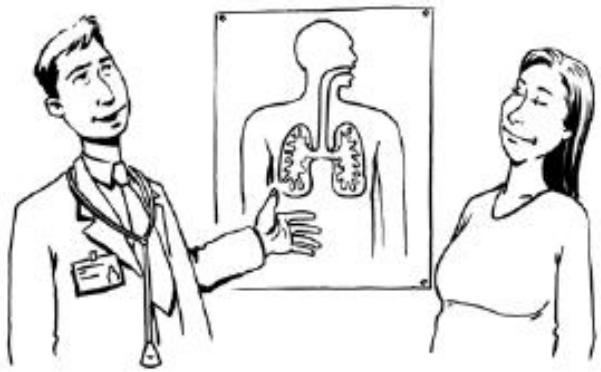
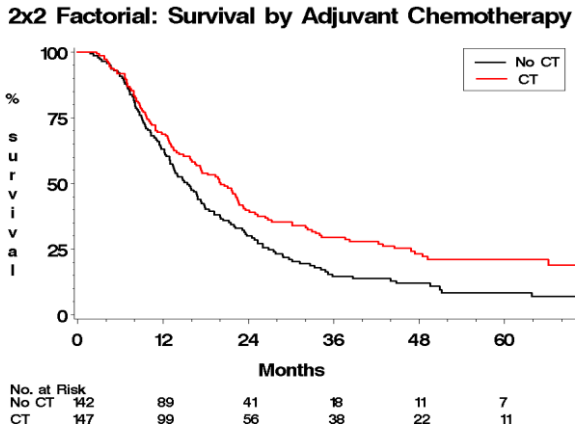
# Use of informatics systems to link laboratory with clinical data and ensure GCP compliance


SANYO
SANYO
Backup
-150°C
freezer
VIP Plus

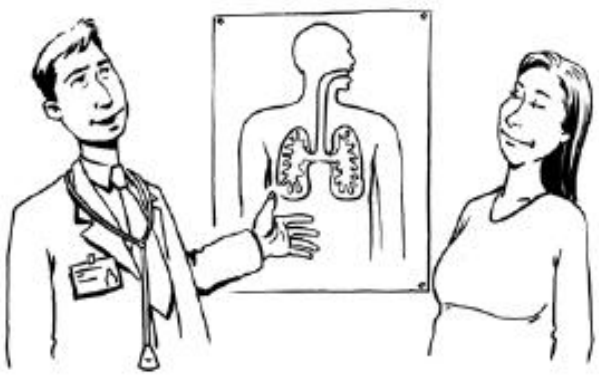



2x2 Factorial: Survival by Adjuvant Chemotherapy
No CT
CT
100
75
50
25
0
% survival
0
12
24
36
48
60
Months
No. at Risk
No CT 142 89 41 18 11 7
CT 147 99 56 38 22 11

Sample

Sample and clinical data

The value of a sample is dependent on the data attached to it

# Biobank data

When storing or moving

| | |
|---|---|
| Location | Where can I put it?<br>Where did I put it? |
| Dates and times | When collected?<br>When processed?<br>When transported?<br>When received?<br>When stored? |
| Nature of sample | Protocol for collection |
| Who? | Who consented, took, processed, stored etc. |
| History | How did it get here?<br>What happened since it it arrived?<br>Adverse events? |
| Aliquots | What happened to the “children”? |
| Quantity | How much is there?<br>How much was there? |

# Regulatory Framework

## Translational work

EU Directives 2001/20/EC and 2005/28/EC
Passed into UK law as statutory instruments
SI 1031, 1928, 2984, 2031

(EU Clinical trial regulations)

England and Wales Human Tissue Act 2004
Scotland Human Tissue Act 2006

Data protection act (1988)

(EU Data protection regulations)

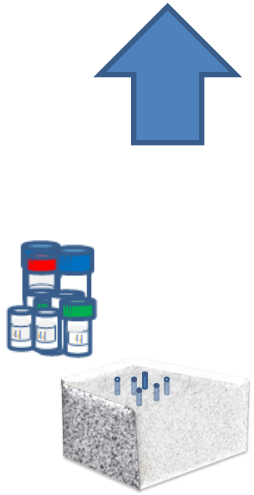
Mental Capacity Act 2005, Access to Health Records Act 1990,
Health and Social Care Act 2001, Children Act 2004

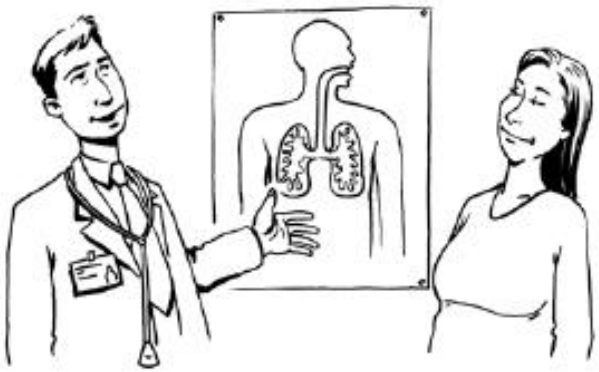
# What is sufficient consent?

**Patients have the right to approve of what is done to their samples**

**In EXCEPTIONAL circumstance the scope of the research may go beyond the original consent obtained, in which case re-consent should be considered**

**Donors have the right at any time to withdraw provision of samples**



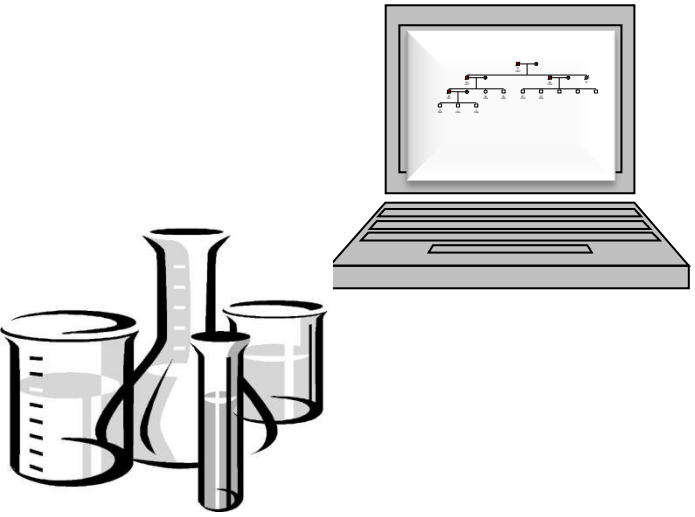
# Biobank data

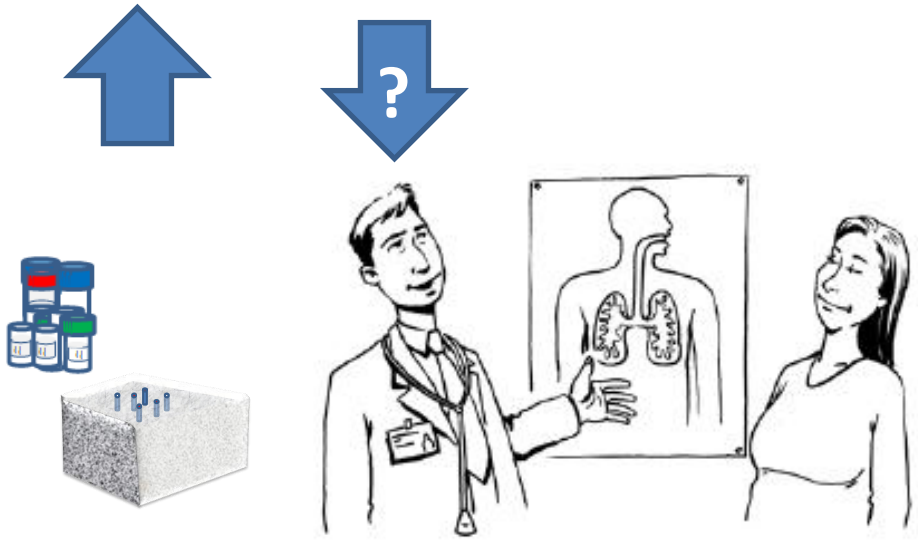
Need to know at point of use

| | |
|---|---|
| Can you use it? | Nature of consent<br>Is there enough left? |
| Should you use it? | SOPs<br>Adverse events |
| What data is already linked to the sample? | Enough information and no more |
| Log an audit of use | |
| Store the data so it is attached to the sample and all related samples | Increase the value of the sample |

# Baseline sample data

Simple descriptive analysis of sample






| | |
|---|---|
| Quantitative | Cell counts<br>[Protein, DNA, RNA etc] |
| Qualitative | Histochemistry<br>Cytochemistry<br>QC Protein, DNA, RNA etc |
| Inclusion or exclusion | Established biomarkers: e.g Pancreatic lipase, triglyceride etc.<br>Somatic genetic markers: K-Ras , p53 etc.<br>Germline genetic markers: BRCA2, PRSS1, PSTI |
| Outcome and Stratification | PK and PD |

Sample

Sample
Diagnosis and demographics

# Patient data

Obtained at point of collection

| | |
|---|---|
| Details of illness | Diagnosis |
| | Aetiology |
| | Stage, Grade etc. |
| Imaging data | Pathology reports |
| | **BLOBS** or links |

BLOBS (Binary Large Objects)

**Advantages:**

"Pictures don't lie"

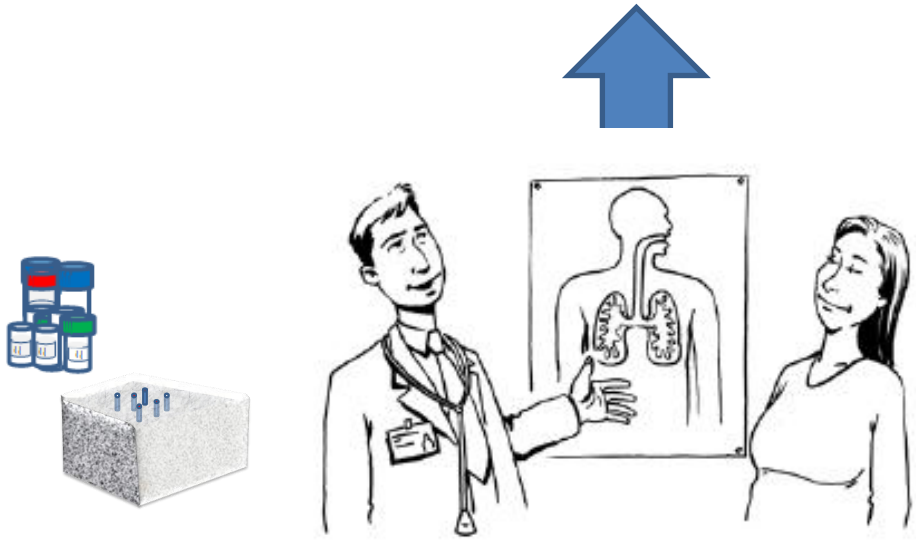
"A picture is worth a thousand words"

(or a BLOB might actually be 1000 words)

**Disadvantages:**

Difficult to search

Very difficult to audit



# Patient data

Obtained at point of collection

| | |
|---|---|
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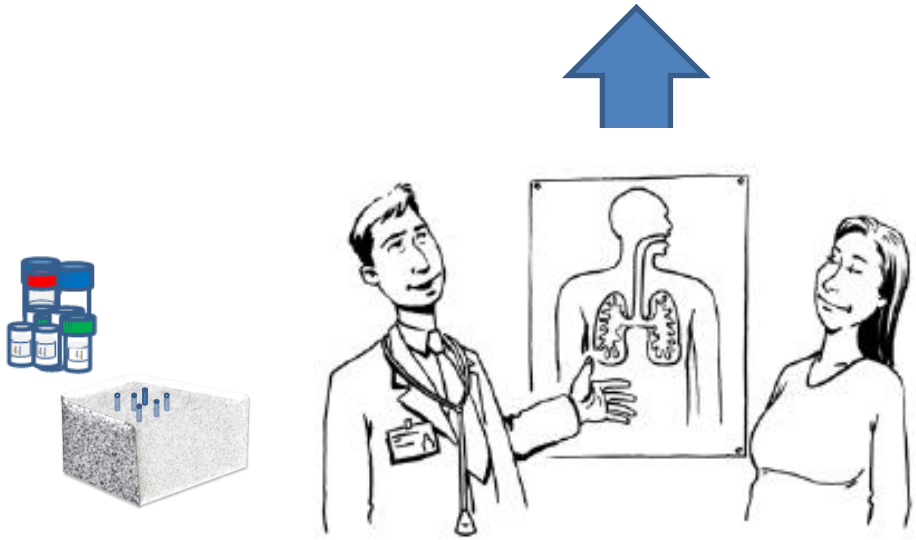
| | BLOBS or **links** |



Links (to another system or cloud)

**Advantages:**

Saves a lot of space

Gives flexibility

Single hub accessed from multiple spokes

**Disadvantages:**

Dramatically reduced control

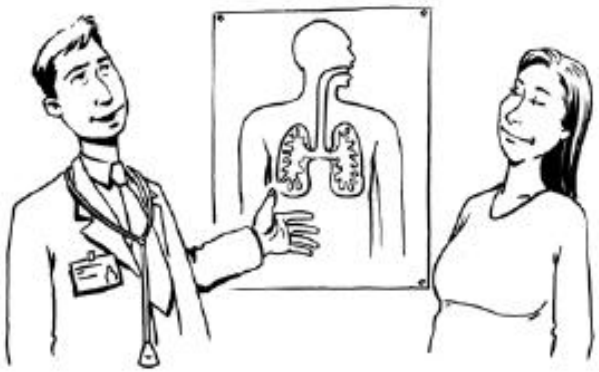
Data protection issues

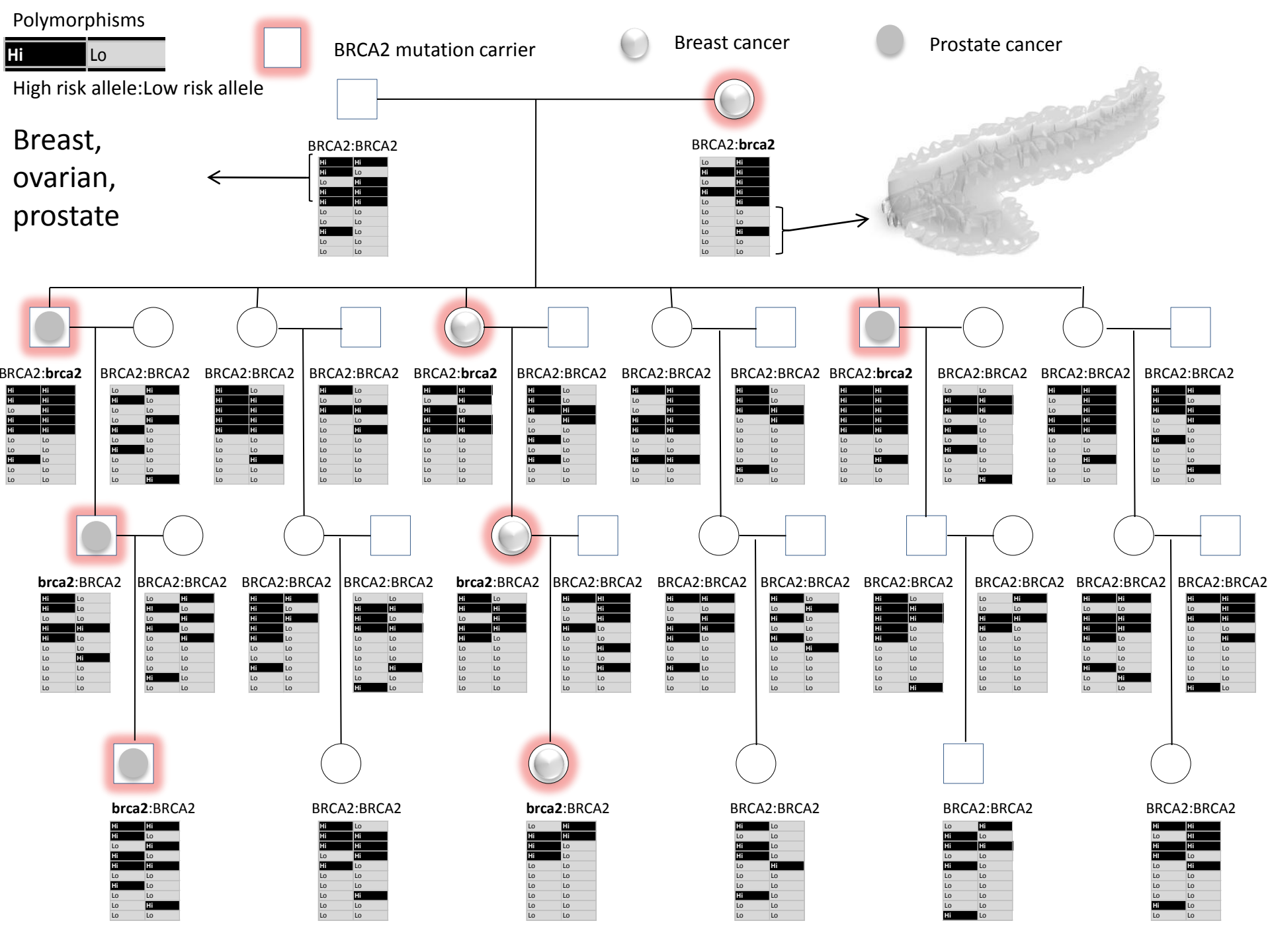
Very difficult to audit

# Patient data

Obtained at point of collection

| | |
|---|---|
| Details of illness | Diagnosis |
| | Aetiology |
| | Stage, Grade etc. |
| Imaging data | Pathology reports |
| | BLOBS or links |
| Gender | Male, Female |
| | Orientation? |
| Age | Year of birth |
| | Date of birth |
| BMI | Height |
| | Weight – history? |
| Family history | Of disease |
| | Of no disease |
| | Family tree |




Polymorphisms
Hi
Lo
High risk allele:Low risk allele
BRCA2 mutation carrier
Breast cancer
Prostate cancer
Breast, ovarian, prostate
BRCA2:BRCA2
BRCA2:brca2
BRCA2:BRCA2
BRCA2:BRCA2
BRCA2:BRCA2
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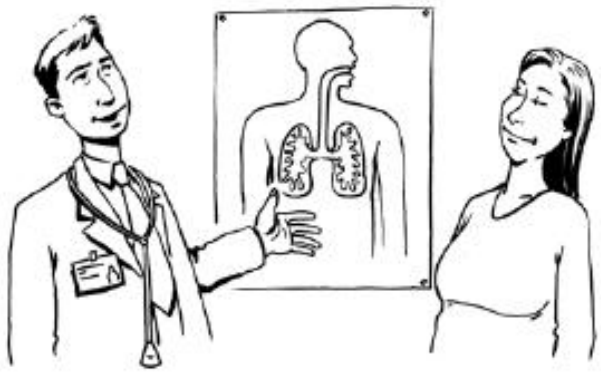

# Patient data

Obtained at point of collection

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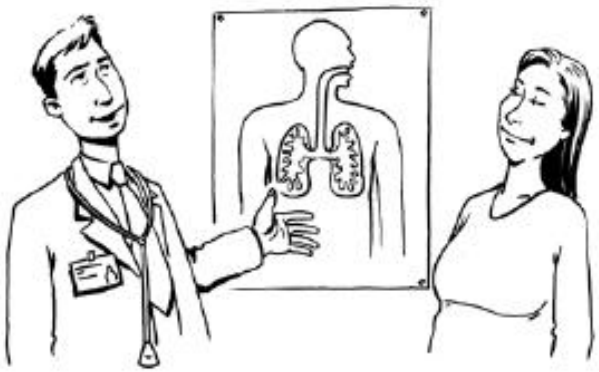
| | Weight – history? |
| Family history | Of disease |
| | Of no disease |
| | **Family tree** |

Advantage: Contextual data

Disadvantage: Data protection issues



# Patient data

Obtained at point of collection

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| Details of illness | Diagnosis |
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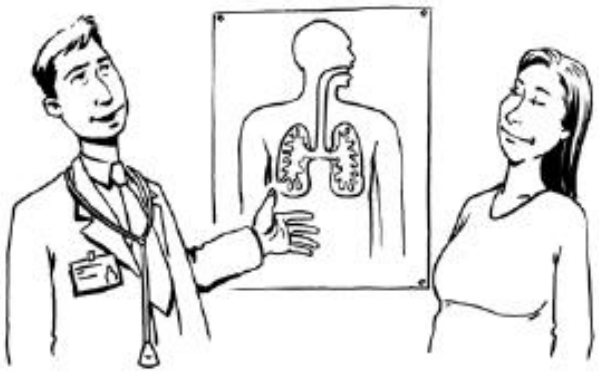
| Gender | Male, Female |
| | Orientation? |
| Age | Year of birth |
| | Date of birth |
| BMI | Height |
| | Weight – history? |
| Family history | Of disease |
| | Of no disease |
| | Family tree |
| Lifestyle | Smoking, alcohol etc. |
| Exposure | Where do they live? |
| Ethnicity and race | Culture and genetics |





# Discovery data

## Omics

| | |
|---|---|
| Proteomic | Tabulated data |
| | Traces and gel images |
| | Array data (image/values/analysis) |
| | Raw mass spec data |
| Metabolomic | Tabulated<br>Traces<br>Raw data |
| Transcriptomic | Tabulated<br>Array (image/values/analysis)<br>RNASeq raw data or analysis |
| Genomic | Exomic |
| | Other targeted |
| | Whole genome |

# S v United Kingdom (2009)
# at the European Court of Human Rights

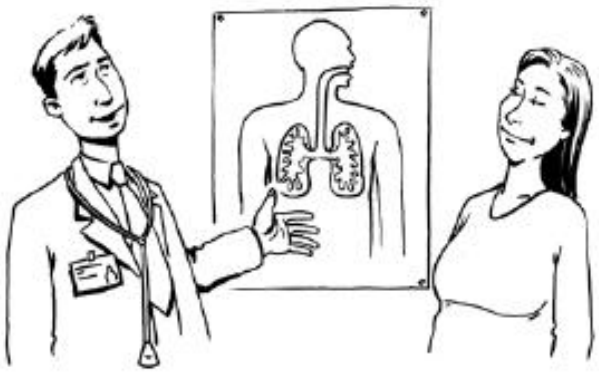
**Personal information is contained in cellular samples. Their retention without consent  interferes with the right to a private life**

**The DNA profile's capacity to provide a means of identifying an individual is in itself sufficient to conclude that their intervention interferes with the right to privacy**

**Retention of samples without consent is a violation of Article 8 of the human rights act.**

# Biomarker data

| | |
|---|---|
| A protein or group of proteins | ELISA<br>Luminex<br>IHC (TMAs) |
| Somatic genetic data or epigenetic | PCR, Sequencing, NGS<br><br>Ras mutation<br>CDKN2A methylation<br>p53 mutation<br>BCR-ABL<br>Etc. |
| Germline genetic data | Sequencing, Arrays<br><br>SNPs<br>BRCA2, MLH1 etc. |



Sample

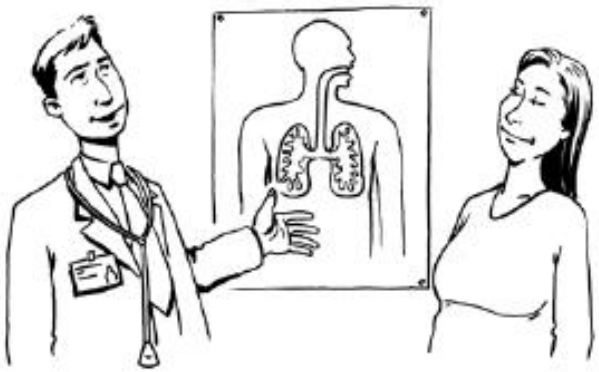
Sample
Diagnosis and demographics

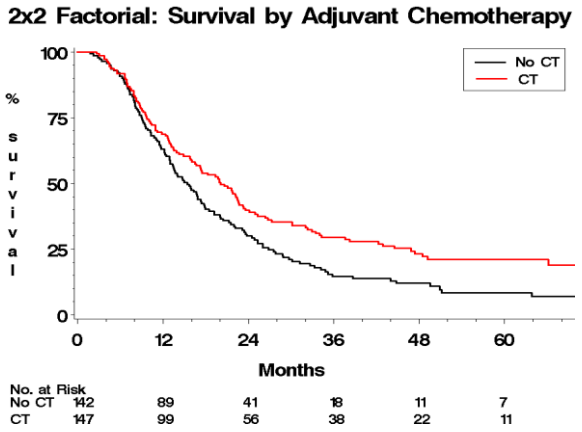

Sample
Diagnosis and demographics
Outcomes

# Trial data

| | |
|---|---|
| Treatment | As randomised<br>As received |
| Outcome | Survival (OS,PFS,<br>Event time etc.) |
| Other | Imaging<br>AE, SUSAR etc |

Subsequent follow up data
(beyond the trial)





Sample

Sample
Diagnosis and demographics


Sample
Diagnosis and demographics
Outcomes

Sample
Diagnosis and demographics
Outcomes

+ Existing sample data

Lab data

Personal Data

Trial data

! Name and date of birth !

NHS Number

Address

Aliquots

Original sample

Patient data

Sample ID

Lab Patient ID

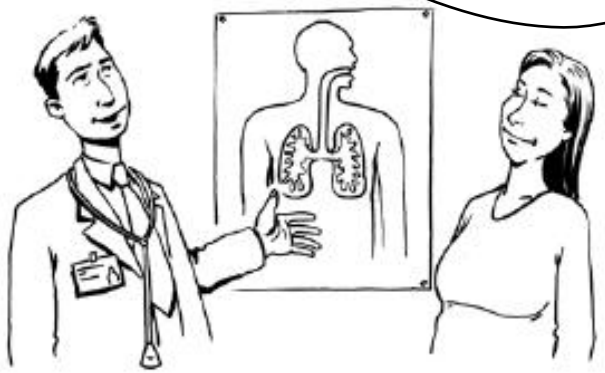
Hospital number

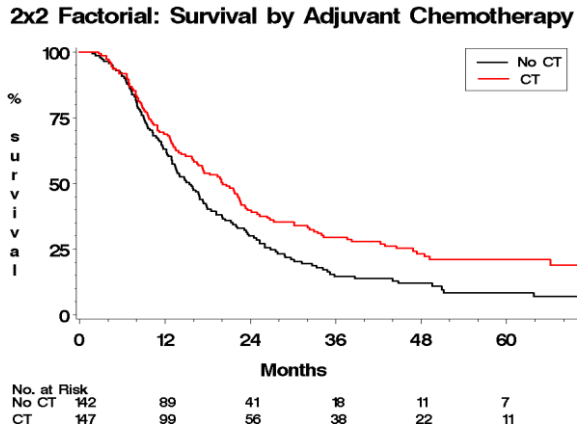
Trial Patient ID

Outcomes

Adverse events

Trial Arm





Narrative recording

Hypothesis

Aims

Objectives

Plan

Protocol

Results

Conclusion

Narrative recording

Easy to understand, efficient and.....

not auditable

Hypothesis

Aims

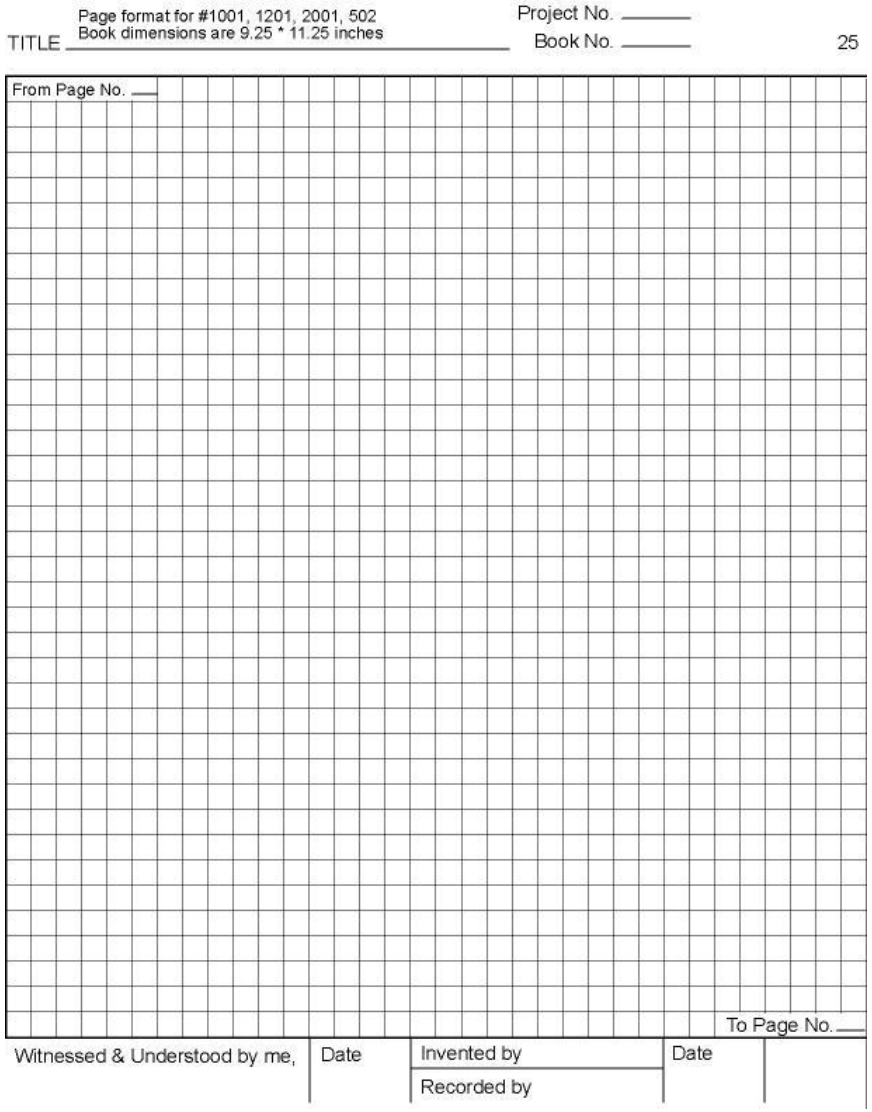
Objectives

Plan

Protocol

Results

Conclusion




Hard to understand, cumbersome and..... auditable

Hypothesis

12/04/2010

Aims

12/05/2010

Objectives

12/06/2010

Plan

12/08/2010

Protocol

12/09/2010

Results

12/12/2010

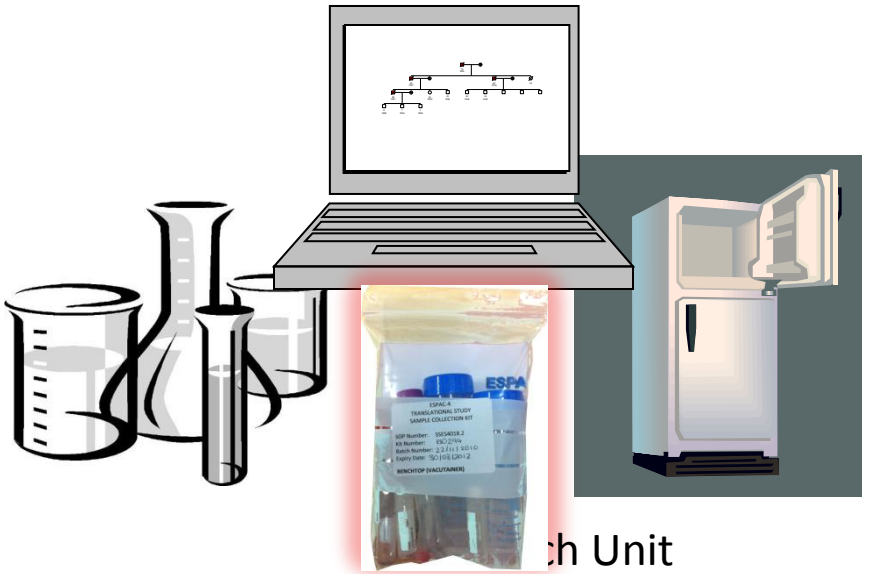
Conclusior

12/07/2012

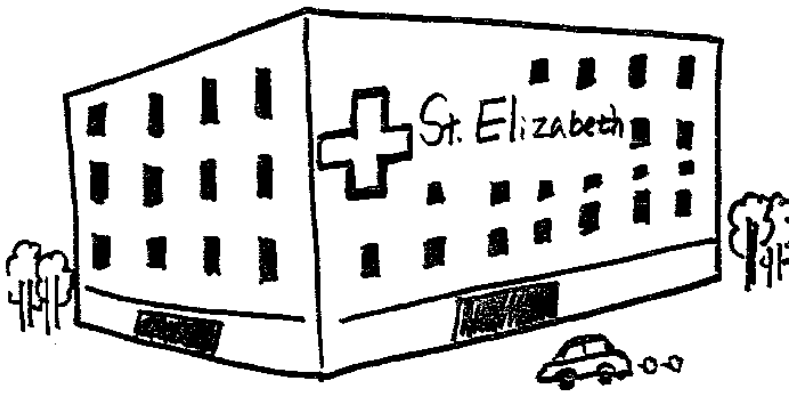
Clinical trials

Trials Units

Translational Research



ch Unit
GCLP facility




Clinical sites

... Any collaborating site providing samples

# Fax

**To:** [redacted] **From:**

**Fax:** 0151 794 8930 **Pages:** 1

**Phone:** 0151 794 8933 **Date:**

**Re:** Plasma Samples **CC:**

| | |
|---|---|
| lumber & Name | ___ _____ |
| Number of patient | _____ |

nt In

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le Ti

se tic

ype

Type A

{Unique kit code} {tube code} {tube number}

Barcode

{Expiry Date}

Ty
(Tic

| | | (HH:MM) | (HH:MM) | have been placed) |
|---|---|---|---|---|
| □ Plasma | ___/___/_____ | __:__ | __:__ | |
| □ Blood Pellet | ___/___/_____ | __:__ | __:__ | |
| □ Serum | ___/___/_____ | __:__ | __:__ | |

Comments

# Checklist form Kit A (Baseline)

Label with Kit code

[redacted] Type A
{Unique kit code}-{tube code}-{tube number}
Bar code
{Expiry Date}

Date _____/_____/_____

| | Initial or give times |
|---|---|
| Verify that Kit labels all have the same code (checklist form, fax form, all tubes) | ☐ |
| EDTA blood drawn | ☐ |
| Serum blood drawn | ☐ |
| CA19-9 blood drawn | ☐ |
| Time at completion of blood draw (24 hour clock) | ____:____ |
| Time when eppendorf and cryotubes placed at -80 degrees/on dry ice (24 hour clock) | ____:____ |
| Time when serum was set to spin (24 hour clock) | ____:____ |
| Time when CA19-9 blood sent for analysis(24 hour clock) | ____:____ |
| Time when cryotubes with serum was placed at -80 degrees/dry ice (24 hour clock) | ____:____ |
| If tubes were temporarily stored on dry ice, time for transfer to -80 degree freezer | ____:____ |

**Send checklist to**

[redacted]
Liverpool Cancer Trials Unit
Cancer Research Centre
200 London Road
Liverpool
L3 9TA

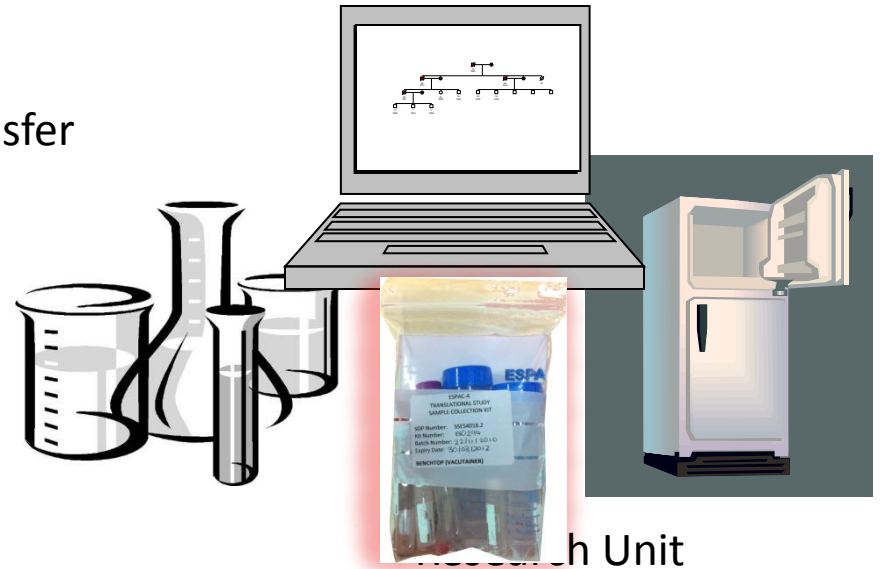
*Contact Numbers*

Tel no: +44 (0) 151 794 8938/8937
Fax no: +44 (0) 151 794 8930/8931
Email: lctu@liv.ac.uk

Clinical trials

Translational Research

Coded data transfer

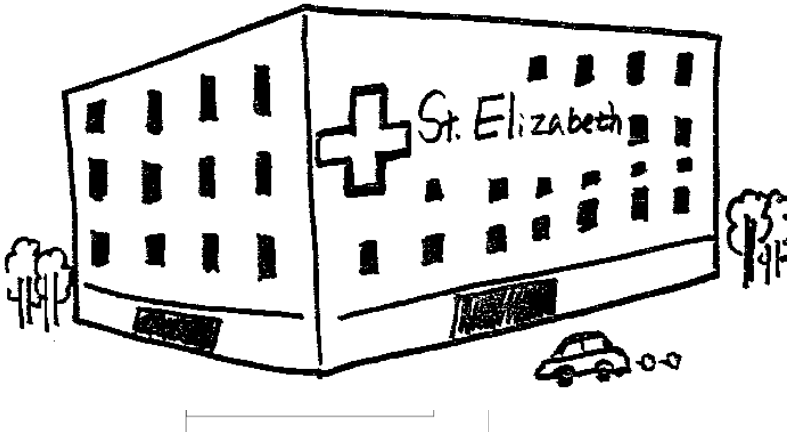


Trials Units

Computer system:
MACRO

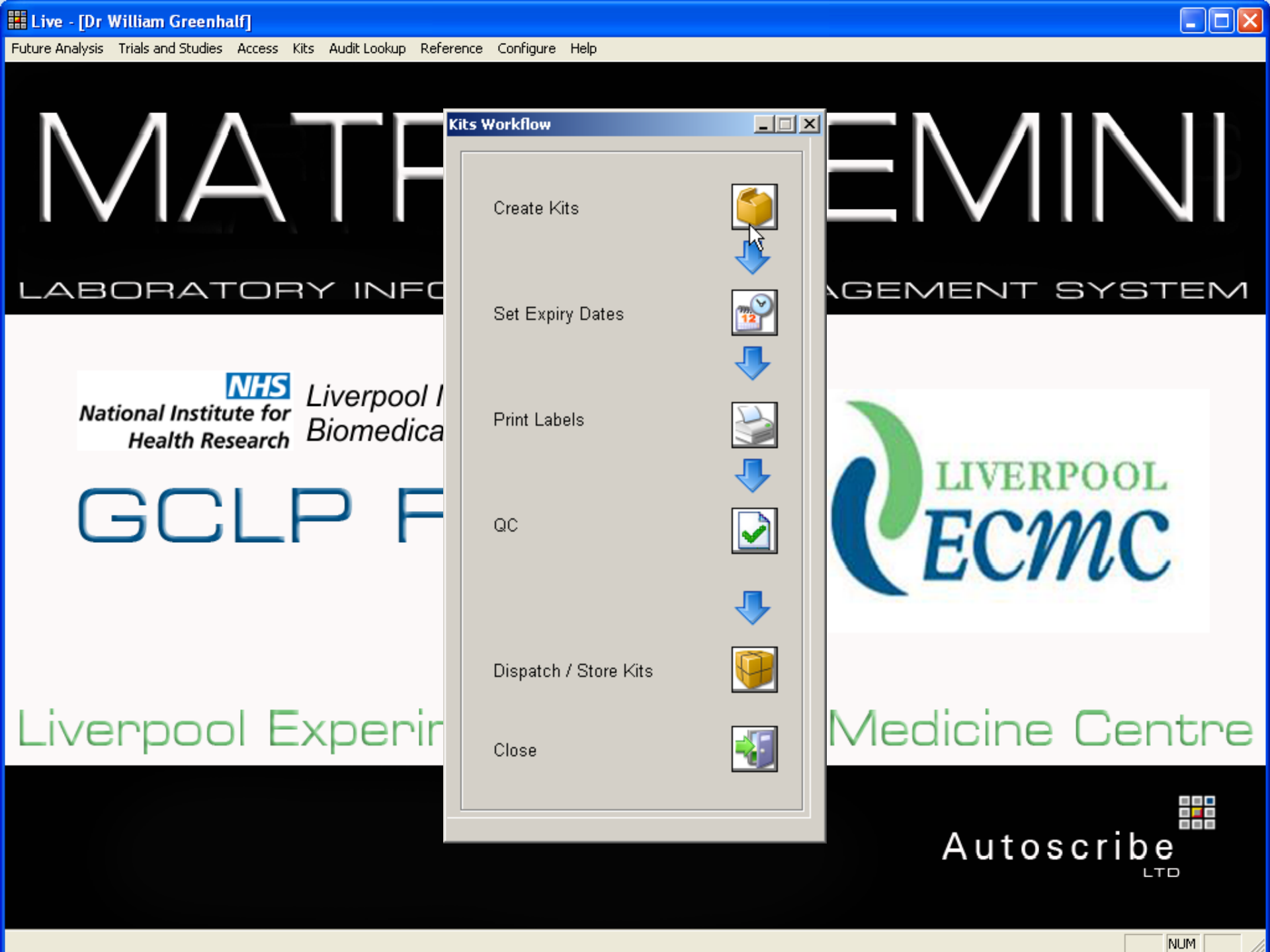
h Unit
GCLP facility

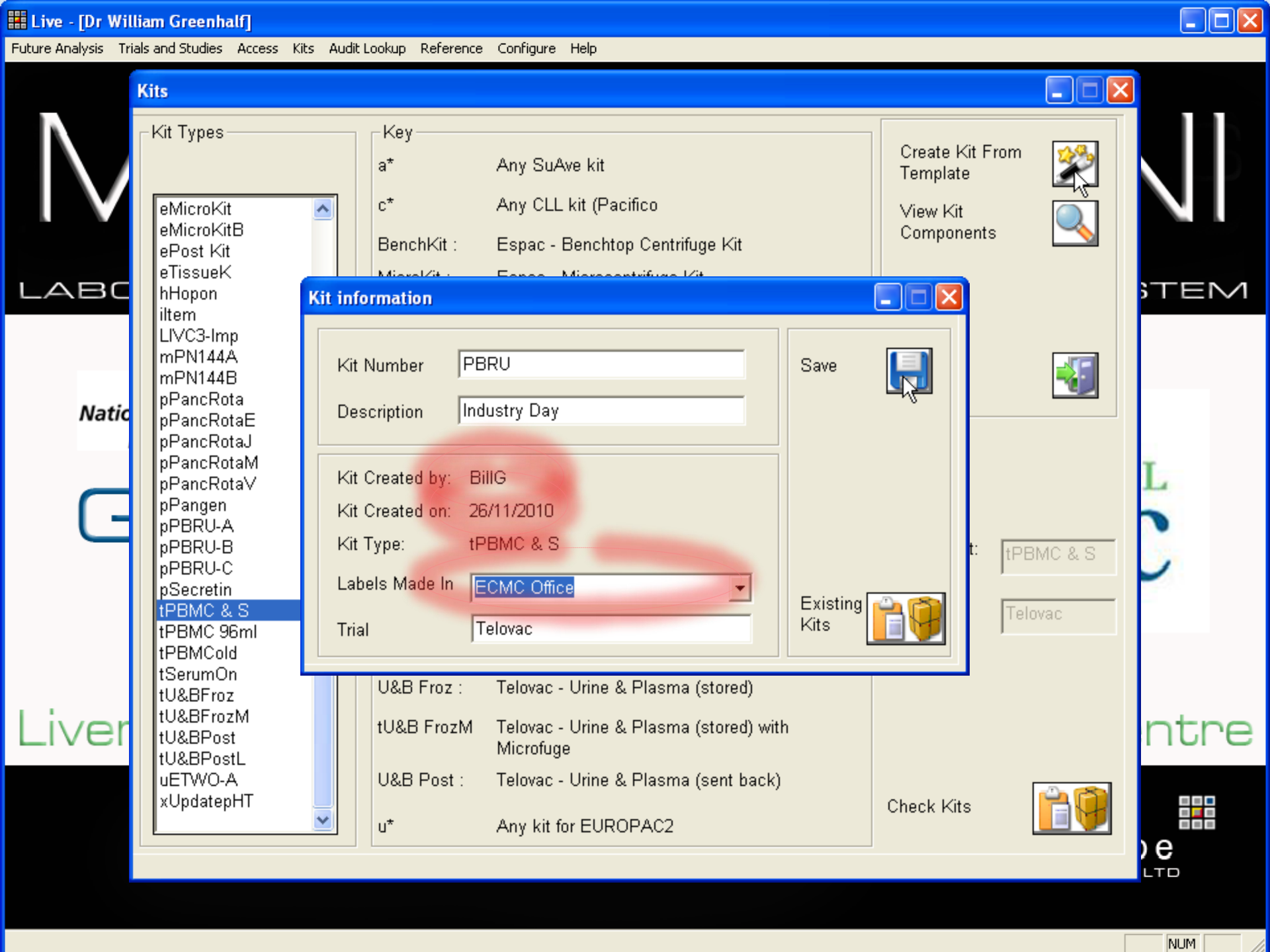
Computer system:
Matrix LIMS




... Any collaborating site providing samples

Clinical sites


Live - [Dr William Greenhalf]
Future Analysis
Trials and Studies
Access
Kits
Audit Lookup
Reference
Configure
Help
Kits Workflow
Create Kits
Set Expiry Dates
Print Labels
QC
Dispatch / Store Kits
Close
LABORATORY INFO
AGEMENT SYSTEM
NHS
National Institute for Health Research
Liverpool I
Biomedica
GCLP F
LIVERPOOL
ECMC
Liverpool Experir
Medicine Centre
Autoscribe
LTD
NUM


Live - [Dr William Greenhalf]
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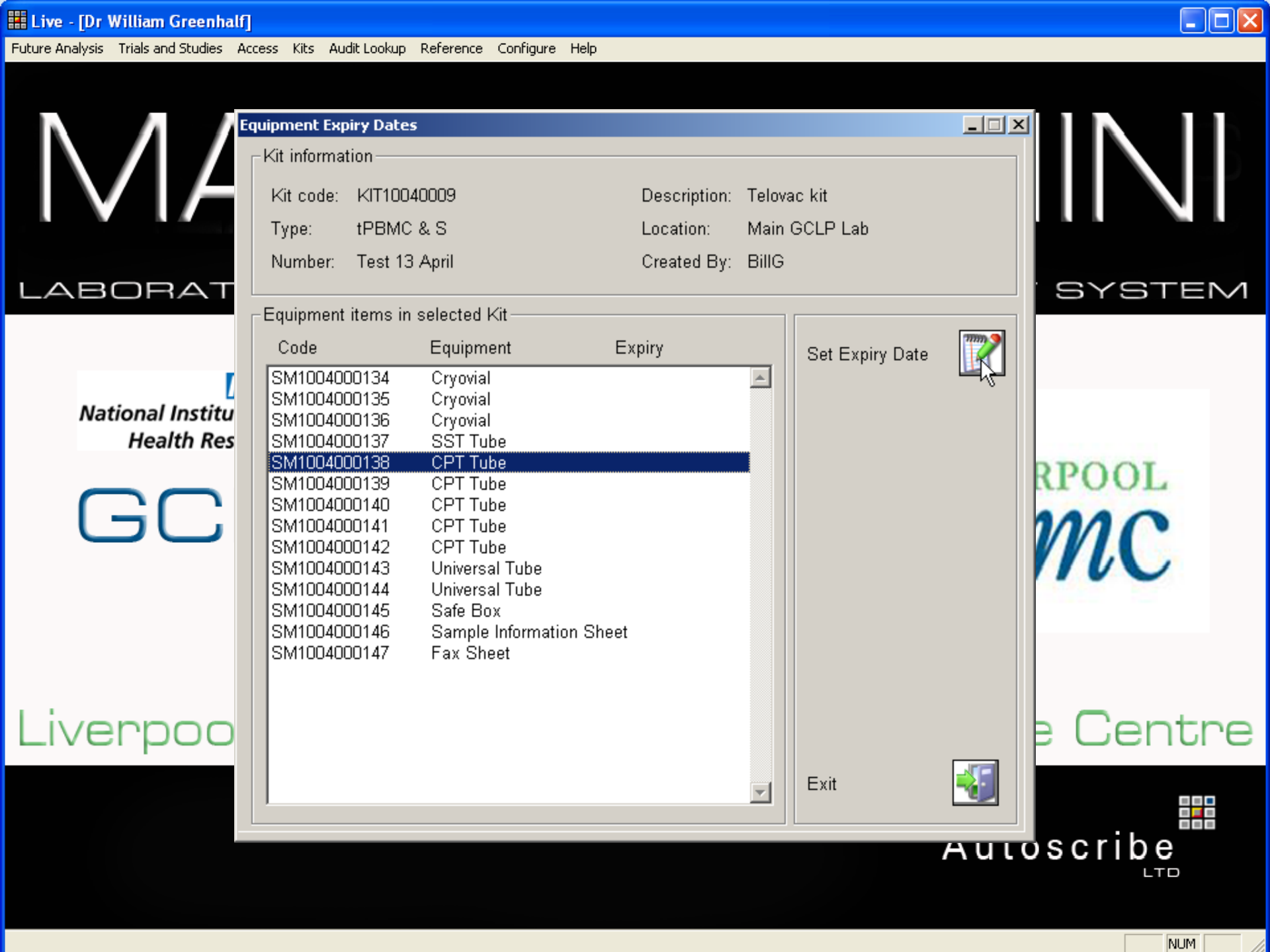
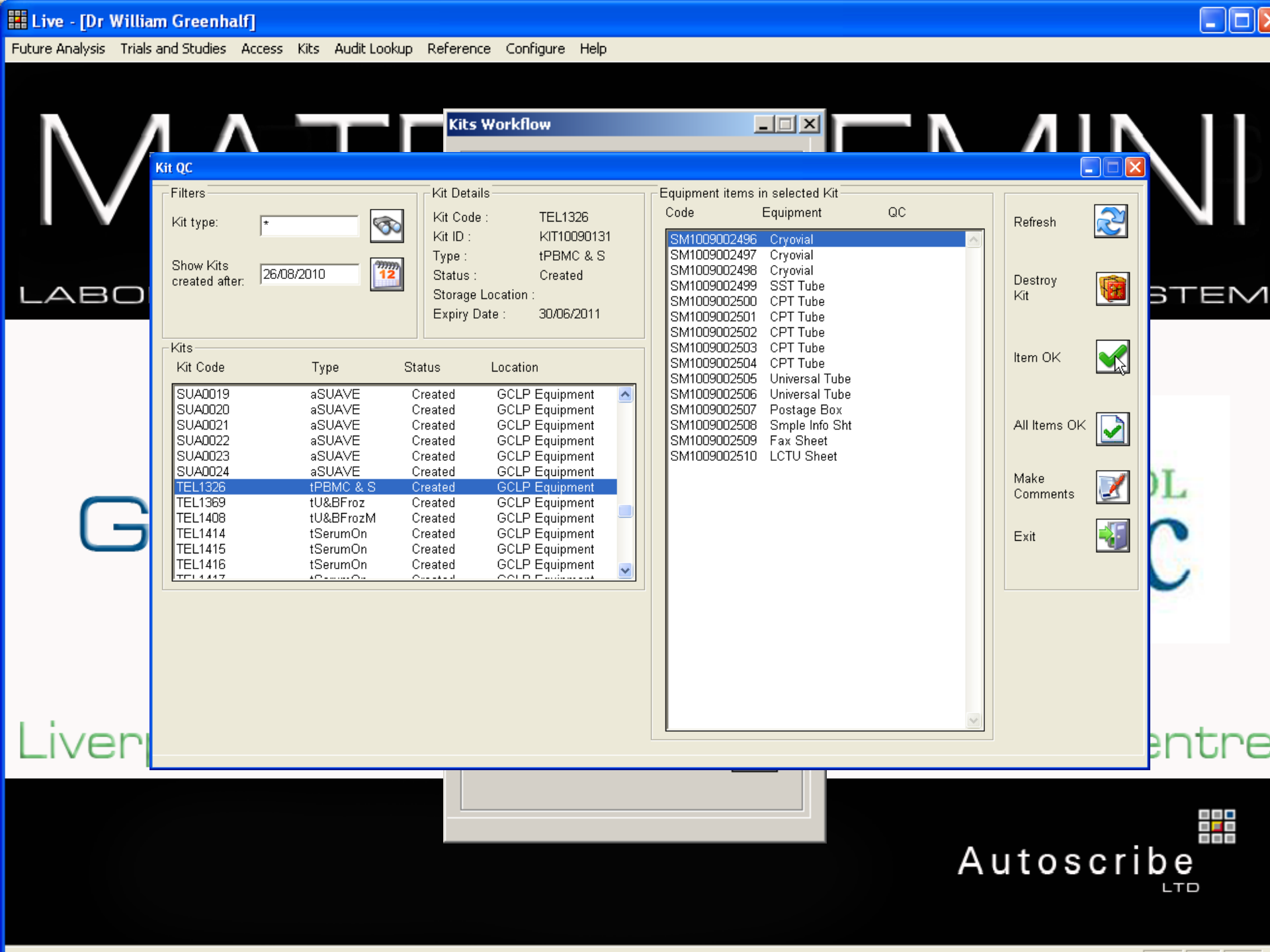
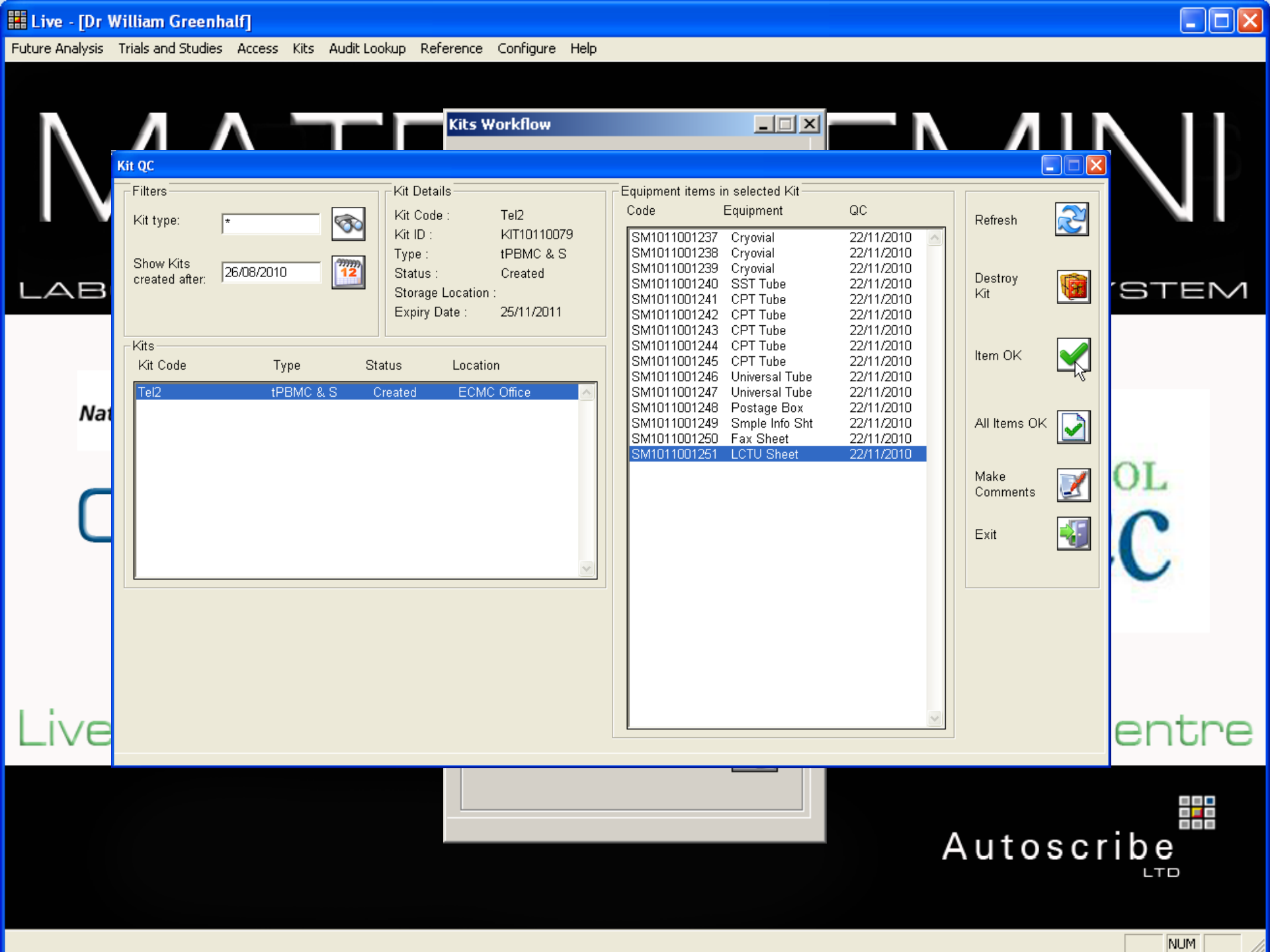
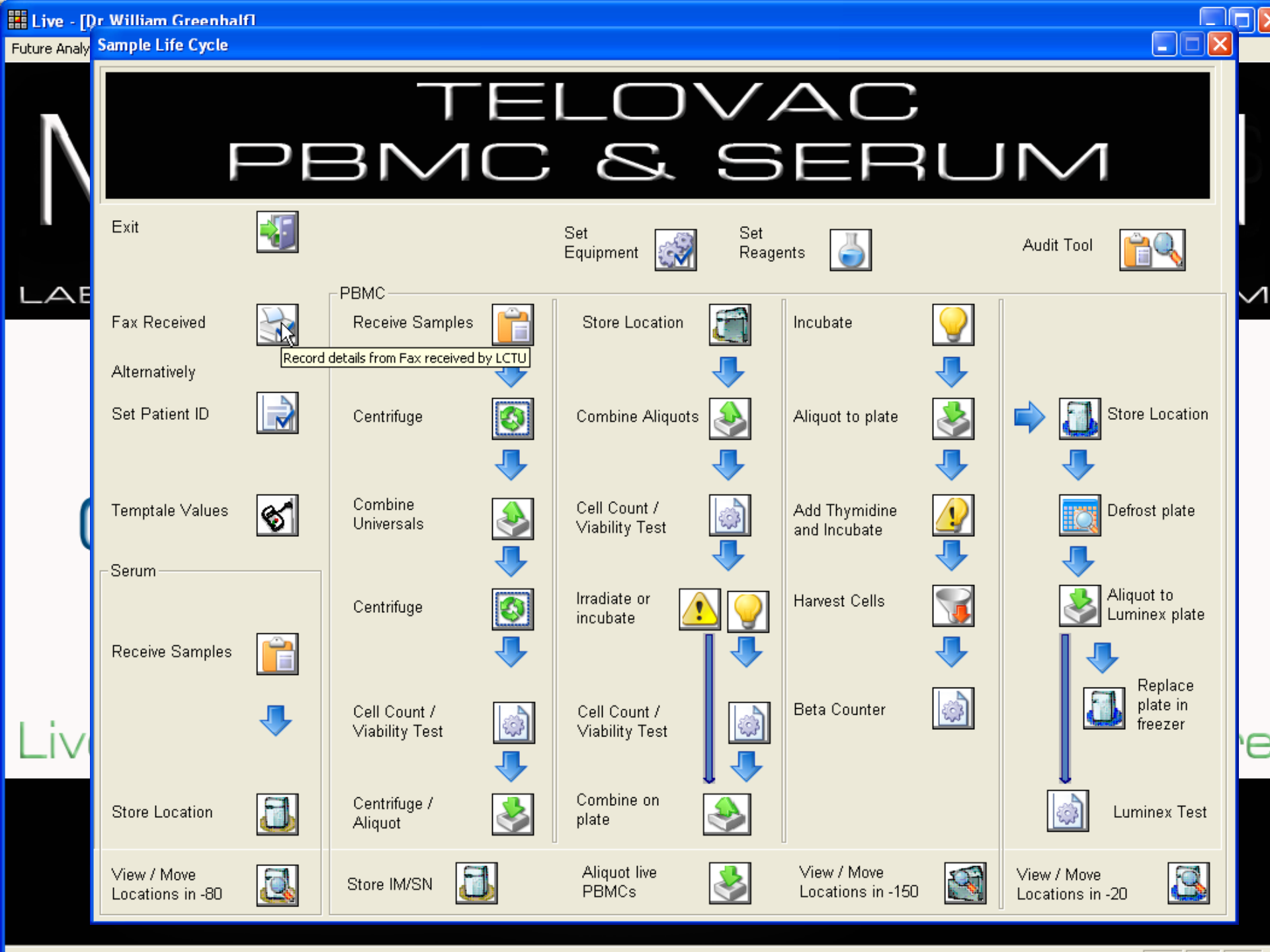
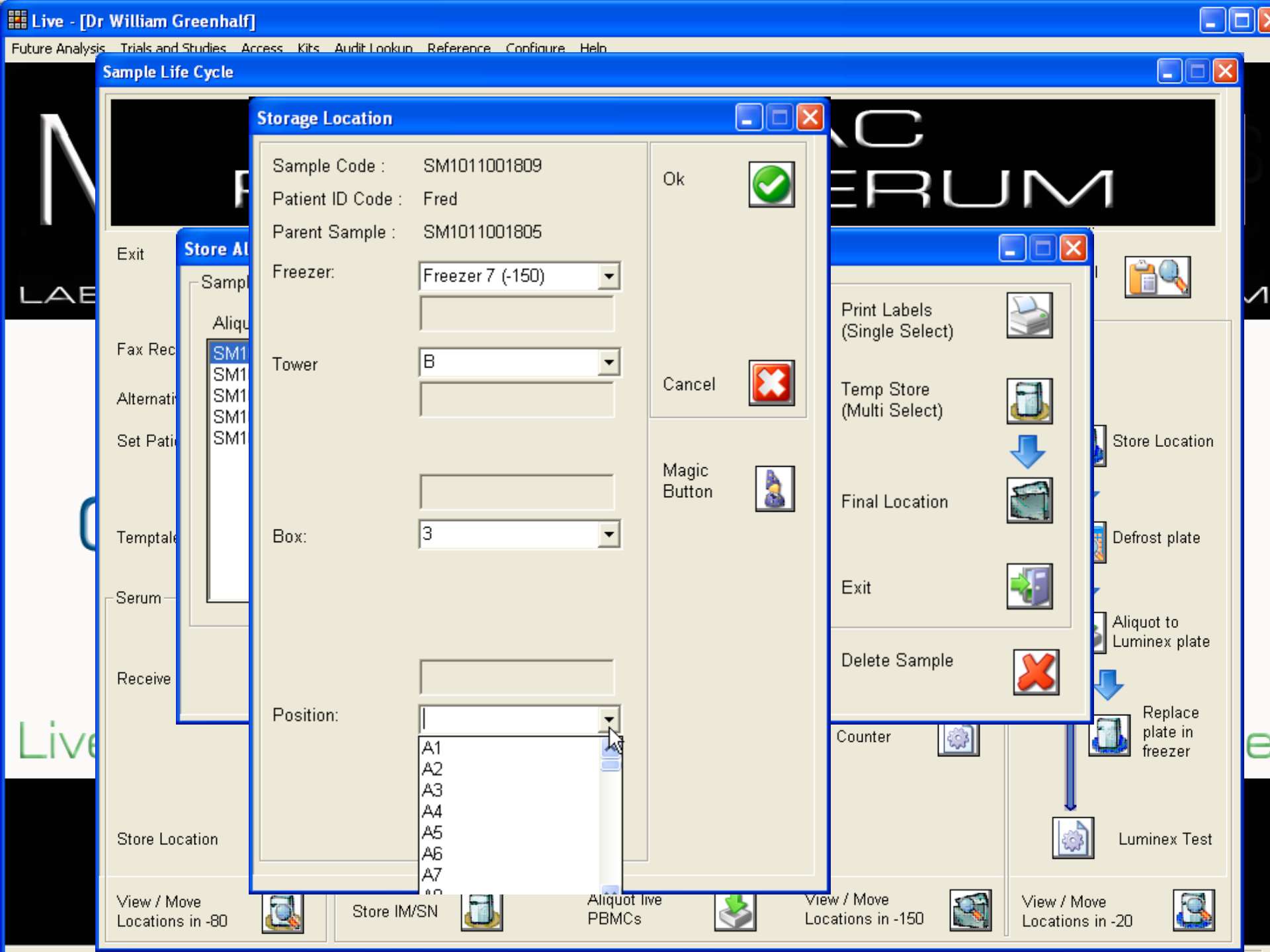
Access
Kits
Audit Lookup
Reference
Configure
Help
Kits
Kit Types
eMicroKit
eMicroKitB
ePost Kit
eTissueK
hHopon
iItem
LIVC3-Imp
mPN144A
mPN144B
pPancRota
pPancRotaE
pPancRotaJ
pPancRotaM
pPancRotaV
pPangen
pPBRU-A
pPBRU-B
pPBRU-C
pSecretin
tPBMC & S
tPBMC 96ml
tPBMCold
tSerumOn
tU&BFroz
tU&BFrozM
tU&BPost
tU&BPostL
uETWO-A
xUpdatepHT
Key
a*
Any SuAve kit
c*
Any CLL kit (Pacifico
BenchKit :
Espac - Benchtop Centrifuge Kit
U&B Froz :
Telovac - Urine & Plasma (stored)
tU&B FrozM
Telovac - Urine & Plasma (stored) with Microfuge
U&B Post :
Telovac - Urine & Plasma (sent back)
u*
Any kit for EUROPAC2
Create Kit From Template
View Kit Components
Check Kits
Kit information
Kit Number
PBRU
Description
Industry Day
Kit Created by:
BillG
Kit Created on:
26/11/2010
Kit Type:
tPBMC & S
Labels Made In
ECMC Office
Trial
Telovac
Save
Existing Kits
tPBMC & S
Telovac
NUM


Live - [Dr William Greenhalf]
Future Analysis
Trials and Studies
Access
Kits
Audit Lookup
Reference
Configure
Help
Equipment Expiry Dates
Kit information
Kit code: KIT10040009
Description: Telovac kit
Type: tPBMC & S
Location: Main GCLP Lab
Number: Test 13 April
Created By: BillG
Equipment items in selected Kit
Code
Equipment
Expiry
SM1004000134 Cryovial
SM1004000135 Cryovial
SM1004000136 Cryovial
SM1004000137 SST Tube
SM1004000138 CPT Tube
SM1004000139 CPT Tube
SM1004000140 CPT Tube
SM1004000141 CPT Tube
SM1004000142 CPT Tube
SM1004000143 Universal Tube
SM1004000144 Universal Tube
SM1004000145 Safe Box
SM1004000146 Sample Information Sheet
SM1004000147 Fax Sheet
Set Expiry Date
Exit
Autoscribe LTD
NUM

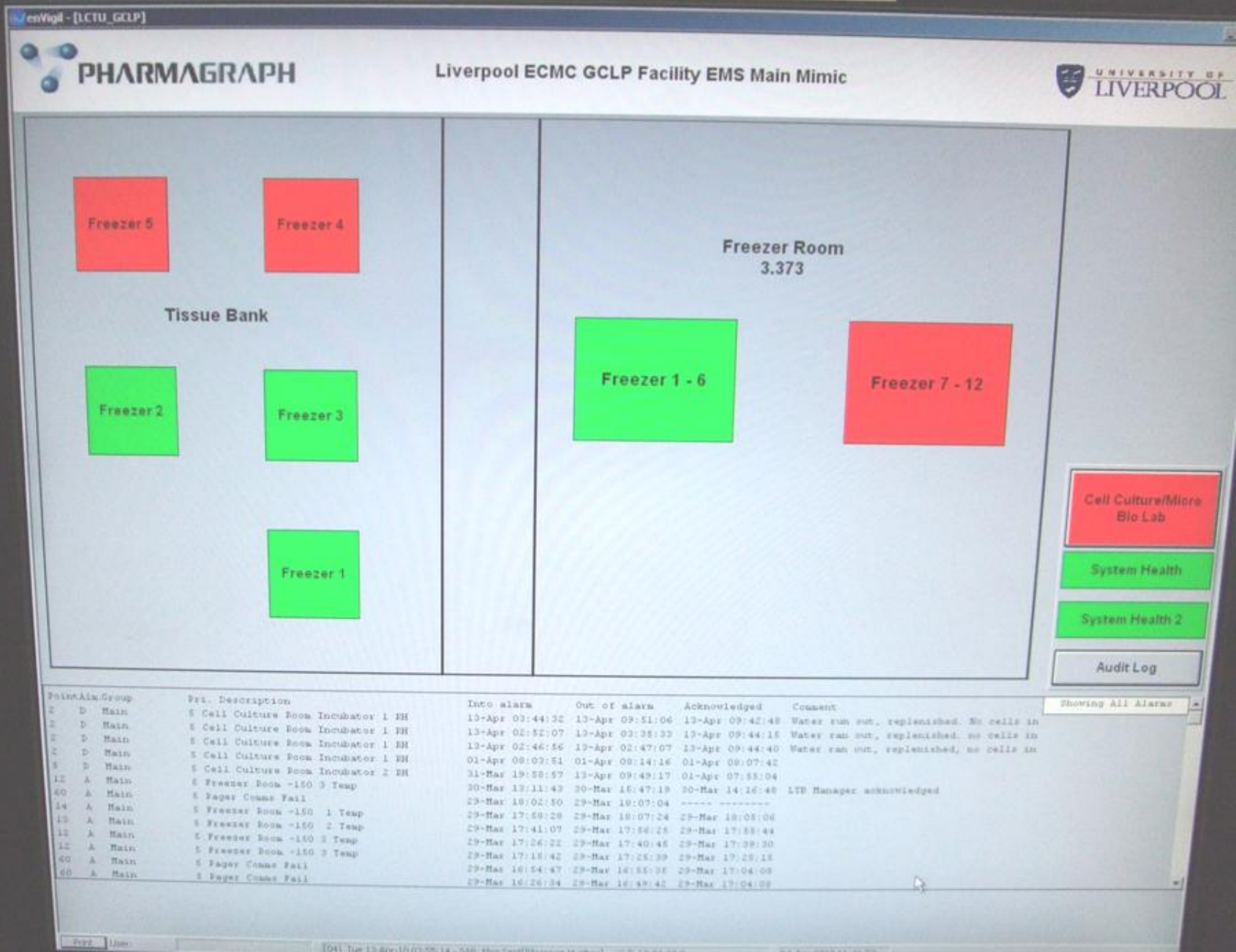

Live - [Dr William Greenhalf]
Future Analysis
Trials and Studies
Access
Kits
Audit Lookup
Reference
Configure
Help
Kits Workflow
Kit QC
Filters
Kit type:
*
Show Kits created after:
26/08/2010
Kit Details
Kit Code : TEL1326
Kit ID : KIT10090131
Type : tPBMC & S
Status : Created
Storage Location :
Expiry Date : 30/06/2011
Kits
Kit Code
Type
Status
Location
SUA0019 aSUAVE Created GCLP Equipment
SUA0020 aSUAVE Created GCLP Equipment
SUA0021 aSUAVE Created GCLP Equipment
SUA0022 aSUAVE Created GCLP Equipment
SUA0023 aSUAVE Created GCLP Equipment
SUA0024 aSUAVE Created GCLP Equipment
TEL1326 tPBMC & S Created GCLP Equipment
TEL1369 tU&BFroz Created GCLP Equipment
TEL1408 tU&BFrozM Created GCLP Equipment
TEL1414 tSerumOn Created GCLP Equipment
TEL1415 tSerumOn Created GCLP Equipment
TEL1416 tSerumOn Created GCLP Equipment
Equipment items in selected Kit
Code
Equipment
QC
SM1009002496 Cryovial
SM1009002497 Cryovial
SM1009002498 Cryovial
SM1009002499 SST Tube
SM1009002500 CPT Tube
SM1009002501 CPT Tube
SM1009002502 CPT Tube
SM1009002503 CPT Tube
SM1009002504 CPT Tube
SM1009002505 Universal Tube
SM1009002506 Universal Tube
SM1009002507 Postage Box
SM1009002508 Smple Info Sht
SM1009002509 Fax Sheet
SM1009002510 LCTU Sheet
Refresh
Destroy Kit
Item OK
All Items OK
Make Comments
Exit
Autoscribe LTD


Live - [Dr William Greenhalf]
Future Analysis
Trials and Studies
Access
Kits
Audit Lookup
Reference
Configure
Help
Kits Workflow
Kit QC
Filters
Kit type:
*
Show Kits created after:
26/08/2010
Kit Details
Kit Code : Tel2
Kit ID : KIT10110079
Type : tPBMC & S
Status : Created
Storage Location :
Expiry Date : 25/11/2011
Kits
Kit Code
Type
Status
Location
Tel2 tPBMC & S Created ECMC Office
Equipment items in selected Kit
Code
Equipment
QC
SM1011001237 Cryovial 22/11/2010
SM1011001238 Cryovial 22/11/2010
SM1011001239 Cryovial 22/11/2010
SM1011001240 SST Tube 22/11/2010
SM1011001241 CPT Tube 22/11/2010
SM1011001242 CPT Tube 22/11/2010
SM1011001243 CPT Tube 22/11/2010
SM1011001244 CPT Tube 22/11/2010
SM1011001245 CPT Tube 22/11/2010
SM1011001246 Universal Tube 22/11/2010
SM1011001247 Universal Tube 22/11/2010
SM1011001248 Postage Box 22/11/2010
SM1011001249 Smple Info Sht 22/11/2010
SM1011001250 Fax Sheet 22/11/2010
SM1011001251 LCTU Sheet 22/11/2010
Refresh
Destroy Kit
Item OK
All Items OK
Make Comments
Exit
Autoscribe LTD
NUM

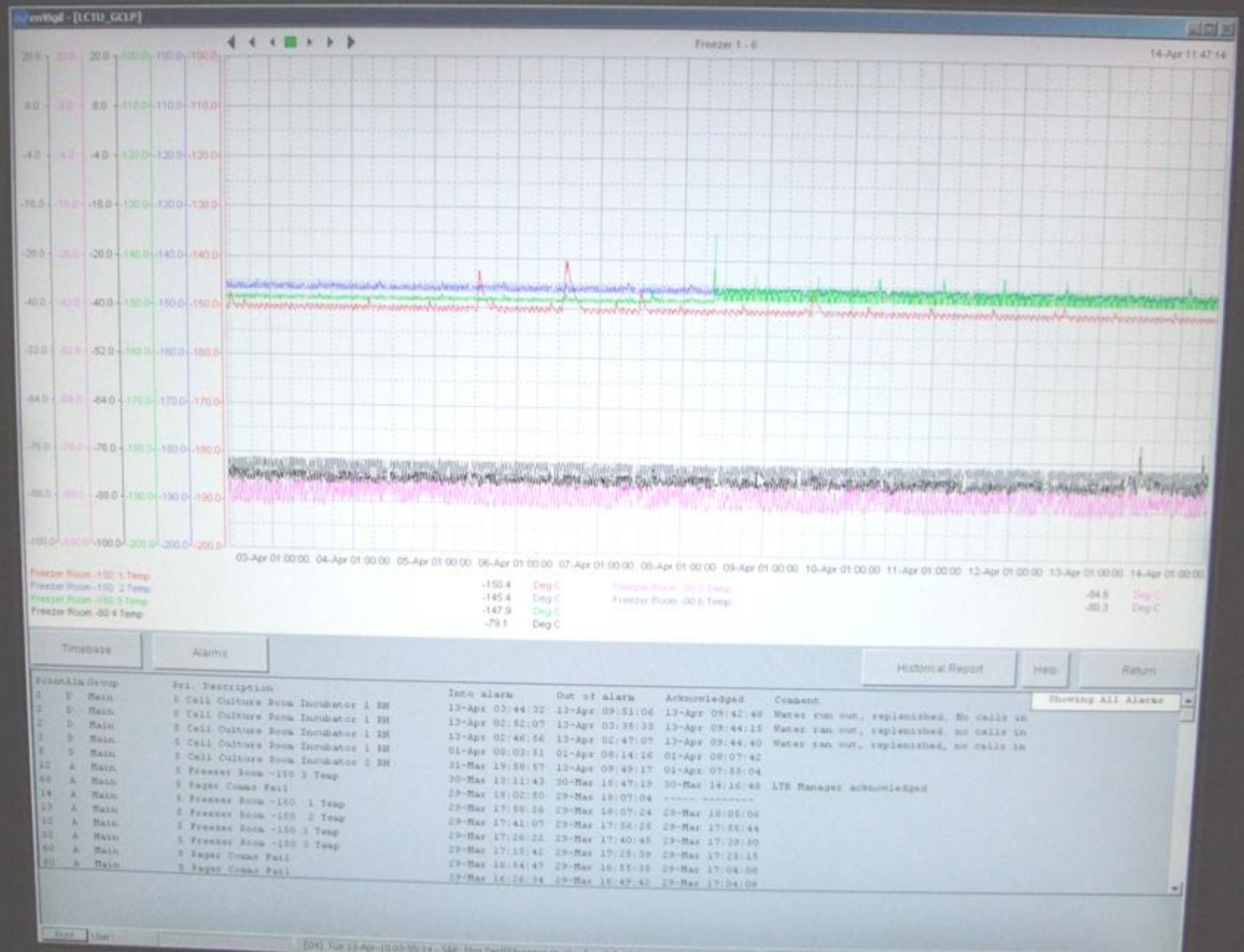

Live - [Dr William Greenhalf]
Future Analy
Sample Life Cycle
TELOVAC
PBMC & SERUM
Exit
Set Equipment
Set Reagents
Audit Tool
PBMC
Fax Received
Record details from Fax received by LCTU
Alternatively
Set Patient ID
Temptale Values
Serum
Receive Samples
Store Location
View / Move Locations in -80
Receive Samples
Centrifuge
Combine Universals
Centrifuge
Cell Count / Viability Test
Centrifuge / Aliquot
Store IM/SN
Store Location
Combine Aliquots
Cell Count / Viability Test
Irradiate or incubate
Cell Count / Viability Test
Combine on plate
Aliquot live PBMCs
Incubate
Aliquot to plate
Add Thymidine and Incubate
Harvest Cells
Beta Counter
View / Move Locations in -150
Store Location
Defrost plate
Aliquot to Luminex plate
Replace plate in freezer
Luminex Test
View / Move Locations in -20


Live - [Dr William Greenhalf]
Future Analysis
Trials and Studies
Access
Kits
Audit Lookup
Reference
Configure
Help
Sample Life Cycle
Storage Location
Sample Code : SM1011001809
Patient ID Code : Fred
Parent Sample : SM1011001805
Freezer:
Freezer 7 (-150)
Tower
B
Box:
3
Position:
A1
A2
A3
A4
A5
A6
A7
Ok
Cancel
Magic Button
Print Labels (Single Select)
Temp Store (Multi Select)
Final Location
Exit
Delete Sample
Exit
Serum
Receive
Store Location
Counter
Store Location
Defrost plate
Aliquot to Luminex plate
Replace plate in freezer
Luminex Test
View / Move Locations in -80
Store IM/SN
Aliquot live PBMCs
View / Move Locations in -150
View / Move Locations in -20

PLEASE SWITCH MONITOR OFF WHEN NOT IN USE



PLEASE SWITCH MONITOR OFF WHEN NOT IN USE



# Conclusion

Samples gain value because of the link to the patient (a person)

Properly informed patient consent is essential and must be verifiable

Patients have the right to privacy

Laboratory data should be acquired empirically
Blinded as far as possible to related clinical data

Potential bias should be identifiable from an easily achievable audit

Regulators (e.g. MHRA) are tasked with ensuring that is achieved

Computer systems can be used to provide a sequential audit trail rather than a narrative

I’d like to discuss Somerset and Edge if I can find a way to cut down the rest of the talk