Managing risk in Cryopreservation



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Bottinghers University Hospitals NWR

Managing risk in Cryopreservation

- · Define risk
- How to identify/quantify risk
- · Risk associated with Cryopreservation
- Specific examples and controls

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What is risk?

- · Risk Probability of an <u>adverse event or hazard</u>
- · Risk Categories
- 1.The unavoidable spontaneous e.g. flood, fire, aliens, management involves coping with the consequences
- 2.Compliance with standards known, planned for, manageable e.g Accreditation, Regulation (EUTD)
- 3. Avoidable risks can be predicted and therefore controlled

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Unavoidable Risk

- Dynamically derived events e.g. infections, epidemics, manmade or natural disasters
- Will occur at some point despite risk avoidance measures
- Outcomes are about coping with the consequences contingency planning (what if



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Compliance with Standards

Voluntary e.g. best practice guidance Mandatory schemes - EUTD

- Accrediting/licensing bodies
 - · ISO
 - · HFEA (UK)
 - · AATB, CAP (US)
 - RTAC (Australia/NZ)
- Medical Devices
 - FDA approval
 - · CE marking
- · Zero tolerance Check compliance by audit

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Avoidable Risk



- Found by: observation, common sense, past experiences
- RM benefits from an open (no blame) reporting culture
- · Learning from mistakes near miss/incident reporting

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Failure to control risk · Loss of Material (patient, research) · Errors in ART · Loss of reputation/referrals/contract · Loss of license · Loss of business · Loss of fingers, toes, eyes, life..... Nottinghers University Hoopitals (IVVII) Formal Risk Identification · Risk Assessment Method for early identification of adverse events (hazards) Implement controls - SOPs - training - equipment - facilities - reduce the chance of those occurring - reduce insurance premiums Bottinghers University Hospitals NWR Assessing risk · Risk Assessment - difficult (prior knowledge) Break down the process - Areas/rooms e.g. cryoroom - Process/Procedures • Incidents - i.e actual occurrences - probability can be estimated - Controls implemented for future - Open reporting culture essential 'Learn by your mistakes and those of others' Rottinghers University Hospitals (MAR)

AZ/NZ543 (risk	60:1999 = conse		ices x l	ikelihoo	od)	
			PPOR	ABILITY		
CONSEQUENCES	Impossible 0	Rare 1	Unlikely 2	Moderate 3	Likely 4	Certain 5
Negligible - 0	0	0	0	0	0	0
Minor - 1	0	1	2	3	4	5
Serious - 2	0	2	4	6	8	10
Major - 3	0	3	6	9	12	15
Fatality - 4	0	4	8	12	16	20
Multiple Fatalities - 5	0	5	10	15	20	25
atality - 4	0	4	8	12	16	

- · 'Risk associated with Cryopreservation'
- The biggies!

 - Injury to personnel
 Loss of stored material

 - 3. Damage to stored material4. Misidentification of material
 - 5. Risk to recipient/ART errors
 - 6. Financial
 - Hudricial
 Litigation (loss of patient material)
 Loss of research material
 Failure to comply with regulation
 Loss of Quality Assurance

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Risk	Area of service
Injury to personnel Loss of stored material	Process
Damage to stored material Misidentification of material	Procedure
Risk to recipient/ART errors Financial	Area or room
Quality assurance/user satisfaction	
Regulation Natural eyents (Flo	ods/Fire/terrorism)
Technical/training	
Professional liabilit	y/Human error
Infection Control Staffing Issues	<u>Causative factors</u>
Facilities (nitrogen	transport and storage)
Product and equipm	ent liability
Security (specimen:	s, facilities, data)
Resources	Mottinghers University Mospitals IVVA

	Campus	Queen				Assess	ment No	o.		Fertra.	003
Nivision: Family Health Issessor: M Tomlinson	Directorate /Department: Job tile:		Ob/Gyn Consults	nt Scienti	at	Location Date:		Fertility Uni 07/07/2009			
						Review	Date:	01/04/2010			
lescription of activity											
Sperm Cryopreservation (for patients and don iupporting information (für example, case of need, explanation this is the awas of highest fisk within the Department. In particula learly	on of activity)	ecimens; st	alf or patier	t injury could	d be costly in	terms of re	putasion, re	gulation and inc	ieed throug	h Higation. S	Equally, th
lisks, Controls and Assessment											
		A. O bjazdives	8 - Harm	- Experience	D-Service Delivery	E- External	Likelih oo d	tisk Score (Highest Score)	Phorby Indiator Rore A-B-C++0	oss the cortod adequately detective fish Tes Filo	s the control measure occumented and communicated? Yes! No
 Risk Mestified Risk of mis labelling of patient flee, stored straw or T cand. 	Controls is place and sop.016-019. Sperm processing, cryopreservation,	3	3	2	3	3	2	6	14	Yes	Yes
Poor service delivery for sperm storage poor quality of donated sperm	and.sop.01+-015/and.sop.021 donor processing	3	3	2	3	3	2	6	14	Yes	Yes
HEALTH AND SAFETY Risk of liquid nitrogen, burns/baphpolation in the cryonom. Other injury e.g. eye damage from exploding valutations.	and.sop.019 Health and safety manual ABAtryosen/ice use of nitrogen course. Trust policy	4	4	3	4	4	2		19	Yes	Yes
Poor invertory control, loss of samples. Inappropriate disposal of samples	and sop.01+015/and.sop.021 donor processing	3	3	2	4	4	2		16	Yes	Yes
Inadvertent thew of frozen samples due to: Equipment failure. Includes: Dry shippers, vapou freezers, pressurised vessels, power	and sop.016-019 ABAlcryoservice r use of nitrogen course. Sample splitting	4	2	3	4	4	3	12	17	Yes	Yes
Loss of frozen specimens during transport Failure of shipper, incorrect filling, shipper damage, lack of care by courier	and.sop.016-019 ABAloryoservice use of nitrogen course	4	2	3	4	4	3	12	17	Yes	Yes
HEALTH AND SAFETY Risk of burns, asphysiation and physical injury Occupational injury during transport of nitrogen culinders.	and.sop.019 Health and safety manual ABAlcryoservice use of nitrogen course	4	2	3	4	4	3	12	17	No7	Yes
Inadvertent thaw of frozen samples due to:			. —	1 -	1 =	. –	1 -			1 =	1 -

Major risk and cryopreservation of Reproductive cells and tissues

- 1. Injury to personnel
- 2. Loss of stored material
- 3. Damage to stored material
- 4. Misidentification of material
- 5. Risk to recipient/ART errors
- 5. Financial
- 6. Regulation
- 7. Quality Assurance

Overarching

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Injury to personnel

Hazards

A - asphyxiation (Death)

T-temperature (Burns)

P - pressure (Explosion)

Other

•Occupational health (transport of LN2)

Who is at risk?

- •1.Delivery/portering/visitors/assessors
- ·2. Laboratory staff

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Injury to personnel Transport of Nitrogen

- Pressurised vessel
 - toppled over' trapping a porter underneath
- Transport in elevators
 - Emergency venting (burst disc)Lift threshold
- Transport by hand
 - Dewars carried by hand (full) upstairs
 - Dilvac

Transport and elevators
• British Compressed Gas Association http://www.bcga.co.uk/

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Injury to personnel Other

1. Burns

PPE, emergency procedures



- 2. Explosion
- · Flasks
- Cryovials
- Ice plugs



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Injury to personnel Explosion Cryovials - shrinkage and

embrittlement in LN2



"0.5ml LN2 in a 1.5 ml vial = 4,053 psi on evaporation Failure of the seal - projectile with an initial velocity of up to 296 miles per hour (132 meters/sec) $\sim 8.4\%$ kinetic energy of a 22-calibre bullet!"

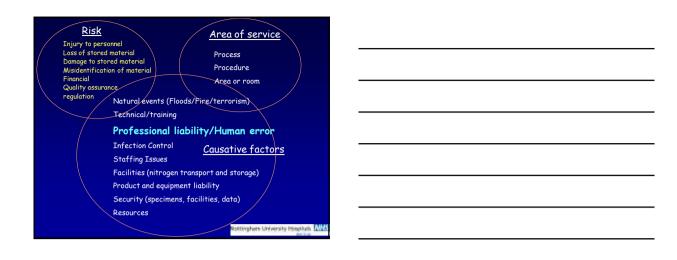
American Industrial Hygiene Association

Letter From A Nobel Prize Laureate on The Loss of Sight In One Eye Due To A Cryogen Accident (top)

70% UK embryologists observed cryovial explosion – use them in liquid phase (Tomlinson and Morroll, 2008)

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Professional Liability/ Human Error*

Association of Clinical Embryologists UK (Tomlinson and Morroll, Human Fertility, 2008)

30% of industry staff received any formal training (senior staff local H&S)
<5% from recognised gas suppliers

10% trainees - had anxiety over N2 use 45% senior staff - " " " "

Unaware of regulations

'Embedded lack of basic knowledge' - At risk

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Injury to personnel

UK Embryology/andrology staff:

- Lack of engagement with the institution
 Poor awareness of any risk management process
- •Facilities poorly sited (5th floor)
- Transport of nitrogen (elevators/stairs)
- Delivery vessels injuring portering staff
- •Concerns over lack of space
- ■Ineffective extraction/O₂ monitoring
- *Lack of PPE or use of PPE
- *High risk Despite heavy regulation and licensing of clinics



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Injury to personnel - Management cont'd

- · Location ground floor (avoid elevators BCGA)
- External wall delivery
- Forced air extraction
- Oxygen monitoring
- Servicing
- Training



Courtesy of Statebourne Cryogenics UK

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Major risk associated with Cryopreservation of Human cells and tissue

- 1. Injury to personnel
- 2. Loss of stored material
- 3. Damage to stored material
- 4. Misidentification of material
 - 5. Risk to recipient/ART errors
 - 5. Financial
 - 6. Regulation
 - 7. Quality Assurance

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Loss or Damage to stored material

- 1. Freezing method
- 2. Storage

 - Nitrogen SupplyEquipment failureAudit/labelling
- 3. Breach of packaging (Contamination)

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BBC	iEWS
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Calbridg Park	Participation of the point before training
Treating their	Process against Nove account of patterns baper at a prod body have been normal after a Racif allowed the samples to partials ribificat.

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Loss or Damage to stored material •1. Cryopreservation Appropriate method ·Avoid contamination (grade A air) Optimised cooling rates Appropriate packaging 40% IVF units had freezer Validation failure at egg retrieval (<60% controls) in place ·Scientifically justified ·Proven efficacy Tomlinson and Morroll, 2008 Spare freezer/Contingency · Appropriate equipment Nottinghern University Hospitals (IVIX) Loss or Damage to stored material 2. Storage Risk Nitrogen Supply · Equipment failure · Identification and Audit · Contamination Bottinghers Shriversity Hospitals IVAR Loss or Damage to stored material Liquid nitrogen supply Delivery failure Natural disaster Breakdown Other

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Delivery vessel failure Staff failure Autofill system failed

Loss or Damage to stored material

Autofill systems

- · Requires vigilance
- Vapour or liquid phase units
 - Solenoid blockage
 - Faulty controller
 - Faulty sensor
- · Failure to fill
- · Fill one preferentially (warm another)





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Loss or Damage to stored material

Liquid nitrogen supply Controls and Management

Deliveries

- Regular delivery to more than cover usage
- Excess storage capacity/spare supply vessel
- Bulk storage (autofill vapour storage)

Manual fill

- Regular documented filling rota
- Regular inspection
- Document losses from each vessel (slow vacuum loss)



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Loss or Damage to stored material

Equipment Failure

Vacuum failure - rare??? UK reports - 2 dewars acute failure in 15 yrs

- Pressurised vessels
- Dewars
- Vapour units
- Dry shippers
- Controller failure (vapour units)
 - 3 major incidents/4-5 years
 - Ongoing Litigation
 - Dry shippers (couriers, keep upright)

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Loss or Damage to stored material

Equipment Failure Controls

- Divide precious specimens across vessels
- Have spare capacity
- · Alarm and monitor vessels
 - Out of hours warning systemFormal staffing rota
- Avoid trauma

 - Flooring (smooth, no trip hazards) Protect shippers clear filling and transport procedure/intructions

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Loss or Damage to stored material

Identification and Audit

- · Poor labelling/Misidentification
 - Patient/recipient error
 - Apparent specimen loss (regulatory, litigation)
 - Warming between fingers

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Loss or Damage to stored material

Identification



- · Broken packaging
- · Label detachment
- 2. Poor Labelling
 - Transcription errors e.g 5 or S
 - · Illegible markings/handwriting
 - · Misaligned markings/bar code





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Loss or Damage to stored material

Identification Risk Management

Controls

- Automated Labelling
- RFID (Radio frequency identification)
- Witness verification
- · Robust labels adheres to packaging in LN2

Doubts over identity

- Discard
- · Record as incident

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Loss or Damage to stored material

Storage review/audit

Mislabelling/Misidentification

"storage centres are expected to carry out reviews at least annually of the status of stored gametes and embryos"

HFEA code of practice, 6th Edition

ACE survey Tomlinson and Morroll (2008) Andrology/Embryology Audit

>50% - observed ejection of sealing plugs <60% - procedures for observation at -140 or below Few used PPE

'Risk to sample harm outweighs the benefits gained from audit' Allow centres a flexible risk based approach depending on size/type of inventory

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Loss or Damage to stored material

Breach of Packaging

Effect of LN2 on materials

Contamination
Loss of material
Hepatitis B incident 1995

Tissue banks and Blood service

- ·Storage system (vapour)
- ·Packaging (double skins)
- ·Screening**

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Summary

- · Risk assessment necessary or scaremongery?
- · Identify potential hazard formally even if low risk
- · Hazards with low risk no controls
- Hazards with high risk implement controls

 - SOPstrainingEquipment/materialsfacilities
- Institute support easier with formal risk assessment

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