors that change expression of the proteins or mRNAs - alterations in the DNA that alter the level of

mRNA expression or change the shape of a protein, or miRNAs, a type of RNA that alters expression of mRNA but is not itself translated into protein. The Wales Cancer Bank helps scientists by providing material in the format they wish to use. In some cases this also means that different scientific groups can look at different types of material from the same patient. For example, one group may be interested in DNA alterations and wish to compare this with expression of RNA or proteins which the Wales Cancer Bank has extracted from the same sample. This maximises the use of a single piece of tissue, and by encouraging cooperation between scientists who specialise in the different specialities of molecular biology that make us what we are, this will speed up the identification of new targets for cancer therapy.

Wales Cancer Bank has supplied more than 1300 samples to 19 projects so far. The projects include those that specifically examine DNA, RNA and protein. The first paper using WCB material is about to be published in the Journal of Proteome Research later this year. The researchers studied proteins in a type of breast cancer that is still difficult to treat – the so-called triple negative breast cancer that expresses no oestrogen, progesterone or Her2 receptors. The aim of the study was to identify new therapeutic targets for this group of breast cancer patients, and to understand how the biology of this type of tumour is different from a closely related type of breast cancer that also does not express oestrogen or progesterone receptor, but does express Her2. The latter group of patients already do have a target for treatment – these patients would be offered Herceptin treatment. The researchers found several different proteins that were expressed differently in the triple negative cancers from the Her2 positive cancers. Some of these are already known to be involved in stimulation of the growth of new blood vessels, and are associated with tumour spread to other tissues (metastasis). They therefore would present potential targets for the development of treatment strategies for this particularly aggressive form of breast cancer.

There will be many more papers published that use WCB samples. The provision of such good quality material to researchers will lead to a much better understanding of human cancer biology, and through this to better, more targeted treatments for a number of different types of cancer.


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RWMB
PT 1A

Applications and Supply of Biomaterials

Sixteen applications for biosamples were received by WCB during the period 1 April 2008 and 31 March 2009, taking the total number of applications received to forty five.Of the sixteen from this reporting year, one was for a clinical trial, one was withdrawn, three were rejected with the suggestion to the researchers that more focussed applications could be submitted for re-review and eleven were approved. Eight of the applications originated from UK university researchers, six from UK biotech and/or pharmaceutical companies and one from a European research centre.

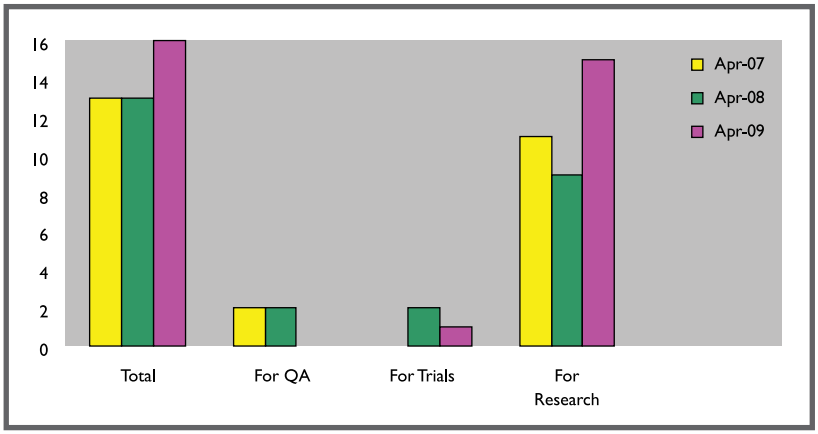

Figure 3 - Applications received

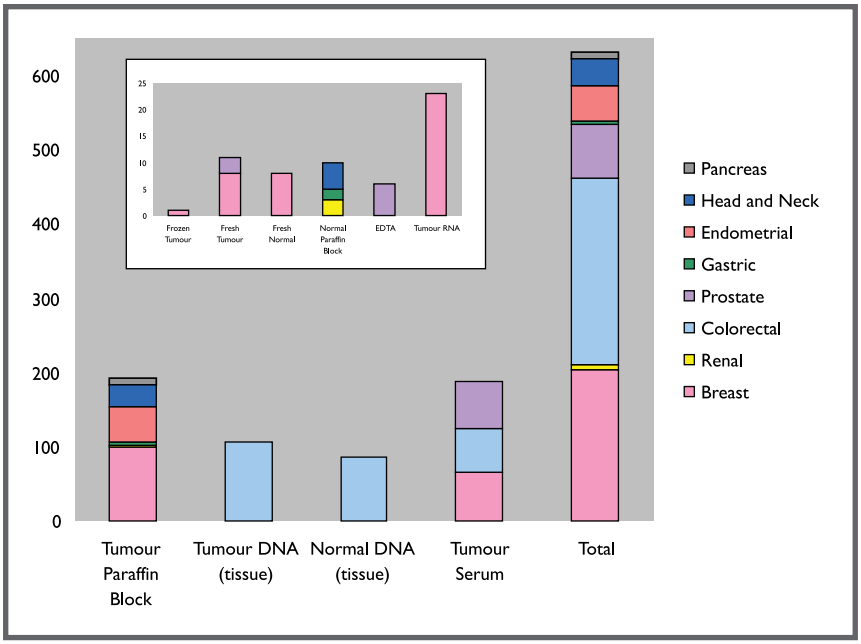

Figure 4 – Samples supplied by tumour type and format

Supply Of Biomaterial

658 samples were supplied to 10 different projects during the year. 67% of those were sent to applications received in previous years and 33% to applications received during this reporting year. The breakdown of sample type and tumour type is shown in Figure 4 below. Some samples were a continued supply to projects reported in last year's annual report. Lay summaries for the new projects supplied can be found in Appendix A. One clinical trial has been supported (SUPREMO) with blocks from WCB.

Advisory Board

Two Advisory Board meetings took place, one in June 2008 and one in February 2009. Several changes have been made to the membership of the Board; Andrea Hague joined the group to represent Velindre NHS Trust due to Tony Hazell's change of affiliation. He remains on the Board in his capacity as Chair of the Nursing and Midwifery Council. Professor Stephen Tomlinson, Provost of Cardiff University joined the Board to represent the University and Barry Furr, formerly Chief Scientist with AstraZeneca has accepted an invitation to join the Board at the next meeting. Professor John Harris has tendered his resignation from the Board as he has so far been unable to attend any meetings held to date, thereby leaving a vacancy for a bioethicist.

HTA/Local Management group

The local management and Human Tissue Authority (HTA) named personnel group met three times over the reporting period. The group continue to manage the WCB activity at local level and look at applicable operational strategies. WCB initiated compliance reports to participating NHS Trusts to provide a communication link between the Trust signatories on the Service Level Agreements (SLA), the local name Person Designated on the HTA licence and the WCB. These reports highlight the annual audit findings for the relevant Trust and detail any areas of concern regarding compliance with both the SLAs and the licensing requirements. Four members of the group were interviewed as part of the HTA inspection in February.

Human Tissue Authority Inspection

In February 2009, the Human Tissue Authority (HTA) inspected five of the WCB collection sites in line with licensing requirements under the Human Tissue Act (2004). Two inspectors from the HTA spent four days inspecting sites in Withybush, Swansea (Singleton and Morriston) and Cardiff (Medical Genetics and UHW) as well as conducting documentation reviews and interviews with staff and personnel named on the licence. The inspection team commented that 'Given the complexity of the samples processed and distributed throughout the sites traceability was excellent', and 'the establishment showed exemplary practices in many areas of operation'. The full report can be found online in Appendix F.

Lay Liaison and Ethics group (LLEG)

The lay liaison and ethics group met twice during the reporting period and continued to develop the awareness raising strategy for WCB via the communication strategy. LLEG members facilitated a workshop with the South East Wales Cancer group (CASE) where WCB and CRW gave overviews of their respective roles in July 2008. The group are actively involved in assisting with the publicity to highlight the upcoming fifth anniversary of the public launch of WCB that took place in June 2004.

MREC

A substantial amendment was successfully submitted to the Wales MREC in June 2008 to increase the biosamples collected by WCB to include fluids, such as ascetic fluid. An annual report detailing projects supplied with WCB samples was sent to MREC in July 2008, as part of the conditions of ethics approval from the committee.

Information Technology (IT)

Development

The WCB system functionality has been extended with the delivery of two bespoke clinical trial modules for the Wales Cancer Trial Unit (WCTU), namely SCOPE and ZICE. An additional module was developed to enable WCTU administrative staff access to the WCB system. This module facilitates the monitoring and auditing of the samples received from the various UK trial centres.

A complete re-write of the patient follow-up data module has been carried out to incorporate lessons learned from the pilot phase. These include new data fields and a module to register WCB donors' participation in clinical trials. A basic Tissue Micro Array (TMA) module was introduced that associates a collection of samples and TMA slides with a TMA. An inventory module has been written to allow WCB sites to record the WCB inventory into a central database. The change management module has been released and enables users to record change management issues directly into the WCB system, thereby establishing a more efficient change management procedure.

CANISC Decoupling

The WCB application was included in the CANISC decoupling project where the citrix and database servers were migrated to a more robust infrastructure supported by Health Solution Wales. As part of this move the WCB IT Manager joined the new CANISC Service Management Board.

Hardware

Two new quad core servers have been purchased and installed in Swansea University. With the development server the WCB software developers can version control their source code in a centrally backed up repository. The second server will be used as a web server for the Mirax digital slides. An additional Terra station was purchased for backing up the digital slides.

System Re-write

The WCB system re-write in ASP and .net has begun with the development of system login and user management screens. The system configuration (24 screens) was completed in addition to the system templates for master and detail screens. Templates were also developed for the business and data access class libraries. The new ASP system uses Component art technology to deliver a rich graphical interface with true AJAX technology.

Figure 5 - The new ASP re-write configuration module

Training

In the last year nine new users were trained to use the WCB system and two system training workshops were delivered. A data leak workshop was also conducted to address concerns of the WCB Advisory Board for possible data leaks.

Governance and Change Management

The system change management has been formalised and uses Agile SCRUM method for new software releases. Regular meetings between the WCB Project Manager and the IT Manager establish the priorities for each software release. The new User Acceptance Test (UAT) environment allows users to test and accept software prior to its release to the production environment.

A review commissioned by the WCB Advisory Board has recommended the setup of an IT Project Board for the WCB re-write project, using PRINCE2 principles, to improve governance. Members of the new board are: Andrew Griffiths (Chair), Director of Service Management, Informing Health Care; Ed Davies, Acting Director of Information Security, ABM trust; Alison Parry-Jones, Project Manager, WCB; and Daniel Naeh, IT Manager, WCB.

Clinical Trials

Hosting

The Wales Cancer Bank is continuing to host sample collections attached to clinical trials. Samples continue to be collected for COIN, XERXES and SCOPE and a new trial collection, ZICE, commenced during 2008.

ZICE

ZICE is a randomised, pragmatic, phase III, open-label, multi-centre, parallel group clinical trial to evaluate and compare the efficacy, safety profile, tolerability and patient satisfaction of daily oral ibandronate 50mg versus intravenous zoledronate 4mg as 3-4 weekly infusions in the treatment of breast cancer participants with bone metastases. The objective of the study is to demonstrate non-inferiority of oral ibandronate 50mg daily in comparison with 3-4 weekly zoledronate 4mg iv infusions and investigate the tolerability and side-effect profile of the two study arms.

Eligible patients with metastatic breast cancer to bone, in whom iv bisphosphonate therapy is indicated, will be randomised to one of the two treatment arms. It is intended that participants in both arms will receive 96 weeks of treatment. At the end of the treatment period, participants will be followed up for a further 3 years. The primary outcome measure is the frequency and timing of skeletal-related events (SREs) over 96 weeks (multiple event analysis). The secondary endpoints include time to first SRE, percentage of participants with any SRE, pain/analgesic scores, Quality of Life, overall survival at 96 weeks and 5 years, safety, and health resource usage at 48 and 96 weeks. A subset of the study population have consented to take part in the ZICE bone marker sub-study, which will measure changes in serum markers of bone metabolism.

The objective of the ZICE bone marker sub-study is to collect and store blood samples to measure bone markers (e.g. CTX, bone specific alkaline phosphatase), and other biomarkers. Analysis/research will assess whether changes in bone markers levels are associated with changes in pain in participants with metastatic breast cancer who are starting on bisphosphonate treatment.

Serum and plasma samples will be taken from a subset of consenting participants. An extra blood sample will be taken at the participant's baseline, 1st interim and 12 week visit, which will be stored at the Wales Cancer Bank for later analysis. All samples will be analysed for bone markers and other potential molecular markers for treatment responses; the baseline samples will be analysed for bone specific alkaline phosphatase and serum CTX levels. Samples at the later time points will be analysed for serum CTX. These samples may also be analysed using newer technologies to see if we can identify better markers of bone activity and the likelihood of benefiting from treatment.

Conferences & Marketing

ISBER

The 2008 Annual ISBER conference was held in May in Bethesda, Maryland. Professor Thomas was invited to contribute to an interesting workshop session aimed at promoting biobanks as critical resources for the host institution, the

research community, and the public. She spoke about engaging institutions and institutional officials in biobanking and suggested ways of getting people involved.

The WCB exhibited and/or presented posters at several events during the year including the 3rd Annual NCRI conference in Birmingham in October 2008, the National Eisteddfod of Wales in August 2008, the joint WCI/Cancer Alliance conference in May 2008 and the WCTN symposium in November 2008.

The Confederation of Cancer Biobanks organised a second workshop event in January 2009 on Ethics and Governance. It was held in London the day before the start of the PathSoc meeting and attracted around 160 attendees from around the UK and Ireland. Dr Alison Parry-Jones gave a talk on 'Generic and Enduring consent' that provoked a lively interactive discussion. Several talks during the day updated the audience on NRES, the HTA and showcased some governance and access models.

The European Science Foundation held a biobank specific event in Spain in November 2008 at which Vicki Woods presented a poster on the QA done at WCB and Dr Alison Parry-Jones gave a talk about patient involvement in WCB. The four day conference was attended by delegates from around Europe and a second biobanking event is being scheduled for 2009.

The Marble Arch working group of International biobank leaders held two meetings during 2008, one in Dublin in April and one in Milan in October. Both meetings were preceded by open meetings for local interested parties.

One of the patient involvement groups in Wales, Cancer in South East Wales (CASE) invited WCB and CRW to give a workshop presentation to the members of the group and local members of the Community Health Council in July 2008. The workshop was well attended and feedback from attendees was very favourable.

CRW held its first scientific symposium in Cardiff in November 2008 and invited Prof Thomas to give a talk about WCB, the progress made and potential gains the WCB could provide for the cancer research community. WCB also displayed two posters detailing the QA processes and a general progress report update. WCB was also present and gave a talk at the annual CRW open day in January 2009 where the charity's supporters are given a chance to hear about the research supported by their donations and also tour the laboratories in Velindre and talk to some of the scientists involved in the work.

Open Day

The WCB held its first open day on 6th January 2009 in Singleton hospital, Swansea. Open days are targeted at university and/or NHS staff interested in setting up a human biobank. Eight visitors joined WCB staff to tour the labs and hear how WCB was set up and functions as a decentralised bank in multiple NHS Trusts around Wales. Following a number of presentations by senior WCB staff the visitors had the chance to talk one to one with WCB nursing, laboratory, IT and admin staff about the specific day to day practicalities of running the bank. An open forum session at the end of the day allowed more general topic discussion and feedback. All of the attendees found the day to be interesting and valuable, especially those in the early stages of setting up human biobanks in their home institutions. Further open days will be held during 2009.


This is such an exciting project – and a real investment by today's generation for the Welsh people of tomorrow.'
Huw Edwards
WALES CANCER BANK

Looking Ahead

Patient Recruitment

The graph below predicts a steady increase in patient recruitment over the coming twelve months. The target recruitment for the coming twelve months has been set at 3500 patients to allow for staff changeover periods which result in fewer patients consented due to induction and training schedules.

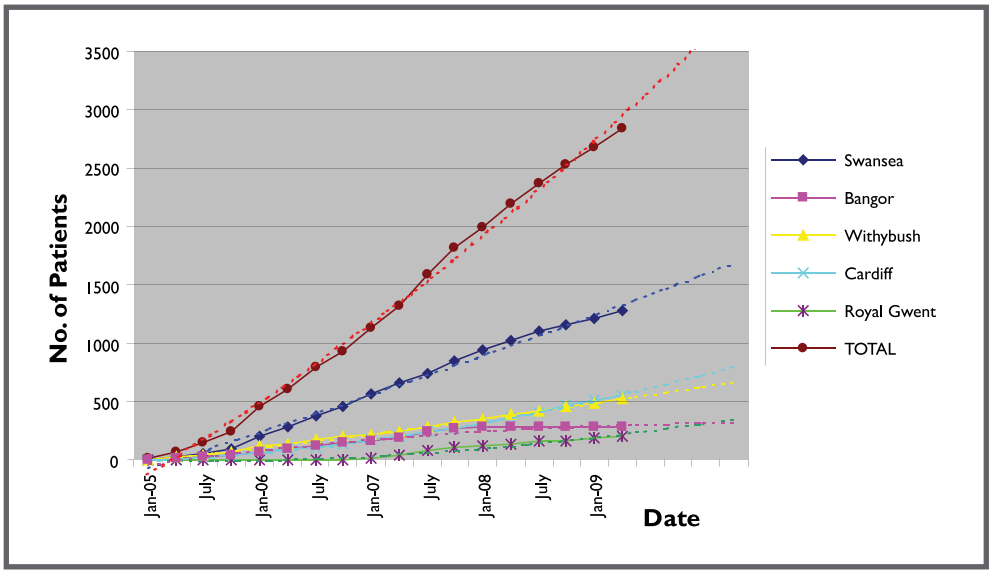

Figure 6 - Forecast of potential future patient recruitment

Expanding collection

Discussions are under way with one hospital in North Wales and a second new site will be identified in the South to utilise the new funding that has been secured from Cancer Research Wales to expand the collection to two new hospital sites in 2009/2010. The new funding from CRW will also enable additional tumour sites to be targeted in current hospitals and the Royal Gwent expansion is one example of how this funding will be used.

Raising awareness

WCB will continue to attend, exhibit and give presentations at national and international meetings during the year, such as the NCRI and ISBER. Publicity within Wales will be addressed with the planned roadshow events for the 5th anniversary celebrations and also National Pathology week in November.

Targets For 2009/10

- Accrue 3500 patients in total
- Supply six new projects with biosamples
- Develop a web accessible version of database
- Collate clinical data for patients consented to end 2008

Financial Statement

	Assembly Funding	CRW	Velindre	CRUK*	General Account	
	Expenditure	Expenditure	Expenditure	Expenditure	Expenditure	Income
STAFF COSTS						
Central Staff	£143,272	£29,543	£31,212			
Swansea Site	£136,454	£27,610				
Cardiff Site	£42,150			£35,849		
Haverfordwest Site	£55,722					
Bangor Site	£9,879					
Newport Site	£15,721					
Sub Total	£403,198	£57,153	£31,212	£35,849		
NON STAFF COSTS						
Office Accommodation	£5,461					
Equipment/Consumables	£27,615	£31,297				
Travel/Conference/Training	£39,608					
Office Expenses/Legal	£47,334					
IT	£11,794	£37,452				
Sub Total	£131,812	£68,749				
Cost Recovery					£527	-£34,589
Trial related					£5,813	-£8,859
Brought Foward 07/08						-£35,115
TOTAL	£535,010	£125,902	£31,212	£35,849	£6,340	-£78,563

* Cancer Research UK (CRUK) funding is via the Experimental Cancer Medicine Centre in Cardiff University

APPENDIX A

PROJECTS SUPPLIED WITH BIOMATERIALS

07/005 – David Millar, Cardiff University

To date, the majority of breast cancer researchers use immortalized cell lines. These cell lines are prone to genetic drift and, in the majority of cases, have been derived from metastatic deposits and not the primary tumour. Thus, a more clinically relevant model would be the use of epithelial cells derived directly from primary breast tumours, as the majority of treatments used today are targeted against the primary tumour. The primary culture of tumour derived cells will therefore be useful for both functional cell and molecular biology studies. To this end a culture system will be established based on the methods of Speirs (2003).

08/001 – Chris Womack, AstraZeneca

This application is for human tissue to support a programme of exploratory research projects that in turn, support and optimise the early stages of cancer drug discovery and development and also to gain information of relevance for design of clinical studies, e.g. "Proof of Mechanism, Proof of Principle and Proof of Concept". Research studies will lead to a better understanding of the natural history of cancer and may generate hypotheses on the predictive value of specific molecular features for the natural history of specific cancer types. This will offer the potential of identifying patients with those tumour types considered most likely to benefit from "molecularly targeted therapies".

08/009 – Gerry Thomas, Imperial College, London

The ret oncogene is known to be associated with specific types of thyroid cancer. Recently is has also been found to be expressed in breast cancer. It is activated by two different mechanisms in breast cancer – by increased expression and by rearrangement of the gene, which results in fusion of part of the end of the gene and an increase in downstream signalling pathways. This project aims to relate expression/rearrangement of the ret gene to specific molecular phenotypes of breast cancer, and to identify the fusion partners when the ret gene is activated by rearrangement in breast cancer. Many drugs that are currently used in cancer treatment to block the development of new blood vessels in tumours also inhibit the signalling pathway for the ret oncogene. The results of this study may lead to identification of subsets of breast cancer patients who may benefit more from these types of treatment regimes than others who do not show activation of the ret gene in their tumours.

08/011 - Oxford Genome Sciences (UK) Ltd, Dr Christian Rohlff

Oxford Genome Sciences (OGeS) will use samples from the Wales Cancer Bank to establish tests for the diagnosis of Cancer and for monitoring patient relapse and progression. OGeS has recently discovered a panel of membrane-associated, transmembrane and secreted proteins that are found to be up-regulated in cancer patients, and to have low normal expression. These proteins were discovered via proteomic detection and prioritised using the company's OGAP® data integration system. OGeS has evidence that some of these biomarkers are likely to be up-regulated in the blood of Cancer patients and may therefore provide specific and sensitive diagnostic biomarkers for the early detection of cancer and for the monitoring of disease progression and relapse. OGeS intends

to conduct an investigation with blood serum samples from the Wales Cancer Bank to confirm whether these proteins are indeed up-regulated in the blood of Cancer patients. If successful, the biomarkers will be taken forward for further investigations for the development of rapid and sensitive tests for Prostate, Breast and Colorectal Cancers.

08/012 – Professor Alan Burnett, Cardiff University

Prostate cancer is thought to originate from cells that are capable of self renewal and the ability to specialise into many different cell types; these cells are known as cancer stem cells. Although conventional chemotherapy is able to reduce the size of prostate tumours it is thought that the continued presence of cancer stem cells results in re-growth and spreading of the tumour. Prostate cancer cells have high levels of a protein called NF-kB which is important for the survival of the cancer cells. Recently we demonstrated that an inhibitor of NF-kB is effective at killing leukaemia cells and myeloma cells and others have shown that it preferentially targets the leukaemia stem cells. We now intend to use this inhibitor in prostate cancer samples to determine whether it is also an effective treatment in this disease and whether it is effectiveness is maintained in prostate cancer stem cells. In this way we hope to develop better treatments for this disease.

APPENDIX B

WALES CANCER BANK AUDIT 2008

The annual audit schedule in 2008 took place between 10th November and 15th December 2008. The Cardiff, Withybush, Swansea and Royal Gwent sites were visited by the WCB Director, Director of Scientific Services, Manager and IT Manager. Medical Genetics was audited by the WCB Manager and Bangor was visited by the WCB Director and Manager. A random selection of donations, spanning all years of collection, was inspected at each site with a sample trail completed for all audited donations. A list of incomplete data was generated to show donations with no samples, no diagnosis, questionable ischaemic times, no questionnaire or no pathology report after two months.

Four sites have been collecting for nearly four years and the 2008 audit was the fourth such internal inspection during this time. Royal Gwent has been collecting samples for two years and this was the second internal audit at the site. The workflows and role responsibilities of staff at each site have local variation in order to fit in with routine clinical practice. Role responsibilities at each site are documented and included in the Service Level Agreements with each NHS Trust.

Each site is covered by a HTA licence to store tissue for research purposes. No major issues were highlighted that could potentially jeopardise the licence at any site. All sites are working within local and WCB guidelines on Health and Safety and adhere to WCB Standard Operating Procedures, although staff are reminded to ensure that they are fully conversant with all SOPs.

Audit Schedule

Site	Date of Audit
Swansea (Singleton, Morriston)	10th November 2008
Withybush	21st November 2008
Cardiff (UHW, Llandough)	24th November 2008
Royal Gwent	24th November 2008
Medical Genetics	8th December 2008
Bangor	15th December 2008

A number of data queries were run to check integrity of data at each site:

1. Female prostate cancer.
2. Incomplete records, i.e those records (donations) having an incomplete record marker recorded against them.
3. Male breast cancer cases.
4. Donations with missing diagnosis.
5. No blood samples for donations over 15 days old.

6. No pathology reports for donations over 15 days old.
7. No tissue sample over 15 days old.
8. Samples without a donation.
9. Query ischaemic time.

Similar data queries will be generated every 3 or 4 months and sent to each site as interim data quality/completeness checks

General

Time fields are still causing some confusion and resulting in erroneous ischaemic times.

Some specialities not on database so pathology reports not able to be completed. Information is held on paper copies but transfer to database not possible. Therefore a number of the missing pathology reports highlighted on the audit paperwork are as a direct consequence of datasets not being available on database. Diagnosis is able to be entered for all specialities but is being omitted to flag as an incomplete record to remind that the dataset is not available.

A separate DNA and RNA audit was conducted earlier in 2008 by staff in Swansea. Some concerns were raised regarding the accuracy of extracted samples following a request for DNA aliquots that were present on the database but not in the freezer. The entire collection of nucleic acids was audited to compare the number of aliquots and their co-ordinates in the freezer against the recorded information on the database. A number of inconsistencies were found including:

- Bags with no samples
- Bags/cryovials with hand written numbers inconsistent with barcode information
- Cryovials labelled as RNA in a bag labelled DNA (and vice versa)
- Unexpectedly high number of cryovials labelled as non-standard aliquots for single donation(s)
- RNA and/or DNA from same extraction in 2 or 3 different storage areas
- Actual storage co-ordinates in freezer inconsistent with database records

Actions

To be implemented centrally:

- Hold training session to clarify all the 'time' fields to ensure accurate data is captured
- Look at workflow in sites to ensure a full range of biosamples is collected in the majority of cases
- Continue 3 monthly local sample tracking exercise. Database manager to generate missing data information and identify five random numbers for local audit. Report to be submitted to central office

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- Distribute updated SOPs that include current sample forms
- Insert tick box to record whether samples go into formalin on same day as operation
- Insert tick box to record if the time the tissue was harvested is unknown. The time field is a critical field to ensure a 'complete' record is achieved. If this is not completed it currently flags the donation as 'incomplete'.
- Instigate an annual 'Assurance statement' following the audit to signatories on the SLA in each Trust to give headline outcomes of audit and show compliance or areas of concern

To be implemented at sites:

- Ensure all samples are barcoded
- Undertake full audit of paraffin block cabinet against database information
- All forms detailing sample handling, time information must be completed
- Diagnosis needs to be entered regardless from paper pathology report
- Incomplete records to be checked every month to enter new data when available
- Ensure training and SOP knowledge is up to date and SOPs are followed
- Ensure cryopen markings on EDTA racks are permanent

DNA/RNA

- Non-standard aliquots of DNA and/or RNA will not be kept from future extractions
- An audit of DNA aliquot amounts to take place by taking 1 of each standard aliquot and confirm amounts by running through the nanodrop.
- Destroy all samples where any ambiguity is involved.
- If the database shows a discrepancy with the number aliquots in the freezer or inconsistent storage co-ordinates then the records on the database need to be amended to match freezer content.
- The SOP for aliquotting to be amended.
- From now on, all aliquots must be placed in a bag and the bag is to be barcoded with the originating block barcode. All aliquots must also be labelled with a barcode detailing the originating block (eg. RVCC000333FT1A). Aliquots do not need to have individual aliquot number suffixes on the aliquot barcode. The total number of aliquots in a bag may be entered manually onto the database.
- A time line of 4 months has been given to complete the 1 standard aliquot of each DNA sample being put through the nanodrop to include a report on the run and to itemise what is left.
- A time line of 6 months has been given for deleting/mirroring the database to the freezer.

Conclusions

All sites are generally operating well and the audit gave a good opportunity for the exchange of views and discussions about local practice and the project in general. Centres must ensure compliance with SOPs, especially with regard to sample identification for tracking purposes. The action points identified involve both central and local activity. It is hoped that all points can be actioned by the end of March 2009.

Regular reviews of data to be encouraged via the quarterly mini audit scheme. The pilot scheme to back fill clinical data has now been rolled out to other sites and most sites have around 80% of the available data captured and entered onto the database by the information assistant in Swansea.

Sample tracking procedures should be reinforced to ensure the exact location of every sample is known and quarterly internal audits will continue in 2009.

The management teams wishes to express its thanks to all staff, not only for their hospitality during the audit visits, but for their continued enthusiastic support for the project.

Notes by centres

Cardiff

The data queries were run against the live WCB database on 19th November 2008 and the results are outlined below.

1. Female prostate cancer – none
2. Incomplete records – 145 instances from Cardiff were found
3. Male breast cancer – n/a, breast samples not collected in Cardiff
4. Donations with missing diagnosis – 58 instances were found at Cardiff
5. No blood samples over 15 days old – 93 instances were found at Cardiff
6. No pathology reports for donations over 15 days old – 73 instances were found at Cardiff.
7. No tissue sample over 15 days old – 14 instances were found at Cardiff
8. Samples without a donation – 1
9. The ischaemic time query returns results for those donations that have either a negative ischaemic time or the ischaemic time is greater than 3 hours - 30 instances to be checked

A list of the missing data was left with the WCB technician and nurse to address. In addition, 12 WCB numbers from UHW, 6 from Llandough, 10 from Medical Genetics and 13 from COIN were randomly chosen to check the data and sample tracking.

Site file was present and up to date with SOPs etc

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UHW

Donation 017

- All paperwork present
- H&E slides barcodes do not have readable numbers only barcode. Need scanning to confirm which slide comes from which block
- Database and paperwork show frozen tumour sample but sample labelled as normal

Donation 096

- All paperwork present
- Paraffin paperwork shows 1 tumour and 1 'background' but both samples labelled as tumour
- Database and paperwork show 4 frozen normal samples but samples labelled as tumour
- H&E slides barcodes do not have readable numbers only barcode. Need scanning to confirm which slide comes from which block

Donation 157

- All paperwork present
- All samples in correct place

Donation 244

- All paperwork present
- All samples in correct place

Donation 247

- All paperwork present
- All samples in correct place

Donation 411

- All paperwork present
- All samples in correct place

Donation 425

- All paperwork present
- All samples in correct place

Donation 502

- All paperwork present
- All samples in correct place
- Blood samples not yet entered on database

Donation 507

- All paperwork present
- Blood paperwork shows samples as post-op but database record shows pre-op
- All samples in correct place

Donation 558

- All paperwork present
- No tissue taken – insufficient
- All samples in correct place

Donation 569

- All paperwork present
- All samples in correct place

Donation 575

- All paperwork present
- No tissue taken – insufficient
- All samples in correct place

Llandough

Donation 173

- All paperwork present
- All samples in correct place

Donation 177

- All paperwork present
- No tissue taken – insufficient
- Clot time for serum >30 minutes
- All samples in correct place

Donation 394

- All paperwork present
- All samples in correct place

Donation 434

- All paperwork present
- All samples in correct place

Donation 482

- All paperwork present
- No tissue – insufficient
- All samples in correct place

Donation 493

- All paperwork present
- No tumour tissue only normal
- All samples in correct place

COIN

13 numbers were chosen and consent information and sample location checked. All 13 samples were recorded on the most recent consent list received from the MRC showing consent for EGFR testing and future research. Sample locations recorded on the WCB database were inaccurate due to sample movement for arraying and kRAS testing but the COIN technician had an additional processing spreadsheet showing accurate locations. Therefore, all samples were located.

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Medical Genetics

10 records showing either EDTA or extracted DNA being present in Medical Genetics were randomly chosen for checking. Donations originated from 3 different collecting sites.

Donations: 001, 277, 405 from Withybush
106, 177, 195, 331, 399 from Swansea
30, 197 from Cardiff

All samples were present in correct place and all internal shipment requests are filed in the site file. Extraction worksheets and lists are filed.

Storage disk for gel view images required and training to upload images to database requested.

Royal Gwent

The data queries were run against the live WCB database on 19th November 2008 and the results are outlined below.

1. Female prostate cancer – none
2. Incomplete records – 4 instances were found.
3. Male breast cancer – n/a, not collecting breast.
4. Donations with missing diagnosis – 13 instances were found
5. No blood samples over 15 days old – none
6. No pathology reports for donations over 15 days old – 13 found
7. No tissue sample over 15 days old – none
8. Samples without a donation – none
9. The Ischaemic time query returns results for those donations that has either a negative ischaemic time or the ischaemic time is greater than 3 hours - none
10. Family History missing– 21 instances were found

A list of the missing data was left with the nurse to address. 9 WCB numbers were randomly chosen to check the data and sample tracking. Numbers generated were 74, 93, 103, 114, 121, 131, 144, 159 and 171.

Site file was present and up to date with SOPs etc

Donation 074

- Three copies of consent form present – query copy in patient notes
- No paraffin form
- All samples in correct place

Donation 093

- No paraffin form
- All samples in correct place

Donation 103

- All paperwork present
- No tissue taken as no malignant tissue found
- All samples in correct place

Donation 086

- All paperwork
- All samples in correct place

Donation 114

- All paperwork present
- No tissue taken – insufficient
- All samples in correct place

Donation 121

- No paraffin form
- All samples in correct place

Donation 131

- Three copies of consent form – query copy in patient's notes
- No tissue taken
- All samples in correct place

Donation 144

- All paperwork present
- All samples in correct place

Donation 159

- All paperwork present
- All samples in correct place

Donation 171

- All paperwork present
- Patient to theatre following day so limited paperwork
- All samples in correct place

Query over information regarding 'harvested op' time field. As samples all go straight into formalin in theatre, a list of 'time put in formalin' to be sent to IT to automatically populate the 'harvested op' time field with 'time put in formalin' minus 1 minute.

Bangor

The data queries were run against the live WCB database on 12th December 2008 and the results are outlined below. As no nurse is present in Bangor only the sample locations were checked.

1. Female prostate cancer – this query produces no results.
2. Incomplete records – 21 instances were found.
3. Male breast cancer – no instances were found.

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4. Donations with missing diagnosis – 2 instances found.
5. No blood samples over 45 days old – 70 instances were found.
6. No pathology reports for donations over 15 days old – 3 instances were found.
7. No tissue sample over 45 days old – 11 instances were found.
8. Samples without a donation – no instances were found.
9. The Ischaemic time query returns results for those donations that has either a negative ischaemic time or the ischaemic time is greater than 3 hours. 5 results were found with negative times.
10. Family History missing - 63 missing forms.

A list of the missing data was sent to the WCB lab staff to address. In addition, 12 WCB numbers were randomly chosen to check the data and sample tracking. Numbers generated were 2, 20, 27, 56, 102, 111, 118, 157, 188, 212, 264 and 274.

Donation 2

- Samples present in correct location and barcoded

Donation 20

- Samples present in correct location and barcoded

Donation 27

- Samples present in correct location and barcoded

Donation 56

- Samples present in correct location and barcoded

Donation 102

- Samples present in correct location and barcoded

Donation 111

- Samples present in correct location and barcoded

Donation 118

- Samples present in correct location and barcoded

Donation 157

- Samples present in correct location and barcoded

Donation 188

- Samples present in correct location and barcoded

Donation 212

- Samples present in correct location and barcoded

Donation 264

- Samples present in correct location. Paraffin blocks and slides not barcoded

Donation 274

- Samples present in correct location. Paraffin blocks and slides not barcoded

2 EDTA samples were present in the freezer that had no WCB identifier. Query as to the origin of the samples. Over half the slides and blocks present were not barcoded.

The scan gun is not working and shipments are being manually entered leading to errors.

Swansea

The data queries were run against the live WCB database on 4th November 2008 and the results are outlined below.

1. Female prostate cancer – none
2. Incomplete records – 382 instances were found.
3. Male breast cancer – 3 instances were found.
4. Donations with missing diagnosis – 195 instances were found
5. No pathology reports for donations over 15 days old – 135 instances found
6. No tissue sample over 15 days old – 8 instance found
7. Samples without a donation – none
8. The Ischaemic time query returns results for those donations that has either a negative ischaemic time or the ischaemic time is greater than 3 hours – 17 instances found
9. Family History missing– 177 instances were found

A list of the missing data was left with the WCB staff to address. In addition, 16 WCB numbers from Singleton and 15 WCB numbers from Morriston were randomly chosen to check the data and sample tracking. Numbers generated for Singleton were 9, 84, 127, 165, 171, 196, 426, 499, 961, 987, 990, 996, 998, 999, 1005 and 1086. Numbers generated for Morriston were 457, 493, 542, 618, 743, 801, 882, 884, 921, 1001, 1004, 1005, 1007, 1008 and 1099.

Singleton

Donation 9

- All paperwork present
- All samples in correct place

Donation 84

- All paperwork present
- No tissue taken
- All samples in correct place

Donation 127

- All paperwork present
- All samples in correct place

Donation 165

- All paperwork present
- All samples in correct place

Donation 171

- All paperwork present
- Path report not signed
- All samples in correct place

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Donation 196
- All paperwork present
- All samples in correct place

Donation 426
- All paperwork present
- All samples in correct place

Donation 499
- All paperwork present
- All samples in correct place

Donation 698
- EDTA co-ordinates listed as D2 and D3 but actual co-ordinates C10 and C11. Donation 677 EDTA in D2 and 3.
- All samples in correct place

Donation 961
- All paperwork present
- No tissue taken
- All samples in correct place

Donation 987
- All paperwork present
- All samples in correct place

Donation 990
- All paperwork present
- Co-ordinates of frozen blocks on database do not match paperwork
- All samples in correct place

Donation 996
- All paperwork present
- All samples in correct place

Donation 998
- All paperwork present
- All samples in correct place

Donation 999
- All paperwork present
- All samples in correct place

Donation 1005
- Paperwork present
- No paraffin block form as blocks went straight to fixative project
- All samples in correct place

Donation 1086
- All paperwork present
- EDTA samples labelled as control samples but should be donor samples
- All samples in correct place

A number of serum samples in 2AB1 not barcoded

Morriston

Donation 457

- All paperwork present
- Pancreas dataset not on database
- All samples in correct place

Donation 493

- All paperwork present
- No tissue taken
- All samples in correct place

Donation 542

- All paperwork present
- All samples in correct place

Donation 618

- All paperwork present
- No tissue taken
- Pancreas dataset not on database
- All samples in correct place

Donation 743

- All paperwork present
- No frozen tissue
- All samples in correct place

Donation 801

- All paperwork present
- All samples in correct place

Donation 882

- Paperwork present
- No paraffin form as blocks went straight to fixative project
- All samples in correct place

Donation 884

- All paperwork present
- Gastric dataset not on database
- All samples in correct place

Donation 921

- All paperwork present
- Paraffin form states only tumour blocks (2) taken but database shows 1 normal block present

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Donation 1001

- All paperwork present
- No tissue taken
- All samples in correct place

Donation 1004

- All paperwork present
- No frozen tissue taken
- All samples in correct place

Donation 1005

- All paperwork present
- All samples in correct place

Donation 1007

- All paperwork present
- No frozen tissue taken
- All samples in correct place

Donation 1008

- All paperwork present
- No frozen tissue taken and only normal paraffin blocks recorded
- All samples in correct place

Donation 1099

- All paperwork present
- Paperwork and database show 2 normal frozen blocks but cryovials in freezer labelled as 1 tumour and 1 normal.

Action

Take H&E of frozen blocks for donation 1099 to determine whether one is a tumour block
Marker pen on EDTA racks is not permanent. Investigate permanent cryomarker pens.

Withybush

The data queries were run against the live WCB database on 18th November 2008 and the results are outlined below.

1. Female prostate cancer – none
2. Incomplete records – 10 instances were found.
3. Male breast cancer – 1 instance found.
4. Donations with missing diagnosis – 1instance was found
5. No pathology reports for donations over 15 days old – 37 instances found
6. No tissue sample over 15 days old – 4 instances found
7. Samples without a donation – 1 instance found
8. The Ischaemic time query returns results for those donations that has either a negative ischaemic time or the ischaemic time is greater than 3 hours – 7 instances found

9. Family History missing– 62 instances were found
10. No blood samples over 15 days old – 17 instances found

A list of the missing data was left with the WCB staff to address. In addition, 17 WCB numbers from Withybush were randomly chosen to check the data and sample tracking. Numbers generated were 002, 014, 059, 118, 136, 204, 233, 253, 262, 301, 354, 362, 409, 424, 443, 450 and 458.

Donation 002

- All paperwork present
- All samples in correct place

Donation 014

- All paperwork present
- Consent boxes (patient and control) ticked not initialled
- All samples in correct place

Donation 059

- All paperwork present
- Boxes on consent form not initialled
- 4 normal blocks annotated as proximal or distal
- PN3A not in block cabinet

Donation 118

- All paperwork present
- Database and paperwork show no tumour blocks and 3 normals but one sample in cabinet is labelled as tumour

Donation 136

- All paperwork present
- Blood form not signed
- Pathology form not fully completed
- No tissue – insufficient
- All samples in correct place

Donation 204

- All paperwork present
- All samples in correct place

Donation 233

- All paperwork present
- Paraffin blocks in row 4 not row 3
- H&E slide for FT2A in slide cabinet but not on database

Donation 253

- All paperwork present
- All samples in correct place

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Donation 262
- All paperwork present
- No tissue taken

Donation 301
- All paperwork present
- All samples in correct place

Donation 354
- All paperwork present
- All samples in correct place

Donation 362
- All paperwork present
- Paraffin samples recorded as 3 tumour and 3 normal on paperwork and three of each present in block cabinet but only 2 of each show on database
- Extra H&E slides for PN1, PN2, PT1 and PT3 in slide cabinet

Donation 409
- All paperwork present
- All samples in correct place

Donation 424
- All paperwork present
- All samples in correct place

Donation 443
- All paperwork present
- Serum samples SD1- 4 in 2 C A 3 not 2 C A 2

Donation 450
- All paperwork present
- All samples in correct place

Donation 458
- All paperwork present
- Additional H&E slide for PT4

APPENDIX C

Site Inspection Report for: **Wales Cancer Bank** Licence No. 12107

Licensed for the Storage of relevant material which has come from a human body for use for a Scheduled Purpose

10 – 13 February 2009

Introduction

1. The Human Tissue Authority (HTA) was set up to regulate the removal, storage, use and disposal of human bodies, organs and tissue for a number of Scheduled Purposes such as research, transplantation, and education and training. The requirements of the HTA are set out in the Human Tissue Act 2004 (HT Act) and the Human Tissue Act 2004 (Ethical Approval, Exceptions from Licensing and Supply of Information about Transplants) Regulations 2006. There are supplementary requirements for those establishments storing tissue for transplantation and they are summarised in HTA Directions 001/2006.
2. As part of the regulatory framework, the HTA licenses establishments and undertakes inspections to assess compliance with expected standards.
3. Under the HT Act, the HTA has a statutory responsibility to make judgements about the suitability of the Designated Individual, Licence Applicant (Holder), premises and practices in relation to the licensed activities. These responsibilities are set out in Schedule 3 to the HT Act, which is the framework for the HTA's approach to licensing and inspection.
4. The HTA must satisfy itself that the Designated Individual (DI) is a suitable person to supervise the activity to be authorised by the licence and that they will undertake the following duties:
   - secure that other persons to whom the licence applies are suitable persons to participate in the licensed activities;
   - secure that suitable practices are used in the course of carrying on the activity; and
   - secure that the conditions of the licence are complied with.
5. The HTA must satisfy itself that the applicant for the licence is a suitable person/entity to be the holder of the licence.
6. The HTA must satisfy itself that the premises are suitable for the activity to be authorised by the licence.
7. To fulfill its statutory responsibilities, the HTA must be able to assess whether an establishment is suitable to carry out one or more of the activities regulated by the HTA. Suitability is assessed through a process of inspection. Inspections can be routine or risk based, announced or unannounced.

Inspection Process

8. HTA defines inspection as a process encompassing desk-based review, on-site assessment and analysis of relevant written, numerical, verbal and visual information to evaluate the establishment's compliance with expected standards. Desk-based reviews, described as phase one inspections, focus on the evaluation of the compliance report submitted by the Licence Applicant and Designated Individual, as well as any additional information provided by the establishment at the request of the HTA. On-site assessments, described as phase two inspections, focus on a review of the establishment's operational policies and procedures, inspection of its premises and scrutiny of its practices. Where the inspection process identifies that a standard is not being met, additional conditions may be placed on an establishment's licence to ensure that appropriate action is taken to address the non-compliance/s.

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9. Both desk-based review and on-site assessments may lead to advice and guidance for improving practice in one or more areas.

Judgements

10. To enable the HTA to make effective judgements about the suitability of the DI and the Licence Holder, the suitability of the premises and the suitability of the practices taking place on the premises under the supervision of the DI, the HTA standards were developed under four high-level headings:
    - Consent
    - Governance and Quality
    - Premises, Facilities and Equipment
    - Disposal
11. The evidence gathering during inspection focuses on these standards, with particular emphasis on any areas identified as requiring special attention in phase one of the inspection, as detailed above.
12. Throughout the inspection process, standards are assessed using the same fourpoint numerical scale used by the DI in the completion of the initial compliance report.

Numerical scale Interpretation

1	Standard not met
2	Standard partially met
3	Standard almost met
4	Standard fully met or exceeded

13. The information gathered throughout the inspection process informs the HTA's licensing decisions within the regulatory framework. Where the HTA is not presented with evidence that the establishment meets the requirements of a standard/s, it works on the premise that a lack of evidence indicates non-compliance. There are varying degrees of non-compliance. The action an establishment will be required to make following the identification of non-compliance is based on the HTA's assessment of risk to patient safety and/or tissue integrity and/or a breach of the HT Act or associated Directions.

The Inspection Report

14. The inspection report represents the findings from the evidence supplied during phase one and phase two of the inspection process, that is from the initial compliance report any additional documentation provided prior to the site-visit and the evidence obtained through interview and observation during the site-visit. Future inspections may identify other areas of non-compliance if new evidence is obtained. Where full compliance with a standard has been established, this is noted. Where standards have been found to be non or partially compliant, details are included of the evidence for this finding.

15. Once the factual accuracy of the report has been agreed with the establishment, it will be published on the HTA website.

Inspection Report for Wales Cancer Bank

16. Wales Cancer Bank obtains tumour samples and normal tissue from living donors following removal of tumours as part of a patient's treatment. Blood samples from donors and from healthy partners of donors are also procured. Tissue is procured at the Wales Cancer Bank hub site at University Hospital Cardiff and at seven satellite sites throughout Wales. Tissue is processed to yield DNA and RNA samples at the Singleton satellite site and blood is processed to yield DNA samples at the Centre for Molecular Genetics (Heath Park site). Tumour material is also processed at all sites to yield paraffin blocks and slides which are stored at all sites. Material is transferred from satellite sites to the hub site and to the Centre for Molecular Genetics. Material is then issued to research projects from the hub site.
17. A phase two inspection of the Withybush Hospital, Singleton Hospital, Morriston Hospital, University Hospital Cardiff and the Centre for Molecular Genetics was carried out on 10 – 13 February 2009. In addition the inspection team viewed the central quality management documentation that is held at the Wales Cancer Bank offices in Grove Mews, Cardiff.
18. The inspection team comprised: Dr Anthony M Noble, HTA lead inspector and Kate Rolfvondenbaumen, HTA inspector.
19. The timetable for the site visit was developed in consideration of the results of phase one of the inspection process and issues common to research licensed establishments. Attention was focused on the audit trail and consistency of procedures between the hub and satellite sites.
20. An audit trail was conducted following the fate of 16 donation records to the derived blocks, slides and blood samples or vice versa. This yielded 152 individual samples that were stored at the 5 sites inspected. In every case the storage records accurately reflected the location of the samples. Consent documentation was available for all specimens and consent was taken by individuals whose consent training records were available in all but one case. Given the complexity of the samples processed and distributed throughout the sites traceability was excellent.

Compliance with standards, Codes of Practice and Directions

Consent

Standard	Assessment	Score
C1 Consent is obtained in accordance with the requirements of the HT Act2004 and as set out in the Code of Practice.	The standard is fully met.	4
C2 Information about the consent process is provided and in a variety of formats.	The standard is fully met.	4
C3 Staff involved in seeking consent receive training and support in the implications and essential requirements of taking consent.	The standard is fully met.	4

APPENDIX C

Governance and Quality

Standard	Assessment	Score
GQ1 All aspects of the establishment's work are supported by ratified documented policies and procedures as part of the overall governance process.	The standard is fully met.	4
GQ2 There is a documented system of quality management and audit.	The standard is fully met.	4
GQ3 Staff are appropriately qualified and trained in techniques relevant to their work and are continuously updating their skills.	The standard is fully met.	4
GQ4 There is a systematic and planned approach to the management of records.	The standard is fully met.	4
GQ5 There are documented procedures for distribution of body parts, tissues or cells.	The standard is fully met.	4
GQ6 A coding and records system facilitates traceability of bodies, body parts, tissues and cells, ensuring a robust audit trail.	The standard is fully met.	4
GQ7 There are systems to ensure that all adverse events, reactions and/or incidents are investigated promptly.	The standard is fully met.	4
GQ8 Risk assessments of the establishment's practices and processes are completed regularly and are recorded and monitored appropriately.	The standard is fully met.	4

Premises, Facilities and Equipment

Standard	Assessment	Score
PFE1 The premises are fit for purpose	The standard is fully met.	4
PFE2 Environmental controls are in place to avoid potential contamination.	The standard is fully met.	4
PFE3 There are appropriate facilities for the storage of bodies, body parts, tissues and cells, consumables and records.	The standard is fully met.	4
PFE4 Systems are in place to protect the quality and integrity of bodies, body parts, tissues and cells during transport and delivery to its destination.	The standard is fully met.	4

PFE5 Equipment is appropriate for use, maintained, quality assured, validated and where appropriate monitored.	The standard is almost met. Locks were present but not in use for freezers storing blood at the Withbush and Centre for Molecular Genetics sites. **See advice and guidance 1.**	3

Disposal

Standard	Assessment	Score
D1 There is a clear and sensitive policy for disposing of human organs and tissue.	The standard is fully met.	4
D2 The reasons for disposal and the methods used are carefully documented.	The standard is fully met.	4

Conclusions

21. During the inspection process, the HTA has made judgements about the suitability of the Designated Individual, the Licence Holder, the premises and the practices taking place on the premises under the supervision of the Designated Individual.

Suitability of PDs, DI and LH

22. Interviews were conducted with the Person Designate (PD) at each site that was inspected. The PD at each site was appropriately qualified and had good understanding of the role and responsibilities. All PDs felt that there was sufficient communication with the Designated Individual (DI). The PDs were not regularly involved in the day to day activities of the Wales Cancer Bank and the DI is advised that additional operational PDs may be added to the licence if she considered that to be appropriate **(See advice and guidance 2).**
23. The Designated Individual was found to be suitable. The corporate structure of the Wales Cancer Bank is not compatible with a Corporate Licence Holder being named. The Licence Holder was found to be suitable.

Suitability of the Premises

24. The premises were found to be fit for purpose. Records were maintained in appropriately secured locations. Samples were also stored in appropriately secured locations. Locks on freezers at the Withybush and Centre for Molecular Genetics sites were not in use (see advice and guidance 1).

APPENDIX C

Suitability of Practices

25. The practices of the establishment were effectively codified in SOPs that were up to date at all satellite sites and reflected actual working practice. The practices of the establishment were found to be suitable in all cases.

Summary comment

26. The HTA is satisfied that the establishment is suitable to be licensed for the purposes that it has set out. The establishment showed exemplary practices in many areas of operation. Conditions (requirements) on the licence at the time of the site visit inspection.
27. There were no conditions on the licence at the time of inspection.
Conditions (requirements) related to areas of non-compliance identified during the inspection process
28. No conditions are proposed to be applied to the licence.

Advice and guidance

29. Below are matters which the HTA advises the DI to consider.

No Regulatory reference
Advice

1. PFE5 The Designated Individual is advised to ensure that locks on freezers at the Withybush and Centre for Molecular Genetics sites are put into use.
2. Persons Designated The Designated Individual is advised to consider naming additional persons designate at satellite sites who are more operationally involved in the activities conducted under the licence.

Report sent to SA for factual accuracy: [date]

Report sent to DI for factual accuracy: [date]

Report returned from DI: [date]

Final report issued: [date]

APPENDIX D

Wales Cancer Bank Personnel List as at 31st March 2009

Staff

Name	Site	Title
Professor Malcolm Mason	Central	Director
Professor Gerry Thomas	Central	Director of Scientific Services
Dr Alison Parry-Jones	Central	Manager
Mr Daniel Naeh	Central	IT Manager
Miss Sarah Phillips	Central	Project Officer
Mr Matthew Shaw	Central	Database Manager
Dr Yasmin Friedmann	Central	Web Developer
Mrs Debbie Way	Central	Clerical officer
Miss Claire Alford	Central/Swansea	Information Assistant
Suzanne Williams	Swansea	Lead nurse
Janette Gwillim	Swansea	Nurse
Catherine Lloyd-Bennett	Swansea	Nurse
Pam Hayward	Swansea	Nurse
Colleen Lloyd	Swansea	Biomedical Scientist
Emma Miles	Swansea	Biomedical Scientist
Alison Davies	Cardiff	Nurse
Kevin Pearse	Cardiff	Nurse
Vicki Woods	Cardiff	Biomedical Scientist
Linda Kirk	Withybush	Nurse
Helen Smith	Withybush	Medical Laboratory Assistant
Lisa Gilby	Newport	Nurse

HTA/Local Management committee

Name	Site	Title
Professor Malcolm Mason	Central	Director
Professor Gerry Thomas	Central	Director of Scientific Services
Dr Alison Parry-Jones	Central	HTA Designated Individual
Professor Nick Stuart	Bangor	HTA Person Designated / Local lead
Professor Julian Sampson	Cardiff	Local lead
Professor Bharat Jasani	Cardiff	HTA Person Designated
Dr Paul Griffiths	Swansea - Morriston	HTA Person Designated
Mrs Christine Davies	Swansea	HTA Person Designated / Local lead
Dr Martin Sevenoaks	Withybush	HTA Person Designated / Local lead
Mr Adam Carter	Royal Gwent	HTA Person Designated
Dr Meleri Morgan	Llandough	HTA Person Designated

WALES CANCER BANK
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