1 Appendices

1.1 Appendix 1 – Ethics Committee Research Proposal Form

Ethics Committee Approval for Study

To be completed by Faculty Research Ethics Committee

We have examined the above proposal and advise

Acceptance **Refusal** **Conditional acceptance** ✓

For the following reason/s:

1. Proposed title to be amended and to read as follows: 'The effect of chemotherapy on patients' nutritional status.' ✗
2. Nursing Managers permissions need to be updated. ?
3. To appoint Local Supervisor, responsible for ethical issues.
4. Not allowed to translate tool to Maltese. ?

Signature

Date 06.01.09

To be completed by University Research Ethics Committee

We have examined the above proposal and grant

Acceptance **Refusal** **Conditional acceptance**

For the following reason/s:

Approved as amended according to new version ~~not~~ attached

Signature Paul Vella

Date 24/3/09

Ethics Committee Approval for Study & Assignment of Tutor & Ethical Supervisor

L-UNIVERSITÀ TA' MALTA
Msida - Malta
ISTITUT GHALL-HARSIEN TAS SAHHA

UNIVERSITY OF MALTA
Msida - Malta
INSTITUTE OF HEALTH CARE

REF. TAGHNA: *OUR REF:*
REF. TIEGHEK: *YOUR REF:*

25th February, 2009

Mr Geoffrey Axiak
32, 'White Rose',
Triq ix-Xitwa
Mosta MST4061

Dear Mr Axiak,

Re: Research Proposal

Reference is made to the submission of your Research Proposal entitled: *'THE EFFECT OF CHEMOTHERAPY ON PATIENTS' NUTRITIONAL STATUS'.*

Following the meeting of the Research Ethics Committee held on 6th January, 2009, the Board is recommending that Dr Donia Baldacchino should act as your local supervisor with responsibility for ethical issues.

Professor V. Ferrito
Chairman
Institute of Health Care
Research Ethics Committee

cc: Dr Donia Baldacchino,
Asst. Co-ordinator, M.Sc./Mid.
Nursing/Midwifery Division
Institute of Health Care
University of Malta

POSTAL ADDRESS: MSIDA MSD 2080, MALTA
TEL: (356) 21333903-6 DDI: (356) 2340 + Extension Number E-MAIL: ihc-web@um.edu.mt

Ethics Committee Approval to Amend Study Title

L-UNIVERSITÀ TA' MALTA
Msida - Malta
ISTITUT GHALL-HARSIEN TAS SAHHA

UNIVERSITY OF MALTA
Msida - Malta
INSTITUTE OF HEALTH CARE

REF. TAGHNA: *OUR REF:*
REF. TIEGHEK: *YOUR REF:*

7th August, 2009

Mr Geoffrey Axiak
32, 'White Rose',
Triq ix-Xitwa
Mosta MST4061

Dear Mr Axiak,

Re: Change in title of Research Proposal

I am pleased to inform you that the Institute of Health Care Research Ethics Committee has approved your request to change your research proposal title from *'THE EFFECT OF CHEMOTHERAPY ON PATIENTS' NUTRITIONAL STATUS'* to ***'THE EFFECT OF CHEMOTHERAPY ON PATIENTS' NUTRITIONAL STATUS AND DISTRESS LEVELS.'***

Professor V. Ferrito
Chairman
Institute of Health Care
Research Ethics Committee

cc: Dr Donia Baldacchino,
Asst. Co-ordinator, M.Sc./Mid.
Nursing/Midwifery Division
Institute of Health Care
University of Malta

POSTAL ADDRESS: MSIDA MSD 2080, MALTA
TEL: (356) 21333903-6 DDI: (356) 2340 + Extension Number E-MAIL: ihc-web@um.edu.mt

1.2 Appendix 2 - Patient Consent Form

Patient Consent Form

I, patient number _____, contact number_____, declare that:

1. I have been informed of the aims and outcomes of this study,
2. I have been told that there are three rounds of data gathering, the first before my treatment starts when I will have my body mass index and distress level assessed and complete a short report on my nutrition to date. The second data gathering point will happen after the commencement of my treatment and assess my experiences of the same. The third data gathering point will be at current treatment completion, when I will again be re-assessed on the above and also asked to reflect on my experiences.
3. I understand that no personal information will be revealed to third parties,
4. I am informed that confidentiality and anonymity will be maintained at all times by I, but that a summary of data collected will be used to inform the educational report written at study end, to guide local practice on patient support and to prepare relevant articles for publication or papers for conference presentation.
5. I am informed that I can retire from participating in the study at any time that I wish, without the need to provide reasons for doing so or without incurring any penalty whatsoever,
6. In the event that the study prompts additional anxieties or queries, not sufficient to prompt my withdrawal, that I may receive additional guidance and support from a qualified healthcare practitioner with expertise in this area
7. I am aware that after the study all data collected will be destroyed after the study report has been assessed and within one month's time as per research ethics committee requirements,

8. I have been informed that at the end of the study I will be able to obtain a summary of the findings, that would be made available at the Medical Investigations and Treatment Unit (M.I.T.U.), Mater Dei Hospital, Malta.
9. I am also aware that I may make any complaint regarding the study or the research process at the M.I.T.U. on the forms provided.

and hence I accept to participate in your study.

Patient Initials_____

Signature of researcher_____ (Geoffrey Axiak)

Signature of research supervisor_____(Dr Bob Price)

Date of consent_____

1.3 Appendix 3 – Patient Information Sheet (English)

Participant Information Sheet

Study Title: Nutrition and cancer chemotherapy treatment

You are being invited to take part in a research study which is being conducted as part of masters degree that I am completing with the Open University, (United Kingdom) but which will also be used to guide our practice on supporting patients during their chemotherapy treatment. Before you decide whether to take part it is important to understand why the research is being carried and what participating in this will involve.

The person who is giving you this information has been asked by me to make a note of your name and contact details, forwarding these to me only if you express interest in assisting with this study. I will then contact you to answer any further questions that you may have, to confirm your wish to proceed, signing a written consent form and to plan the three times that we will meet. You may change your mind at any time, without cost to your future care and support, simply by contacting the Nurse-in-Charge of MITU or if you prefer by telephoning on hospital extension number **7217**, paging me on the internal paging system on pager number **356 2141**, on mobile number **99822288** or by writing to me **Geoffrey Axiak** at **Clinical Nutrition Services, Level -1, Out-Patients' Block, Mater Dei Hospital**.

What is the purpose of the study?

The research aims are to

Help us to better understand the part that nutrition plays in the support of patients who receive chemotherapy treatment

To appreciate what it is like to deal with the side effects of cancer chemotherapy

To understand how you evaluate your experiences at completion of a first course of treatment

To complete requirements associated with an education qualification that I am studying.

Whilst at this stage we cannot be sure what the resultant data will teach us, it is hoped that a better understanding of the above will play a part in the briefing and professional update of staff who support patients and assist them during their treatment.

Why have I been invited?

We have invited you to contribute to the research study because you have recently been scheduled (and for the first time) to receive cancer chemotherapy treatment. I am especially interested in how patients receiving such treatment experience its effects and any possible associations that there might be with their nutrition.

Do I have to take part?

You are at complete liberty to decide whether to take part in this research study, or to decline and all without penalty to the treatment care and support that you receive. There are no financial incentives to take part in the study. Should you decide to take part, you have the right to change your mind later, withdrawing from the study at any time and without giving a reason (see above for guidance on how to do this).

What will happen to me if I take part?

Should you feel comfortable to participate in the study I will visit you on three occasions to gather information. None of the research requires you to have different treatment or to undergo injections or other invasive procedures.

On the first of these visits I will invite you to ask any remaining questions and to sign a written consent form before we proceed further. You will be given a copy of the signed consent form to keep, alongside this information sheet.

Visit 1 will happen after your admission to hospital and before your chemotherapy treatment commences. During this visit I will make an assessment of your nutritional status and invite you to complete a short questionnaire on how you see the same. I anticipate that this visit will take no more than 15-20 minutes of your time.

Visit 2 will be scheduled for between 5 days and 10 days after your chemotherapy treatment has commenced. Should you have been discharged from hospital in the interim then I will arrange a suitable time to visit you at home or an agreed other venue so that the data can be collected. During this visit I will ask you to complete a short sheet detailing your experience of chemotherapy and its side effects. I anticipate that this visit will take about 10-20 minutes.

Visit 3 will be scheduled for the point at which you complete your first course of chemotherapy treatment and at this point you will be asked to complete a short questionnaire (this will take approximately 30 minutes to complete). Once again I will schedule with you a convenient time and place to complete this work. The focus of interest during this visit will be your experiences of treatment and what seemed supportive there.

Will my taking part in the study be kept confidential?

If you agree to participate in the study you will be allocated a code to ensure your anonymity. The only individuals who will have access to the data will be I, his research supervisor and any examiners charged with assessing the work undertaken. Research supervisors and examiners though will not have access to details of your identity. To protect research paperwork from misuse, I will ensure that these are securely stored in a locked cabinet. Any work completed on this study using a computer will be password protected and will NOT be transported using a laptop computer.

A summary of the results of this study will be made available to you and other participants through MITU (please state whether you would like copy of the same at visit 3 or before and whether you would like it posted to you or not). Your personal identity though will not be revealed to others there, or indeed in any papers for publication, conference presentation or research report that follows. If you would like to have the study results posted to you just leave your details with the **Nurse-in-Charge of MITU** and she will post copies of the results to all interested people at the end of the study.

Potential disadvantages to taking part in the study

I have indicated above the anticipated time that I think it will take for you to share information with me. You may find that you become tired, if this occurs please indicate this to me and I will adjust the pace of our discussion or reschedule a meeting. You may find that sharing your experiences in this way affect you emotionally. If so, I can arrange for you to speak with a qualified healthcare professional who can assist you.

Possible advantages to taking part in the study

There are no guaranteed personal advantages in taking part in this study, though you may find it supportive to discuss your experiences with I. The chief advantages may lie with other patients whose treatment and support are improved as a result of what we understand from this and other such studies.

What if there is a problem?

If you wish to complain or comment on Is conduct, you can do so by writing to the **Nurse-in-Charge** of **MITU** and she is instructed to forward it to the person involved in forwarding requests to the Ethics Committee of the Institute of Health Care, University of Malta..

Alternatively, you may also choose to contact my research supervisor to express your concerns. His details are as follows:

Dr Bob Price

Director, Postgraduate Awards in Advancing Healthcare Practice/MSc in Nursing

Health and Social Care Faculty

The Open University

Walton Hall

Milton Keynes MK7 6AA

United Kingdom

What will happen if I do not want to carry on with the study?

If you wish to withdraw from the study, you can do so at any time by notifying MITU staff or myself. No reason has to be given for your decision and this will not affect the care that you receive. Withdrawal from the study will mean the removal of all information collected with you to that point unless you give me written permission to draw on the incomplete data.

What will happen to the results?

The results of the study will be written up as part of I's MSc Dissertation. Summary of the research may be published within the healthcare press and observations on the study shared at conference. In all instances, your personal details will not be shared with recipients of my report. Data collected during this study will be destroyed after a month from the completion of the study.

Who has reviewed the study?

The study has been reviewed by the Research Ethics Committee of the Institute of Health Care, University of Malta and by my Research Supervisor.

Contact Details

If you have any queries or would like more information you can contact me on hospital extension number **7217**, by paging me on the internal paging system on pager number **356 2141**, on mobile number **99822288** or by writing to me **Geoffrey Axiak** at **Clinical Nutrition Services, Level -1, Out-Patients' Block, Mater Dei Hospital**.

If you decide to participate

Once you have read this information and if you indicate an interest in participating in the research study please retain this copy of the briefing information for future reference. You contact details will be passed to me from the professional who has alerted you to the study and I will contact you in seven more days time..

Thank you for taking the time to read this information and considering participating in the research study.

_____	_____
Patient's Initials	Patient Contact Number
_____	_____
Researcher's Signature	Signature of Nurse-in-Charge, MITU
GEOFFREY AXIAK	(witness)

1.4 Appendix 4 – Patient Information Sheet (Maltese)

Formola t'Informazzjoni Għall-Pazjenti

Isem tal-Istudju: L-ikel u l-kimoterapija

Inti mistieden tieħu sehem f'din ir-ricerka li qed nagħmel biex inġib Masters mill-Open University (fl-Ingilterra) imma li wkoll se tintuża biex nirranġaw il-mod li bih ngħinu lill-pazjenti tagħna li jkunu qed jircievu l-kimoterapija. Qabel ma tiddeciedi jekk tixtieqx tieħu sehem huwa mportanti li tifhem għal xhiex qed isir dan l-istudju u x'jinvolvi jekk tieħu sehem fih.

Il-persuna li qed tagħtik din l-informazzjoni intalbet tikteb ismek u d-dettalji fejn nistgħu insibuk, u tagħtihom lili biss jekk tiddeciedi li tieħu sehem. Imbagħad jien nikkuntattjak biex nirrispondi xi mistoqsijiet li jista' jkollok, biex nikkonferma li tixtieq tkompli, tiffirma formola ta kunsens u nippjanaw tliet laqgħat. Tista' tibdel il-ħsieb meta trid, mingħajr effett fuq il-futur jew l-għajnuna tiegħek, billi tkellem lin-Nurse-in-Charge tal-MITU jew iccempilli fuq extension tal-isptar numru 7217, jew bil-pager fuq numru 356 2141, jew bit-telefon cellulari numru 99822288 jew billi tiktibli bħala Geoffrey Axiak u tibagħtha Clinical Nutrition Services, Level -1, Out-Patients' Block, Mater Dei Hospital.

X'inhu l-iskop tal-istudju?

l-iskopijiet tar-ricerka huma:

- Biex jgħajnuna nifhmu aħjar x'inhi l-importanza tal-ikel fl-għajnuna li għandu bżonn xi ħadd li jircievi l-kimoterapija
- Biex napprezzaw xi jfisser li tħoss l-effetti ħżiena tal-kimoterapija
- Biex nifhmu kif t'evalwa l-esperjenzi tiegħek meta tispicca l-ewwel kors ta trattament
- Biex nispicca l-istudju li qed nagħmel

Fil-waqt li issa ma nistgħux inkunu certi x'se tgħallimna din ir-ricerka, qed nittamaw li se nifhmu aktar kif nistgħu ngħinu lill-pazjenti waqt il-kimoterapija u b'hekk ngħallmu wkoll lil min jieħu ħsiebhom.

Għalfejn ġejt mistieden/mistiedna?

Aħna stidinnik biex tgħinna peres li dan l-aħħar inti kellek bzonn tircievi l-kimoterapija għall-ewwel darba. Nixtieq inkun naf l-aktar kif il-pazjenti jesperjenzaw l-effetti ħziena tat-terapija u xi għaqda li jista' jkun hemm mal-ikel.

Irrid bil-fors nieħu sehem?

Inti liberu tiddeciedi jekk tieħux sehem fir-ricerka, mingħajr ma jeffetwa l-kura jew l-għajnuna li tircievi. M'hemm l-ebda incentiva finanzjarja biex tieħu sehem fl-istudju. Jekk tiddeciedi li tieħu sehem, tista' tibdel il-ħsieb u tieqaf meta trid mingħajr ma tagħti raġunijiet (ara aktar il-quddiem kif tagħmel hekk).

X'se jiġrili jekk nieħu sehem?

Jekk tieddeciedi li tieħu sehem jiena se niltaqa' miegħek għal tliet darbiet biex niġbor xi nformazzjoni. Din mhix se tibdel xi trattament li tircievi jew tinvolvi xi ħaġa nvażiva.

Waqt l-ewwel viżta nistaqsik jekk għandekx xi mistoqsijiet jew dubji u biex tiffirma formola ta kunsens qabel ma nkomplu mexjin aktar. Tingħata kopja għalik biex iżżommha, ma din il-formola. Din se tkun kif tidħol l-isptar u qabel ma tibda' t-trattament. Hemm nistaqsik biex tara int x'inhu l-istatus nutrizzjonali tiegħek u biex timla' kwestjonarju qasir fuq hekk. Dan ma jdumx aktar minn 15 sa 10 minuta.

It-tieni viżta hija ppjanatha għall bejn il-ħames u l-għaxar ġurnata wara li tibda' t-trattament. Jekk tkun intbagħadt id-dar nirranġaw ħin bejnietna l-isptar jew xi mkien ieħor fejn niltaqgħu. Hawn nistaqsik timla' kwestjonarju qasir dwar kif tħossok dwar il-kimoterapija. Dan idum bejn 10 u 20 minuta.

It-tielet viżta ppjanatha għal meta tispicca l-ewwel trattament tiegħek u hawn nitolbok timla' kwestjonarju qasir (ta madwar 30 minuta). Għal dan nerġgħu niftehmu ħin u post fejn tixtieq. Se niffokaw fuq l-esperjenzi tiegħek waqt it-trattament u x'għajnuna sibt.

Jekk nieħu sehem, dan jibqa' konfidenzjali?

Jekk tieħu sehem tingħata numru biex ismek jibqa' mhux magħruf, ħlief għar-ricerkatur, is-supervisor tiegħu u xi eżaminaturi li jeżaminaw xogħlu. Is-supervisor tiegħu u xi eżaminaturi ma jkollomx access għad-dettalji personali tiegħek. Il-karti kollha se jinżammu imsakkrin u kull xogħol lest jinżamm imsakkar b'password u ma jinġarrx fuq laptop.

Se nagħtuk kopja tar-riżultati fil-qosor (u għalhekk għidilna jekk tixtieqx kopja waqt it-3 viżta u jekk tixtieqhiex bil-posta jew le). Ħadd ma jingħata d-dettalji personali tiegħek u lanqas ma jidhru f'artikli, ricerki jew konferenzi. Fil-kas li tixtieq kopja bil-posta ħalli d-dettalji tiegħek man-Nurse-in-Charge tal-MITU u hi timpostalek ir-riżultati kif jispicca l-istudju.

Żvantaġġi li jista' jkollu l-istudju

Jien tajtek il-ħin kemm nistgħu ndumu meta niltaqgħu. Jista' jkun li tkun għajjien. Fil-kas informani u nagħmlu appuntament ieħor. Tista' ssib li taqsam din l-informazzjoni jaffetwak emozzjonalment fil-kas, nista' nirranġalek biex tkellem persuna kwalifikata biex tgħinek.

Vantaġġi li jista' jkollu l-istudju

M'hemm l-ebda vantaġġ garantit, izda tista' ssib li meta tiddiskuti mar-ricerkatur dan jgħinek. L-akbar vantaġġ jista' jkun li tgħin pazjenti oħra meta jieħdu t-trattament minħabba riżultati li joħorġu minn dan l-istudju.

X'jiġri jekk ikun hemm xi problema?

Jekk tixtieq tagħmel ilment fuq ir-ricerka jew ir-ricerkatur, tista' tikteb lin-Nurse-in-Charge tal-MITU u hi mitluba tgħaddih lill-Kumitat tal-Istitut għall-Ħarsien tas-Saħħa li jieħu ħsieb l-Etika, fl-Universita ta' Malta.

Inkella tista' tkellem lis-supervisor tar-ricerkatur. Id-dettalji tiegħu huma:

Dr Bob Price

Director, Postgraduate Awards in Advancing Healthcare Practice/MSc in Nursing

Health and Social Care Faculty

The Open University

Walton Hall

Milton Keynes MK7 6AA

United Kingdom

X'jiġri jekk ma nkunx irrid inkompli nieħu sehem fl-istuju?

Jekk tkun tixtieq tirtira mill-istudju, tista' x'ħin trid billi tavża lili jew l-istaff tal-MITU. M'għandekx bżonn tagħti raġuniijiet u dan ma jaffetwax il-kura tiegħek. Meta tirtira, titneħħa l-informazzjoni kollha tiegħek li tkun inġabret sa dak il-ħin sakemm ma tagħtinix permess bil-miktubbiex nuża l-informazzjoni li tkun tajtni sa dak il-ħin.

X'se jiġri bir-riżultati?

Ir-riżultati tal-istudju se jinkitbu bħala parti mit-teżi tal-MSc li qed jagħmel ir-ricerkatur. Ir-riżultat ta dan l-istudju jistgħu jiġu ppublikati fuq xi rivista tas-saħħa jew imsemmija f'xi konferenza. Summary of the research may be published within the healthcare press and observations on the study shared at conference. F'kull każ, id-dettalji personali tiegħek qatt m'huma se jkunu żvelati. L-informazzjoni li tinġabar tiġi maħruqa wara xahar minn meta jintemm dan l-istudju.

Min qara dan l-istudju?

l-istudju inqara mill-Kumitat tal-Etika fir-Ricerka, tal-Universita ta Malta u s-supervisor tiegħi.

Kif Tikkuntattjani

Jekk ikollok xi mistoqsijiet jew tkun tixtieq aktar informazzjoni tista' ccempilli fuq l-extensjoni tal-isptar numru 7217, jew bil-pager fuq numru 356 2141, jew fuq it-telefon cellulari numru 99822288 jew billi tiktibli: Geoffrey Axiak u tibagħtu il-Clinical Nutrition Services, Level -1, Out-Patients' Block, Mater Dei Hospital.

Jekk tiddeciedi li tieħu sehem

La darba tkun qrajt din l-informazzjoni u jekk turi nteress li tieħu sehem fl-istudju, jekk jogħġbok żomm din il-kopja tal-informazzjoni bħala referenza għall-quddiem. Il-persuna li qaltlek dwar dan l-istudju se tgħaddili id-dettalji tiegħek u jien se nikkuntattjak fi żmien ġimgħa.

Grazzi tal-ħin li ħadt biex taqra din l-informazzjoni u talli kkonsidrajt tieħu sehem f'din ir-ricerka.

_____	_____
Firma tal-pazjent	Numru telefoniku tal-pazjent
_____	_____
Firma tar-ricerkatur	Firma tan-Nurse-in-Charge, MITU
GEOFFREY AXIAK	(xhud)

1.5 Appendix 5 – Patient Complaint Form (English)

Patient Complaint Form

I would like to complain about:

☐ The way I is conducting the study

☐ The tools that are being used for the study

☐ The information that is being collected during the study

☐ Other:

_____

_____

I feel that:

_____

_____

_____

I propose that:

_____

_____

_____

☐ I would therefore like to retire my participation from this study with immediate effect. I therefore ask I not to publish or use any data that he collected from me during the course of this research project.

☐ I would still like to participate in this study on condition that the above complaint/s are dealt with immediately.

Patient initials (optional)[1]:_____

Patient Contact Number (optional)[2]:_____

Date:_____

This complaint form is to be presented to the Nurse-in-Charge of the M.I.T.U., Mater Dei Hospital.

1.6 Appendix 6 – Management Consent Forms

[1] **You have a right to remain anonymous and leave this form unsigned if you wish.**
[2] **You have a right to remain anonymous and leave this line empty if you wish.**

Nursing Ward Manager's Approval to Conduct the Study

Managers' Consent Form

I, (name) Mary Grace Cardona., (name in BLOCKS) MARY GRACE CARDONA accept to authorize you to conduct your study with the patients under my care, after I have been informed of the aims and outcomes of this study and understand that no personal information will be revealed and that confidentiality and anonymity will be maintained at all times by the researcher.

Manager's Signature Cardona.

Name in full MARY GRACE CARDONA.

Nomenclature/Grade A/N.O.

Date of consent 15th February 2009.

Signature of researcher (Geoffrey Axiak)

Nursing Departmental Manager's (Responsible for Researcher) Approval to Conduct the Study

Re: Study on "The Effect of Chemotherapy on Patients' Nutritional Status"

Managers' Consent Form

I, (name) ISABELLE AVALLONE, (name in BLOCKS) _____, accept to authorize Mr Geoffrey Axiak to conduct a study with the patients undergoing chemotherapy at the MITU, after I have been informed of the aims and outcomes of this study and understand that no personal information will be revealed and that confidentiality and anonymity will be maintained at all times by the researcher, whilst adhering to the regulations of the University Research Ethics Committee and Data Protection.

Manager's Signature I Avallone

Name in full ISABELLE AVALLONE

Nomenclature/Grade DNM

Date of consent 16-02-09

Signature of researcher _____ (Geoffrey Axiak)

Nursing Departmental Manager's (Responsible for Unit) Approval to Conduct the Study

Re: Study on "The Effect of Chemotherapy on Patients' Nutritional Status"

Managers' Consent Form

I, (name) Lawrence Azzopardi, accept to authorize Mr Geoffrey Axiak to conduct a study with the patients undergoing chemotherapy at the MITU, after I have been informed of the aims and outcomes of this study and understand that no personal information will be revealed and that confidentiality and anonymity will be maintained at all times by the researcher, whilst adhering to the regulations of the University Research Ethics Committee and Data Protection.

Manager's Signature [signature]

Name in full LAWRENCE AZZOPARDI

Nomenclature/Grade D-N M.

Date of consent 19-02-09

Signature of researcher [signature] (Geoffrey Axiak)

1.7 Appendix 7 – Approval from the Ethics Committee of the University of Malta

Ethics Committee Approval for Study

To be completed by Faculty Research Ethics Committee

We have examined the above proposal and advise

Acceptance **Refusal** **Conditional acceptance** ✓

For the following reason/s:

1. Proposed title to be amended and to read as follows: 'The effect of chemotherapy on patients' nutritional status.' ✗
2. Nursing Managers permissions need to be updated, ?
3. To appoint Local Supervisor, responsible for ethical issues.
4. Not allowed to translate tool to Maltese. ?

Signature

Date 06.01.09

To be completed by University Research Ethics Committee

We have examined the above proposal and grant

Acceptance **Refusal** **Conditional acceptance**

For the following reason/s:

Approved as amended according to new version ~~not~~ attached

Signature Paul Abela

Date 24/3/09

Ethics Committee Approval for Study & Assignment of Tutor & Ethical Supervisor

L-UNIVERSITÀ TA' MALTA
Msida - Malta
ISTITUT GHALL-HARSIEN TAS SAHHA

UNIVERSITY OF MALTA
Msida - Malta
INSTITUTE OF HEALTH CARE

REF. TAGHNA:
REF. TIEGHEK:

OUR REF:
YOUR REF:

25th February, 2009

Mr Geoffrey Axiak
32, 'White Rose',
Triq ix-Xitwa
Mosta MST4061

Dear Mr Axiak,

Re: Research Proposal

Reference is made to the submission of your Research Proposal entitled: *'THE EFFECT OF CHEMOTHERAPY ON PATIENTS' NUTRITIONAL STATUS'.*

Following the meeting of the Research Ethics Committee held on 6th January, 2009, the Board is recommending that Dr Donia Baldacchino should act as your local supervisor with responsibility for ethical issues.

Professor V. Ferrito
Chairman
Institute of Health Care
Research Ethics Committee

cc: Dr Donia Baldacchino,
Asst. Co-ordinator, M.Sc./Mid.
Nursing/Midwifery Division
Institute of Health Care
University of Malta

POSTAL ADDRESS: MSIDA MSD 2080, MALTA
TEL: (356) 21333903-6 DDI: (356) 2340 + Extension Number E-MAIL: ihc-web@um.edu.mt

Ethics Committee Approval to Amend Study Title

L-UNIVERSITÀ TA' MALTA
Msida - Malta
ISTITUT GHALL-HARSIEN TAS SAHHA

UNIVERSITY OF MALTA
Msida - Malta
INSTITUTE OF HEALTH CARE

REF. TAGHNA:
REF. TIEGHEK:

OUR REF:
YOUR REF:

7th August, 2009

Mr Geoffrey Axiak
32, 'White Rose',
Triq ix-Xitwa
Mosta MST4061

Dear Mr Axiak,

Re: Change in title of Research Proposal

I am pleased to inform you that the Institute of Health Care Research Ethics Committee has approved your request to change your research proposal title from *'THE EFFECT OF CHEMOTHERAPY ON PATIENTS' NUTRITIONAL STATUS'* to ***'THE EFFECT OF CHEMOTHERAPY ON PATIENTS' NUTRITIONAL STATUS AND DISTRESS LEVELS.'***

Professor V. Ferrito
Chairman
Institute of Health Care
Research Ethics Committee

cc: Dr Donia Baldacchino,
Asst. Co-ordinator, M.Sc./Mid.
Nursing/Midwifery Division
Institute of Health Care
University of Malta

POSTAL ADDRESS: MSIDA MSD 2080, MALTA
TEL: (356) 21333903-6 DDI: (356) 2340 + Extension Number E-MAIL: ihc-web@um.edu..mt

1.8 Appendix 8 – Approval from National Comprehensive Cancer Network (N.C.C.N.) (2008) to use the Distress Thermometer Score

National Comprehensive Cancer Network®
275 Commerce Drive
Suite 300
Fort Washington, PA 19034
215.690.0300
Fax: 215.690.0280
www.nccn.org

May 14, 2008

Geoffrey Axiak, M.Sc. Nursing

R.C.N., London

32, Winter Street

Mosta

MST 4061

Dear Mr. Axiak:

On behalf of the National Comprehensive Cancer Network ("NCCN") I am writing to grant you limited one time permission to reproduce the **Distress Thermometer Screening Tool FIGURE (DIS-A)** from the NCCN **1.2008 Distress Management** Guidelines for use in your dissertation. Permission is granted solely for the purposes described herein which you represent and warrant to be for non-promotional educational use only. The following qualifications also apply to the permission granted by this letter:

1. You agree to include a citation giving full credit to the NCCN for these Guidelines as follows:

   Reproduced with permission from The NCCN 1.2008 **Distress Management** Clinical Practice Guidelines in Oncology. ©National Comprehensive Cancer Network, 2008. Available at: http://www.nccn.org. Accessed [Month and Day, Year] To view the most recent and complete version of the guideline, go online to www.nccn.org

2. Permission is for one time use only and expires after one year.

3. You agree that you will not translate, change, adapt, delete, extract portions, or modify the content of the NCCN **1.2008 Distress Management** Guidelines.

4. Permission is for reproduction of the Guidelines in print media only. **No Electronic Rights** (including CD-ROM and Internet) are granted. Reproduction of the Guidelines into any other medium, including but not limited to electronic media, is explicitly prohibited. You further agree that any reproduction of the Guidelines will include

NCCN's URL address www.nccn.org, to link to the most updated version of the NCCN **Distress Management** Guideline.

5. Permission is granted for reproduction in the English language only.

6. You agree that the following statements shall be conspicuously included in all guideline reproductions:

   "These Guidelines are a work in progress that will be refined as often as new significant data becomes available." "The NCCN Guidelines are a statement of consensus of its authors regarding their views of currently accepted approaches to treatment. Any clinician seeking to apply or consult any NCCN guideline is expected to use independent medical judgment in the context of individual clinical circumstances to determine any patient's care or treatment. The National Comprehensive Cancer Network makes no warranties of any kind whatsoever regarding their content, use or application and disclaims any responsibility for their application or use in any way."

   "These Guidelines are copyrighted by the National Comprehensive Cancer Network. All rights reserved. These Guidelines and illustrations herein may not be reproduced in any form for any purpose without the express written permission of the NCCN."

7. You acknowledge that the NCCN is sole owner of the Guidelines, and any derivative works created from the Guidelines. You further acknowledge that the NCCN is the owner of the name "National Comprehensive Cancer Network, Inc.®," and "the NCCN®" and any derivatives thereof (the "Marks"). You agree that you shall not use the Marks in any manner or for any purpose other than to acknowledge ownership of the Guidelines by the NCCN as described in this letter. Your use of the Marks and/or Guidelines for the purposes described herein in no way constitutes an endorsement of your works or opinions by the NCCN. You acknowledge that use of the Marks and reprinting of the Guidelines pursuant to the permission granted hereunder shall not create in your favor any right, title, or interest in or to the Marks and/or the Guidelines. The permission granted hereunder is for a one-time use of the Marks and/or Guidelines. You agree that each use of the Marks and/or the Guidelines by you, beyond or in addition to that described herein, shall require written approval by the NCCN.

8. Your use of the Marks and/or Guidelines as described herein shall signify your acceptance of the terms and conditions of this letter. The NCCN reserves the right to at any time revoke the permission granted hereunder if, in its discretion, the NCCN determines that you have violated or are in violation of the terms of this letter of permission.

Thank you for your interest in the work of the NCCN.

Sincerely,

Lynn Cherrin, MS

Project Assistant

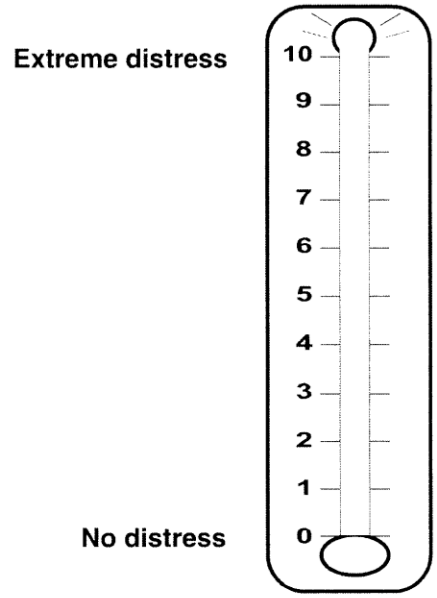
NCCN

Axiak/5-14-08

1.9 Appendix 9 – Distress Thermometer Problem Score

SCREENING TOOLS FOR MEASURING DISTRESS

Instructions: First please circle the number (0-10) that best describes how much distress you have been experiencing in the past week including today.



Second, please indicate if any of the following has been a problem for you in the past week including today. Be sure to check YES or NO for each.

YES	NO	Practical Problems
❑	❑	Child care
❑	❑	Housing
❑	❑	Insurance/financial
❑	❑	Transportation
❑	❑	Work/school
		Family Problems
❑	❑	Dealing with children
❑	❑	Dealing with partner
		Emotional Problems
❑	❑	Depression
❑	❑	Fears
❑	❑	Nervousness
❑	❑	Sadness
❑	❑	Worry
❑	❑	Loss of interest in usual activities
❑	❑	**Spiritual/religious concerns**

YES	NO	Physical Problems
❑	❑	Appearance
❑	❑	Bathing/dressing
❑	❑	Breathing
❑	❑	Changes in urination
❑	❑	Constipation
❑	❑	Diarrhea
❑	❑	Eating
❑	❑	Fatigue
❑	❑	Feeling Swollen
❑	❑	Fevers
❑	❑	Getting around
❑	❑	Indigestion
❑	❑	Memory/concentration
❑	❑	Mouth sores
❑	❑	Nausea
❑	❑	Nose dry/congested
❑	❑	Pain
❑	❑	Sexual
❑	❑	Skin dry/itchy
❑	❑	Sleep
❑	❑	Tingling in hands/feet

Other Problems: _____

_____

1.10 Appendix 10 – Study Report to Ethics Committee

This dissertation involves a correlation study aimed to identify a possible relationship between nutritional status (actual and perceived) and chemotherapy-induced distress in patients treated for haematological cancers. As well as providing a physical support to

patients, it is surmised that nutrition might have some sort of relationship also with their levels of distress, perhaps helping them to cope with challenges they meet. Whilst this study might not demonstrate a definite causative relationship between correlates, there seemed value in exploring possible relationships that might be examined further in future research. All patients were recruited from those admitted for a first treatment at a specific unit at the general hospital in Malta (between March and May 2009), under the care of the same Medical Consultant.

Ethics & Consent Issues

The participants were given pre-validated tools that could be filled in by the patients themselves. The scope of this was to increase the validity and reliability of the study. Consent to carry out the study was obtained from all the hospital authorities and from the Ethics Committee of the Institute of Health Care.

Methodology

The study sample consisted of seven men and six women. Although their treatment regimes differed in small degree, the side-effects of the treatment, those causing the distress to the patients were similar. Sample size was limited due to the short data collection period available, although I obtained a sample size amounting to 50% (n= 13) of the total patient population during this period. The objectives of this study ranged from identifying a possible correlation mentioned above, comparing actual patients' nutritional status with their own perceived status, and also comparing their nutritional status across the treatment cycle. A subsidiary objective of the study, after all correlation data had been collected, was to invite patients to report whether they perceived their nutritional status as insulating them in some way against the side effects of treatment.

Results

Individual patient profiles showed no relationship between any of the variables compared, i.e. nutritional status, distress and other variables like patient-perceived nutritional status, the use of steroids and nutritional supplements. That means that, on an individual basis, patients did not seem to follow any trends. Their nutritional status and distress were based mostly on personal factors influenced by patient preferences, family support and past experiences. After conducting statistical analysis on the data obtained, the study showed no correlation between actual nutritional status and patient distress before chemotherapy started (P-value 0.309), although significant correlations were then found once the side-effects of treatment started to be experienced by the patients, up to the end of the treatment (P-values 0.508, 0.528 respectively). Secondary relationships were also found between B.M.I. (actual nutritional status) and patient-perceived nutritional status (P-value of 0.027 at data collection point 1 and 0.041 at data collection point 3).

Conclusion

Although statistically some correlations and relationships were found between nutritional status and patient distress, individual patient profiles did not show the same trends. The results of this study are therefore not conclusive although they start to shed light on the role of nutritional support in haematological cancer patients, an area of medicine which is rather scarcely researched and provides a basis for future research. It prompts for further studies going deeper into topic area, studying the various variables that might influence the patients' distress and nutritional status, treatment, different side-effects and other factors that are ingrained and form part of the daily treatment of these patients

1.11 Appendix 11 – Study Tool - Adapted from Distress Thermometer Problem Score

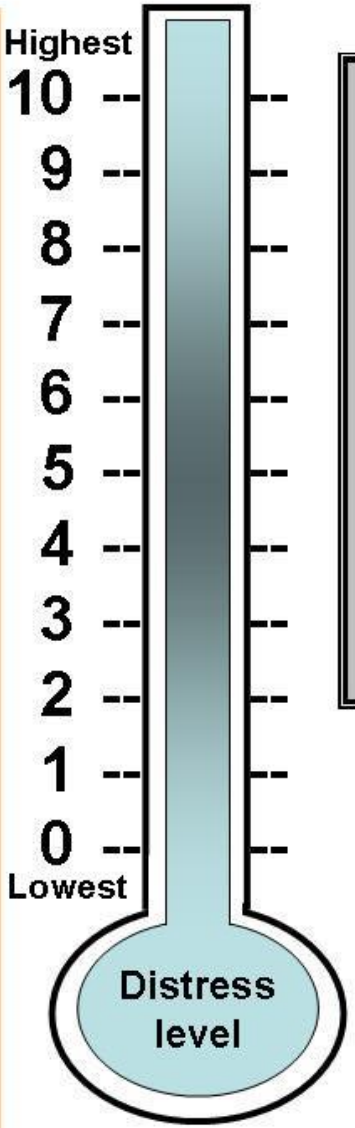
Patient Contact Number:_____

Date of assessment:_____

Yes	No	Physical Problems
____	____	Appearance
____	____	Constipation
____	____	Diarrhoea
____	____	Fatigue
____	____	Indigestion
____	____	Mouth Sores
____	____	Nausea
____	____	Pain
____	____	Feeling swollen
____	____	Sleep

Assessment Number:_____

(1 – Before treatment
2 – At onset of side-effects
3 – At end of treatment)



PATIENT DISTRESS MEASUREMENT TOOL

Modified from the Distress Thermometer Problem Score (NNCN, 2008)

Instructions:

1. Mark your distress level in the thermometer provided.
2. Tick the Physical Problem/s in the list on the left.

1.12 Appendix 12 – Study tool - Set of questions given to patients at data collection point 1

Patient Questionnaire 1

Date :_____

Patient Number_____ Contact Number_____

Please mark the answer to the following questions as you feel it is appropriate:

Question	Under-weight	Normal	Over-weight	Obese
1. I think that at the moment I am…				
	Completely agree	**I tend to agree**	**I tend to disagree**	**I disagree completely**
2. I would like to weigh more right now				
3. I would like to weigh less right now				
4. Enjoying my food is important for my morale				
5. I feel well informed about healthy eating				

1.13 Appendix 13 – Study tool - Set of questions given to patients at data collection point 3

Patient Questionnaire – Last Assessment

Date :_____

Patient Number_____ Contact Number_____

Please mark the answer to the following questions as you feel it is appropriate:

Statement	Under-weight	Normal	Over-weight	Obese
1. I think that my present nutritional status is...				
	Agree completely	**Agree to some extent**	**Disagree to some extent**	**Disagree completely**
2. Because my appetite remained good I was less anxious about treatment side effects				
3. Because I eat a balanced diet I was less anxious about treatment side effects				
4. Eating a balanced diet helped my body limit the side effects of chemotherapy				
5. Because diet is important to my moral, receiving help with nutrition during treatment was important				
6. Being well informed about a healthy diet will help me cope with any future treatment that I might need				

1.14 Appendix 14 – Summary of patient data

Data by Patient at the Three Data Collection Points

Patient Number	Data Collection Point 1								Data Collection Point 2		Data Collection Point 3							Accuracy of Patients' Preceived Nutritional Status		Chemotherapy treatment taken	Chemotherapy treatment strength	Steroids taken		Nutritional Supplementation Taken	
	BMI (kg/m2)	BMI Explained	Barthel Index Score (%)				Patient Distress Score	Patient Distress Score Explained	Patient Distress Score	Patient Distress Score Explained	BMI (kg/m2)	BMI Explained	BMI Trend	Patient Distress Score	Patient Distress Score Explained	Perceived Nutritional Status Trend	Patient Distress Score Trend								
1	29.9	Overweight	100.0	100.0	100.0	100.0	3.0	Medium	3.0	Medium	29.9	Overweight	Same	2.0	Low	Decreased	Decreased	Improving	1	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	No	0
2	21.9	Normal	100.0	100.0	100.0	100.0	3.0	Medium	2.0	Low	21.9	Normal	Same	3.5	Medium	Same	Increased	Inaccurate (underestimate)	0	Fludarabine, Cytarabine, Donorubicine	3	Yes	1	Yes	1
3	20.9	Normal	100.0	100.0	100.0	100.0	5.0	Medium	3.0	Medium	20.9	Normal	Same	3.0	Medium	Same	Decreased	Inaccurate (underestimate)	0	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	Yes	1
4	25.4	Overweight	100.0	100.0	100.0	100.0	5.0	Medium	5.0	Medium	23.8	Normal	Decreased	5.0	Medium	Increased	Same	Inaccurate (inconsistent)	0	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	Yes	1
5	24.2	Normal	95.0	95.0	95.0	95.0	2.0	Low	2.0	Low	24.2	Normal	Same	2.0	Low	Same	Same	Accurate	2	Cytarabine, Mitoxantrone	2	Yes	1	Yes	1
6	27.3	Overweight	100.0	95.0	100.0	98.3	5.0	Medium	6.0	Medium	27.3	Overweight	Same	5.0	Medium	Increased	Same	Improving	1	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	No	0
7	31.1	Obese	95.0	95.0	95.0	95.0	2.0	Low	2.0	Low	29.3	Overweight	Decreased	2.0	Low	Increased	Same	Improving	1	Cytarabine, Vincristine	2	No	0	No	0
8	23.4	Normal	100.0	100.0	100.0	100.0	9.0	High	2.0	Low	24.2	Normal	Increased	2.0	Low	Increased	Decreased	Improving	1	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	No	0
9	23.0	Normal	100.0	100.0	100.0	100.0	1.0	Low	1.0	Low	23.0	Normal	Same	1.0	Low	Same	Same	Accurate	2	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	Yes	1
10	26.4	Overweight	100.0	90.0	90.0	93.3	5.0	Medium	8.0	High	25.0	Normal	Decreased	8.0	High	Increased	Increased	Improving	1	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	Yes	1
11	28.9	Overweight	100.0	70.0	70.0	80.0	2.0	Low	8.5	High	31.1	Obese	Increased	8.5	High	Decreased	Increased	Inaccurate (inconsistent)	0	Vincristine, Cyclophosapha mide	2	No	0	Yes	1
12	33.1	Obese	100.0	65.0	65.0	76.7	5.0	Medium	8.0	High	36.7	Obese	Increased	10.0	High	Same	Increased	Accurate	2	Vincristine, Donorubicine, Asparaginase, Methotrexate	4	Yes	1	No	0
13	25.4	Overweight	100.0	90.0	100.0	96.7	8.0	High	9.0	High	26.0	Overweight	Increased	9.0	High	Same	Increased	Inaccurate (underestimate)	0	Fludarabine	2	No	0	Yes	1

1.15 Appendix 15 – Extra Table

Cancer Site	Overall Rank	Number of new cases in men (to the nearest	Number of new cases in women (to the nearest

		1000)	1000)
Lung	1	902,000	337,000
Breast	2	-	1
Colon/rectum	3	499,000	446,000
Stomach	4	558,000	318,000
Liver	5	398,000	166,000
Prostate	6	543,000	-
Cervix uteri	7	-	471,000
Oesophagus	8	279,000	133,000
Bladder	9	260,000	336,000
Non-Hodgkin's Lymphoma	10	167,000	121,000
Oral cavity	11	170,000	97,000
Leukaemia	12	144,000	113,000
Pancreas	13	116,000	216,000
Ovary	14	-	192,000
Kidney	15	118,000	71,000

Table 1 - Cancers with the highest incidence worldwide, 2000 (Evans, Newnham & Moller, 2006, p. 60)

1.16 Appendix 16 – Glossary and Definitions

Glossary

A

- Agony suggests pain too intense to be borne (MWOD, 2009).

- Anorexia - a nutritional status with a Body Mass Index which is not within the normal range, i.e. below 18 kg/m^2 (Fyke, 2002).

B

- Basal Metabolic Rate (B.M.R.) is the minimum amount of energy that a person requires to maintain his/her normal body functions, while at rest or asleep.

- Body mass index is defined as the individual's body weight divided by the square of their height. The formulas universally used in medicine produce a unit of measure of kg/m^2 (Wikipedia, 2007). This ratio is widely used to assess a person's weight for nutritional status

C

- Cancer cachexia – a syndrome that occurs during the terminal course of the disease in approximately 70% of cancer patients, but it is also sometimes evident at clinical presentation (Bozzetti, 2001, p. 641). Rivadeneira *et al.* (1998, p. 69) mention define it as *"a complex multifactorial syndrome, characterised by anorexia or the spontaneous and unintended loss of appetite, generalised host tissue wasting, skeletal muscle atrophy, immune dysfunction, and a variety of metabolic alterations*".

D

- Distress – In medicine it occurs when an individual cannot adapt to stress (Wikipedia, 2009a). It also signifies is a kind of suffering (Wikipedia, 2009), and "*unpleasant*

feelings or emotions that may interfere with one's ability to cope with cancer, its physical symptoms, and its treatment" (American Cancer Society and National Comprehensive Cancer Network, 2004). N.C.C.N. (2008) add that distress covers a wide range of feelings, from powerlessness, sadness and fear, to depression, anxiety, and panic. According to MWOD (2009) synonyms of distress include suffering, misery, and agony and mean the state of being in great trouble. Distress implies an external and usually temporary cause of great physical or mental strain and stress (MWOD, 2009). Dictionary.com (2009) defines distress as great pain, anxiety, or sorrow; acute physical or mental suffering; affliction; trouble; a state of extreme necessity or misfortune.

- Dysphagia – difficulty with swallowing (Molassiotis & Foubert, 2006).

E

F

- Fatigue – tiredness in humans (Wikipedia, 2009b). It is a feeling of tiredness, weariness, exhaustion and lethargy (MedlinePlus, 2009).

G

H

- Haematological cancers include acute and chronic leukaemia, lymphoma, multiple myeloma (NICE, 2008; R.C.P. London, 2008).
- Hodgkin's Lymphoma (HL) is characterised by the orderly spread of disease from one lymph node group to another together with the development of systemic symptoms with advanced disease (Wikipedia, 2008b). According to The Leukemia & Lymphoma Society (2008) about 11.5% of people with lymphomas have Hodgkin's lymphoma. The rest have one of many different kinds of non-Hodgkin's lymphoma.

I

J

K

L

1. Leukaemia is a type of cancer that affects the bone marrow, which is the soft, spongy centre of the bone that produces cells (Health Insite, 2008).

M

- Malignant lymphomas are composed of lymphocytes and might arise anywhere in the body where lymphoid tissue is present and, rarely, even in organs like the brain

(Bosman, 2006). Lymphomas can be further subdivided into Hodgkin's and non-Hodgkin's lymphoma.

- Malnutrition, defined simply, is often defined as a nutritional status with a Body Mass Index which is not within the normal range, i.e. below 20 or above 25 kg/m^2. This is a condition that develops when the body does not get the right amount of the vitamins, minerals and other nutrients it needs to maintain healthy tissues and organ function (Fyke, 2002). Malnutrition can encompass a wide range of deficiencies (e.g. protein-energy malnutrition (PEM)) and excesses (e.g. obesity).
- Misery – stresses the unhappiness attending especially sickness, poverty, or loss (MWOD, 2009).
- Mucositis is the painful inflammation and ulceration of the mucous membranes lining the digestive tract, usually as an adverse effect of chemotherapy and radiotherapy treatment for cancer. Mucositis can occur anywhere along the gastrointestinal (GI) tract, but oral mucositis refers to the particular inflammation and ulceration that occurs in the mouth. Oral mucositis is a common and often debilitating complication of cancer treatment (Wikipedia, 2009c).
- Myeloma (also known as multiple myeloma or plasma cell myeloma) (Multiple Myeloma Research Foundation (MMRF), 2008). This is a cancer of the plasma cell, that is an integral part of the immune system. It involves the formation of excessive numbers of abnormal plasma cells in the bone marrow and overproduction of intact monoclonal immunoglobulin or Bence-Jones protein resulting in hypercalcaemia, anaemia, kidney damage, increased susceptibility to bacterial infection and impaired production of normal immunoglobulin. Often it is also characterised by diffuse osteoporosis in the pelvis, spine, ribs and skull (MMRF, 2008; Wikipedia, 2008d).

N

- Non-Hodgkin's lymphoma (NHL) describes a group of cancers which arise from lymphocytes. NHL may develop in any organ associated with the lymphatic system, such as the spleen, lymph nodes or tonsils). Most cases start with infiltration of lymph nodes, but some are restricted to other lymphatic organs. Diagnosis of NHL is by a biopsy of the tissue involved. NHL subtypes are categorised according to their aggressiveness, namely indolent (or low-grade), aggressive (or intermediate-grade) or highly aggressive (or high-grade). The treatment in these cases varies from a period of observation to chemotherapy and/or radiotherapy, depending on the grade of the tumour (Wikipedia 2008c).

O

- Odynophagia – sensation of pain behind sternum as food or fluid is swallowed (Molassiotis & Foubert, 2006)

P

- Protein-Energy Malnutrition (PEM) occurs when a person's diet provides enough energy but lacks the protein minimum. In most cases the deficiency will be dual. PEM may also occur in persons who are unable to absorb vital nutrients or convert them to energy essential for healthy tissue formation and organ function (Smith, 1999).

Q

R

S

- Suffering – conscious endurance of pain or distress (MWOD, 2009).

T

- *Tumour Lysis Syndrome (TLS)*. This is a metabolic derangement that occurs with tumour breakdown following the initiation of cytotoxic therapy. TLS results from the rapid destruction of malignant cells and the abrupt release of intracellular ions, nucleic acids, proteins and their metabolites into the extracellular fluid.

U

V

W

X

Y

Z