# NATIONAL APPLICATION FORM FOR ETHICAL APPROVAL OF A RESEARCH PROJECT

## NAF-2009-v1

The application guidelines (NAFG-2009-v1) are to be read before completing this form to ensure that the questions are answered appropriately.

The electronic version of this form is formatted the same way as the paper version so that, for example, where an answer needs six lines, six lines are formatted, but where an answer only needs one line, one line is formatted. Please note the number of lines allowed for a question before answering it and make sure that you do not use extra lines.

You may find it helpful to print out the application form before completing it to help you to keep to the page limits allowed. **No extra pages should be added,** except where specified, as appendices.

The relevant paragraphs of the Operational Standard for Ethics Committees (Ministry of Health document) have been included in subject headings for reference.

The page breaks are not to be deleted as this will affect the formatting of the form.

When collating your application, please ensure that the information sheet, consent form and any attachments are placed behind the application form before copying. Applications not correctly collated, ie not in complete sets ready to be sent to committee members will be returned.

**Do not include this page with your application.**

# Checklist for Applicants – attach to front of application

**Before sending your application form, please check to make sure that all relevant information has been attached. If not applicable to the application write N/A. Protocols, information sheets, consent forms, questionnaires, advertisements, letters of invitation, data collection or other study forms must have a version number and date (marked *).**

**Please note: Incomplete applications will not be considered. Pending is an option only for written confirmation of Maaori consultation, SCOTT approval, and Locality assessment by organisation. For multi-region studies, the documentation for one site must be complete.**

| **Reference** | **Item** | **Yes, pending or N/A** |
|---|---|---|
| Observational Studies Guidelines 5.11 | * Study protocol – must be supplied with all applications | Yes |
| Page 21 of NAFG, QE on NAF | * Consent form | Yes |
| Page 23 of NAFG, QE on NAF | *Information sheet | Yes |
| QA5.4 on NAF | * Questionnaire/interview guidelines | N/A |
| Page 8 of NAFG, QA2 of NAF | Scientific assessment | Yes |
| QA5.3 of NAF | Statistical report | N/A |
| QD2, NAFG page 8 Q A4 | * Advertisement, letter of invitation | No |
| Section F of NAFG, Page 15 | Evidence of Māori consultation | Pending |
| Part 4 of NAF | Declaration signed by principal investigator, Head of Department or Dean (for each site) | Yes |
| Part 4, Form A or B of NAF | Accident compensation declaration correctly witnessed | Yes |
| NAFG page 20, NAF page 28 | Form/s for registered and unregistered medicines | N/A |
| Pages 11 and 35 (Appendix 1) of NAFG, QB17 on NAF | Standing Committee on Therapeutic Trials (SCOTT) approval attached if drug is unregistered in New Zealand | N/A |
| Locality assessments form(s) NAFG pages 18-20 | Completed by ethics committee if required, or completed by locality organisation(s) if received at time of submission | Yes |
| NAFG pages 30-32 | Part 5: If there any use of tissue (includes blood, saliva, skin) | Yes |
| Appendix 2 of NAFG | Part 6: If the research involves any gene or genetic studies | N/A |
| Appendix 2 of NAFG | Part 7 if the study involves xenotransplantation | N/A |
| NAFG pages 33-34 | Part 8 if any participants are unable to consent themselves including children | Yes |
| Parts 6 and 7, Appendix 2 of NAFG | GTAC approval if required | N/A |
| QB17 of NAF, Appendix 4 of NAFG | National Radiation Laboratory risk assessment if required | Yes |
| **Company sponsored studies** | Investigator brochure (if product is unregistered in New Zealand) | N/A |
| | Signed indemnity agreement (sponsor/institution/investigator) | N/A |
| | Current company insurance certificate | N/A |
| If yes to C.6 | Evidence of sponsor indemnity insurance to cover C.6 | N/A |
| If yes to C.6 | Evidence of hospital/institution indemnity insurance to cover C.6 | N/A |
| If yes to C.6 | Evidence of Investigator indemnity insurance to cover C.6 | N/A |

# NATIONAL APPLICATION FORM FOR ETHICAL APPROVAL OF A RESEARCH PROJECT

| Ethics reference number and date received (for office use only) |
|---|

## Part 1: Basic Information

1. Full project title (include protocol number if applicable)

Randomised control trial of an intervention programme based on the cystic fibrosis model of care in children less than two years of age admitted to hospital with severe lower respiratory tract infection to prevent chronic lung disease.

2. Short project title (lay title)

Healthy Lungs

3. Principal investigator's name and position

Dr Adrian Trenholme

4. Contact address of principal investigator


Kidz First Children's Hospital Administration
Middlemore Hospital
Private Bag 93311, Hospital Road
Otahuhu
Auckland

| | |
|---|---|
| Work phone no. | (09) 2760044 ext 7016 |
| Emergency no.* | (021) 576 818 |
| Fax | (09) 276 0192 |
| Email | atrenholme@middlemore.co.nz |


5. Principal investigator's qualifications and experience in the past five years (relevant to proposed research)

Dr Adrian Trenholme is currently employed at Counties Manukau District Health Board (CMDHB) and is a consultant in Paediatrics. He has experience as Principal Investigator in numerous trials at Kidz First Children's Hospital (CMDHB). These include Epidemiology of severe lower respiratory illness in the paediatric population in Counties Manukau, Respiratory health outcomes of young infants admitted to hospital with severe lower respiratory infection in the first two years of life in Counties Manukau, a phase 3 study of Motavizumab (MEDI-524) in 2005, lead NZ investigator for a phase 2 study of Motavizumab (MEDI-524) in 2006, and is currently lead NZ investigator for a phase 2 clinical trial to study a single 30 mg/kg or 100mg/kg IV dose of Motavizumab (MEDI-524) vs. placebo for the treatment of children hospitalized with RSV illness.

6. Co-investigator's name(s), qualifications and position(s) and,. if more than one locality; principal investigator at **each** locality

| | |
|---|---|
| A | Dr Catherine (Cass) Byrnes – Respiratory Paediatrician and Senior Lecturer, Starship Children's Health and University of Auckland |
| B | Dr Harley Aish – General Practitioner, Bairds Rd Family & Christian Health Centre |
| C | Mr Henare Mason - Te Kahui ora Maaori Health CMDHB |
| D | Karen Hoare – Nurse Practitioner and Lecturer, University of Auckland. |
| E | Dr Diana Lennon FRACP Paediatrics - Professor of Community Paediatrics, University of Auckland |
| F | Joanna Stewart – Biostatistician, School of Population Health, University of Auckland |
| G | William Leung – Health Economist, University of Auckland |

7.1 Address of A above

| | | |
|---|---|---|
| Paediatric Department<br>Faculty of Health & Medical Sciences<br>University of Auckland<br>Private Bag 92019<br>Auckland 1142 | Work phone no. | (09) 373 7599 ext 89770 |
| | Emergency no.* | (021) 245 9115 |
| | Fax | (09) 3737486 |
| | Email | c.byrnes@auckland.ac.nz |

7.2 Address of B above

| | | |
|---|---|---|
| Bairds Rd Family & Christian Health Centre<br>120 Bairds Road<br>Otara<br>Manukau 2025 | Work phone no. | (09) 2746654 |
| | Emergency no.* | (021) 241 5544 |
| | Fax | (09) 274 6694 |
| | Email | harley@aish.co.nz |

7.3 Address of C above

| | | |
|---|---|---|
| Counties Manukau District Health Board<br>Private Bag 93311<br>Otahuhu<br>Auckland1640 | Work phone no. | (09) 276 0000 |
| | Emergency no.* | (021) 663 271 |
| | Fax | |
| | Email | MasonH@middlemore.co.nz |

7.4 Address of D above

| | | |
|---|---|---|
| Greenstone Family Clinic<br>157 Great South Road<br>Manurewa<br>Auckland | Work phone no. | (09) 267 8702 |
| | Emergency no.* | (09) 267 8702 |
| | Fax | |
| | Email | |

7.5 Address of E above

| | | |
|---|---|---|
| Department of Paediatrics: Child & Youth Health<br>University of Auckland<br>Private Bag 92019<br>Auckland | Work phone no. | (09) 3737599 ext 89190 |
| | Emergency no.* | 021 694 832 |
| | Fax | |
| | Email | d.lennon@auckland.ac.nz |

7.6 Address of F above

| | | |
|---|---|---|
| Section of Epidemiology and Biostatistics<br>School of Population Health<br>University of Auckland<br>Private Bag 92019<br>Auckland | Work phone no. | (09) 923 6360 |
| | Emergency no.* | (09) 923 6360 |
| | Fax | |
| | Email | j.stewart@auckland.ac.nz |

7.7 Address of G above

| | | |
|---|---|---|
| School of Population Health<br>University of Auckland<br>Private Bag 92019<br>Auckland | Work phone no. | (09) 373 7599 |
| | Emergency no.* | |
| | Fax | |
| | Email | w.leung@auckland.ac.nz |

(* option for ethics committee's information only)

8. Where this is supervised work

| | |
|---|---|
| 8.1 Supervisor's name | N/A |
| Position | |
| Daytime phone number | |

| | |
|---|---|
| 8.2 Signature of supervisor (where relevant)<br>Declaration: I take responsibility for all ethical aspects of the project | |

9. List locality organisation/s involved, including contact address, and complete the locality assessment in Part 4: Declarations (refer to the Guidelines (NAFG-2009-v1))

Middlemore Hospital, Counties Manukau District Health Board in conjunction with following PHOs:

- Bairds Rd Family & Christian Health Centre, Otara
- Greenstone Family Clinic, Manurewa
- Mangere family Doctors, Mangere

10. I wish the protocol to be heard in a closed meeting. ☐ Yes ☑ No

If the answer is yes, please provide a reason why you wish the protocol to be heard in a closed meeting in accordance with the Official Information Act 1982.

11. If the study is based, in part or in full, overseas, which countries are involved?

N/A – Study is based in New Zealand

12. Has this application been reviewed by another ethics committee in New Zealand or overseas? ☐ Yes ☑ No

(If yes, advise which country, the name of the committee/s and the decision/s of the committee/s)

Please note a copy of the report/s may be requested.

13. **Human tissue** – Does the project involve collection or use of human tissue? If **yes**, complete Part 5. ☑ Yes ☐ No

14. **Gene studies** – Does this research involve any gene or genetic studies? If **yes**, complete Part 6. ☐ Yes ☑ No

15. **Xenotransplantation** – Does this research involve the transplantation of living biological material from one species to another? ☐ Yes ☑ No

If **yes**, complete Part 7.

16. **Consent** – Are all participants able to provide consent for themselves? If **no**, complete Part 8. ☐ Yes ☑ No

17. **Lay summary** – give a brief **lay (non-technical)** summary of the study (not more than 200 words) such as you would give as an explanation to participants.

We are seeking a workable solution to the inequitable and escalating numbers of Maaori and Pacific children with chronic lung disease which the current healthcare system is struggling to accommodate. The primary aim is to determine whether an international model of care from the specialised patient population of CF delivered in tertiary hospitals can be adapted as an intervention programme and be delivered in a local and community setting to NZ Maaori and Pacific paediatric populations at high risk of developing chronic lung disease. Parents of children admitted to hospital with a severe lower respiratory tract infection will be approached for consent, and be randomised to an 'intervention programme group' or a 'control group' of usual care. Both groups will be followed throughout the two years of the study and will receive a medical examination to assess their respiratory health at 24 months.

18. Proposed starting date (dd/mm/yy) — 01/08/10

19. Proposed finishing date (dd/mm/yy) — 31/07/13

20. Duration of project in New Zealand (mm/yy) — 3 years

21. Proposed final report date (mm/yy) — 31/12/13

22. Has the clinical trial been registered? ☐ Yes ☑ No

If **yes**, name the register.

If **no**, has registration been applied for? ☐ Yes ☑ No

**Comment**:

The study will be registered on the Australian New Zealand Clinical Trials Registry (ANZCTR) prior to any recruitment activities commencing.

# Part 2: Ethical Principles

## A. Validity of research *(Operational standard paragraphs 53–59)*

**SCIENTIFIC BASIS**

### A1. Aims of the project

A1.1 What is the hypothesis/research question(s) and/or the specific aims of the project? (State briefly.)

Comment**:**

**Hypothesis:** An early intervention programme based on Cystic Fibrosis (CF) care will reduce respiratory morbidity as determined by moist cough in clinic (MCIC) and/or chest Xray (CXR) abnormalities by 50% in 24 months.

**Aims:** To reduce respiratory morbidity in the predominantly Maaori and Pacific children of South Auckland (SA) which develops subsequent to an admission for severe lower respiratory infection (LRI) by adapting the model of care employed for children with CF.

To determine if this also decreases the presence of Chronic Suppurative Lung Disease CSLD (including bronchiectasis) at age 2 to 4 years.

To do a cost benefit analysis of the intervention programme.

### A2. Scientific background of the research

A2.1 Has this project been scientifically assessed by independent review? ☑ Yes ☐ No

| | |
|---|---|
| If **yes**, describe the process, for example, HRC funding assessment process. *A copy of the report should also be attached. The researcher's response may also be included.* | The study has been reviewed through the HRC funding assessment process. (See attached approval letter). |
| If **no**, do you intend to have the project scientifically assessed and by whom? | |

A2.2 Describe the scientific basis of the project **(300 words maximum**). Where this space is inadequate, continue on a separate sheet of paper. *Do not* delete page breaks or renumber pages.

Lower respiratory infection is a significant problem for NZ children, as shown in a pilot study following children after a hospital admission with a severe lower respiratory infection (?ref). One year post the index hospital admission, 2/3 of the children had signs of chronic lung disease. The proposed programme of intervention is regular clinical follow-up to ensure resolution of respiratory illness, and/or additional respiratory management, as well as health resilient behaviours for the child and family. This is an adaptation of two models of care; (1) early intervention in children with cystic fibrosis internationally, (2) community based care in adults with chronic lung disease in South Auckland. The study aims to reduce respiratory morbidity in these predominantly Maaori and Pacific children of South Auckland, which develops subsequent to an admission for severe lower respiratory infection. This type of randomised interventional study has never been previously undertaken. It will provide direct health benefit whilst determining the feasibility of instituting a new health care delivery model in the community and also collecting informative data for this disadvantaged population within the next five years. A cost benefit analysis will determine continued use of the programme locally and potentially nationally and internationally.

## A3. Study design

A3.1 Describe the study design. Where this space is inadequate, continue on a separate sheet of paper. *Do not* delete page breaks or renumber pages.

A randomised controlled intervention study in which 400 South Auckland children will be enrolled with half having an intensive intervention programme performed by an integrated multidisciplinary team with a minimum of three monthly clinic visits at a community health centre located in Mangere, Otara or Manurewa. The clinic will be allocated in negotiation with each family. The control group will receive current 'usual care' as currently practised in SA with GP and paediatrician review on an 'as needed' basis. Both groups of children will be assessed after 24 months by a paediatrician in training with paediatric specialty oversight who is independent to the study. This examination will be offered at Counties Manukau District Health Board site.

**Continued on separate sheet of paper** A3.1.0

## A4. Participants

A4.1 How many participants do you intend to recruit? (Include details for each locality organisation.)

400 children will be recruited, 200 children will be randomised to the intervention group and 200 to the control group.

A4.2 Give a justification for the number of research participants proposed, giving the details of power calculations when appropriate.

400 children will be randomised 1:1 to intervention and control groups. Assuming 80% retention, 160 per group will be available at 2 year follow up: Note this retention has been demonstrated in our previous South Auckland studies. With this sample size and assuming 40% of the controls have chronic respiratory symptoms (less than seen in the one year follow up study) there will be 91% power to detect a 50% reduction at the 1% level of significance (i.e. 20% of the intervention group having chronic respiratory symptoms). There will be 80% power to detect 45% reduction, at the 1% level. Should the rate in the control group only be 30%, there will still be 90% power to detect a 50% reduction at the 5% level of significance. The South Auckland area includes 113,000 children< 15 years of age including 26% Maaori and 29% Pacific with 71% of children living in the lowest socioeconomic quintile.

A4.3 If randomisation is used, explain how this will be done.

Randomisation of patient number to intervention or control will be achieved using block randomisation, with random block size, to ensure the participants are balanced in the 2 groups. A set of 400 sealed, numbered envelopes containing the study arm for that number will be provided by CCREP to the study coordinator. The next sequential study number will be allocated to a study participant immediately following consent. Randomisation will take place after consent and the completion of the gathering of the baseline data by opening the envelope for that study number.

## A5. Statistical method

A5.1 Is the method of analysis quantitative? ☑ Yes ☐ No

Or qualitative? ☐ Yes ☑ No

If the method of analysis is **wholly qualitative**, go to question A5.4.
If the method of analysis is **wholly or partly quantitative**, complete the following:

A5.2 Describe the statistical method that will be used to analyse the data.

The primary hypothesis of a difference in chronic respiratory morbidity at 24 months post index hospital admission between the intervention and control groups will be tested using logistic regression with chronic respiratory morbidity documented as 'present' or 'absent' as the outcome. Age, ethnicity, deprivation index, and group will be explanatory variables. The "intention to treat" population will be used for all those completing the 24 month follow up. A further exploratory analysis will be done including the interactions of the other variables with group to ensure there is no evidence indicating the possibility of a differential effect of the intervention.
Other outcomes will be investigated with the same explanatory variables using binary or ordinal logistic regression or linear regression, depending on the distribution of the variable.

A5.3 Has specialist statistical advice been obtained about this study? ☑ Yes ☐ No

If **yes**, from whom? (A brief statistical report should be included if appropriate.)

Joanna Stewart (Biostatistician) is a co-investigator on this study and is providing statistical advice for this project.

A5.4 If the method of analysis is **wholly or partly qualitative**, specify the method. Why is this method appropriate? If interviews are to be used, include the general areas around which they will be based and a copy of the interview guide, if one is to be used. Copies of any questionnaires that will be used must be included.

N/A

## A6. Expected outcomes or impacts of research

A6.1 What is the potential significance of this project for improved health outcomes?

This seeks to apply a low technological, multi-disciplinary clinical intervention by current personnel to reduce the precursors of chronic lung disease for children at risk by 50% within 24 months. If proven successful and cost effective, we will have developed an evidence based standard of care and a community based programme applicable throughout New Zealand and internationally to improve health care delivery to high risk populations. It will improve current inequity of health outcomes and be able to prevent lifelong disease.

A6.2 What is the potential significance of this project for the advancement of knowledge?

We seek to reduce the respiratory disease in this cohort of children who are in the intervention programme and we have estimated a 50% decrease. We will prove that this model of care works for a high risk group in preventing further respiratory disease in a community setting in the population of South Auckland.

The programme will see benefits in real time and, if proven successful, the results will be translated and used to develop and apply new standards of care to this high risk group which will ultimately be relevant locally, throughout New Zealand and internationally.

A6.3 What steps will be taken to disseminate the research results?

This research group is already made up of multidisciplinary personnel from community and hospital settings with leaders in Maaori and Pacific health involved. All will be involved in dissemination of the results of the research and with the recommendation (if successful) of a continued programme within the current health service - locally and nationally. This will include dissemination to:

- General practices and conferences
- Nursing practices and conferences
- Maaori Health stakeholders including District Health Boards Maaori Boards and Maaori health hui
- POU, Maaori Health Governance at CMDHB
- Pacific Stake holders including District Health Boards
- Clinical Governance Forum CMDHB
- Paediatric Conferences
- Lay Health groups
- Media - especially local and national radio and TV with Maaori and Pacific media streams
- Submitted for peer review journal publications
- Offered to Ministry of Health

## A7. Publication of results

Will any restriction be placed on publication of results? ☐ Yes ☑ No

If **yes**, please supply details.

## A8. Funding

A8.1 How will the project be funded?

A funding grant has been provided by the Health Research Council (see attached)

A8.2 Does the researcher, the host department, the host institution or the locality organisation have any conflict of interest, eg, financial interest, in the outcome of this research? If **yes**, please give details. ☐ Yes ☑ No

## A9. Incentive payments

A9.1 Have you read and understood the description of incentive payments in the Guidelines? ☑ Yes ☐ No

**Note: Details about any payment (in money or kind) or reward made to participants recruited into the project are to be provided in question E10.**

A9.2 Does the funding available to the project depend upon the number of participants recruited, eg, is the funding on a per participant basis?. If **yes**, give details of the amount per participant. Where there is a significant difference between these, this incentive to recruit should be declared in the information sheet.

☐ Yes ☑ No

A9.3 Does the funding available to the project include any form of incentive (in money or kind) for the early or complete recruitment of a specified number of participants, eg, bonus payments to the researcher, host department or host institution? If **yes**, give details.

☐ Yes ☑ No

However we have budgeted for families to receive petrol and parking vouchers, and for long visits food vouchers or a meal.

A9.4 Will **all** funding available to the project be passed through an audited research account or cost centre? If **yes**, give details. If **no**, specify why not.

☑ Yes ☐ No

The funds will be managed by the Centre for Clinical Research and effective practice (CCRep) and will be held in audited research accounts.

## B. Minimisation of harm *(Operational standard paragraphs 60–68)*

B1. How many visits/admissions of participants will this study involve? Clarify what is in addition to standard treatment. Give also an estimate of total time involved for participants.

Both groups will be followed for a two year period.

Control Group

This group will receive standard care with a 24-month follow up visit. The total time commitment with a consenting visit and a final follow up visit will be approximately 6 hours. There will be brief but regular (7) phone and/or home visits (for those without phones) 7 in total undertaken by the community health worker/s to maintain contact.

Intervention Group

This group will have clinic visits at months 1,3, 6, 9, 12, 15, 18, 21 and 24, after the initial consenting visit. It is anticipated that they will also have an average of two additional clinic visits to follow up on required interventions. This will mean a time commitment of approximately 20 hours.

B2. Who will carry out the research procedures?

The research procedures will be carried out by the staff at each of the primary care sites. Each primary care centre will be staffed by a GP, nurse practitioner and practice nurse supported by the study respiratory nurse and community health worker. All staff will undergo an intensive education programme relating to all aspects of the intervention.

B3. What other research studies is the lead investigator currently involved with?

Dr Adrian Trenholme:
NTX/08/087/069 Epidemiology of severe lower respiratory illness in the paediatric population in Counties Manukau.
NTX/09/02/003 A prospective randomised trial comparing nasogastric with intravenous hydration in hospitalised children with severe bronchiolitis requiring hydration
NTX/09/09/091 Ti Piripohotanga; A randomised trial of a family-centred tobacco control program about environmental tobacco smoke (ETS) to reduce respiratory illness in Maaori infants.
NTY/08/06/055 Longitudinal study of New Zealand children and Families: Cord blood study.

Dr Catherine Byrnes:
MEC/09/10/112 Port CF Data Registry.
NTY 07/01/001 Bronchiectasis Interventional Study.
AKL/2000/23 A multicentre randomised controlled trial of bronchoalveolar lavage therapy in young children with cystic fibrosis.

B4. Where will the research procedures take place?

Study procedures will take place at Kidz First Children's Hospital, Starship Hospital and the three primary care sites (GP clinics in Otara, Mangere and Manurewa).

B5. How do the research procedures differ from standard treatment procedures?

The children randomised to the intervention arm of the study will receive an adapted programme based on the CF model of care for early childhood. The essence of this model of care is for regular review from infancy, early detection of deviation from normal health and early intervention to prevent ongoing disease. This will mean additional monitoring of health status at scheduled clinic visits over a two year period. Every child in the study will receive an additional clinic visit at 24 months where they will see a specialist paediatric doctor who is independent of the study. At this clinic they will be clinically assessed for signs of any respiratory illness and/or chronic disease. This screening will include a chest x-ray and for those that have consented, a blood test to check their iron and vitamin D levels.

B6. What are the benefits to research participants of taking part in the project?

If the study hypothesis is correct there may be a benefit to the intervention group in the study. At the point of consent all participants will be made aware of this within the written information and at point of consent. All the participants will receive medical review by senior paediatric trained staff at 24 months and will subsequently be referred to specialist health care providers if required. The intervention group will also receive regular clinical review and required treatment during the two year period

It is hoped that this study will help health care professionals at CMDHB further develop strategies to reduce the impact of lower respiratory infection in the South Auckland region. Any medical problems identified during clinic visits will be managed by the clinic paediatrician or referred on to the appropriate medical agency including an identified respiratory paediatrician if further respiratory investigation is warranted.

B7. Describe any methods for obtaining information. Attach questionnaires and interview guidelines. (If National Health Index (NHI) information is used, see the Guidelines (NAFG-2009-v1).)

For each enrolled child a review of hospital medical records for medical history will obtained to review the number of hospital admissions, length of stay and severity of illness. Additional clinical information will be obtained from direct parent/legal guardian enquiry collected on a case report during clinic visits regarding general health, immunisation status, well child appointments/assessments, growth and development, and frequency of illness. The parent/legal guardian will also be asked for permission (see consent form attached) to contact the GP to record if the child has attended their GP for respiratory complaints (for example coughs, colds and/or wheezing events). The number of visits to the GP for these types of complaints will be recorded along with any medications for wheezing events.

B8. Briefly describe the inclusion/exclusion criteria and include the relevant page number(s) of the protocol or investigator's brochure.

Inclusion criteria: Children <2 years age admitted to SA with *severe* LRI (pneumonia and/or bronchiolitis - admission ≥5 days and/or supplemental oxygen for > 48 hours and/or admission to Intensive care unit, and/or consolidation on CXR) between 1st Aug 2010 & 31st Oct 2011.
Exclusion criteria:

- Children with more than two prior admissions to hospital with LRI
- Prematurity <32 weeks gestation
- Children with a diagnosis of chronic lung disease
- Children known to have chronic health problems of clinical significance affecting daily life:
    - cardiovascular
    - neurological
    - immunodeficiency
    - multiple congenital abnormalities
    - enteral feeding

B9. What are the physical or psychological risks or side effects to participants or third parties? Describe what action will be taken to minimise any such risks or side effects.

Psychological Risk: We believe this study caries minimal psychological risk, the demographic and clinical information collected for this study will only be obtained following informed consent from each parent/legal guardian involved. If any parent/care giver should become distressed during any aspect of the study procedures support services will be offered to the participants. All research staff collecting information will the trained in 'Good Clinical Practice' Standards (*ICH GCP Glossary 1.24)*. The health and disability advocacy service phone number is listed on the patient information sheet along with the principal investigators contact details.

Consent will be requested for each child to have a chest x-ray (PA and Lateral) taken at the 24 month clinic visit. This is equivalent of 2.4 days usual background radiation exposure. Where consent is given, a blood test will be taken twice in the intervention group and once in the non-intervention group. This will be obtained by a finger prick and could result in some bruising.

B10. What facilities/procedures and personnel are there for dealing with emergencies?

The investigator and the research team are experienced in managing the risks associated with the conduct of clinical trials. Equipment, supplies, and properly skilled medical personnel will be accessible for use in an emergency in the event of an unexpected reaction.

Participants will be issued with an emergency contact number for a member of the study team should they experience a medical emergency between study visits and participant medical records will be clearly marked to indicate their participation in this study.

B11. What arrangements will be made for monitoring and detecting adverse outcomes?

A doctor will supervise all clinic visits and all information retrieved. One of the study investigators will always be on-call to answer any questions or review any information if required.

B12. If the study is a clinical trial, are participants to be provided with a card confirming their participation, medication and the contact phone number of the principal investigator? ☑ Yes ☐ No

B12.1 Do you intend to inform the participant's GP that their patient is a participant in this study? (If yes, consent from the participant is required.) ☑ Yes ☐ No

B12.2 Do you intend to inform the GP of all clinically significant abnormal results obtained during study conduct? ☑ Yes ☐ No

B13. Is the trial being reviewed by a data and safety monitoring board (DSMB)? ☐ Yes ☑ No

If **yes**, who is the funder of the DSMB? ☐ HRC ☐ Sponsor ☐ Other

If **'Other'**, please specify.

B14. What are the criteria for terminating the study?

There is no foreseen reason why this study would be terminated for safety reasons. However, the principal investigator would have the ability to terminate the study following discussion with the wider research investigator group if any concerns were recognised. Should the intervention or randomisation prove to be unacceptable in this community such that it was not possible to recruitment the study would be terminated. Individual participants will be withdrawn from the study if the parent/legal guardian withdraws consent.

B15. Will participants be exposed to any potential toxins, mutagens or teratogens? ☐ Yes ☑ No

If **yes**, specify and outline the justification for their use.

B16. Will any radiation or radioactive substances be used? ☑ Yes ☐ No
**Note: If any form of radiation is being used, please answer B16.1–B16.2.**
**If no, go to question B17.**

B16.1 How many x-rays or other procedures are planned for the purposes of this study, ie, that are not part of standard treatment?

Each participating child will have one chest x-ray at the 24 month visit.

B16.2 Under whose licence is the radiation being used?

Dr Russell Metcalfe
Paediatric Radiologist
Starship Children's Hospital

B16.3 Has the National Radiation Laboratory (NRL) risk assessment ☐ Yes ☑ No

been completed?

If **yes**, please enclose a copy of the risk assessment and a contact name and phone number.

If **no**, please explain why not.

No – Report from Dr Russell Metcalfe supplied which contains information from James Dudson (Medical Physicist) as to the background radiation risk.

NRL assessment is no longer required.

B17. Will any medicines be administered for the purposes of this study? ☐ Yes ☑ No

B17.1 If **yes,** is Standing Committee on Therapeutic Trials (SCOTT) approval required? ☐ Yes ☐ No

B17.2 Has SCOTT approval been given? (Please attach.) ☐ Yes ☐ No

B18. Does the study involve the use of health care resources? ☑ Yes ☐ No

If **yes**, please specify:

Clinic visits will be conducted at DHB and GP locations. Clinical supplies, staffing and x-ray costs are incorporated into the budget for the study provided by the obtained HRC investment signal funding (see attached).

B19. What effect will this use of resources have on waiting list times for patients, that is, for diagnostic tests or for standard treatments?

We do anticipate that there may be an increase in referrals to secondary and tertiary health providers for the children enrolled in this study. This point has been discussed with management at CMDHB and they are supportive of this study and will ensure that this is monitored and appropriate clinical services provided. The study investigators will continue to liaise with CMDHB service management in ensuring that we are only using facilities when they are not required for the provision of public health services.

## C. Compensation for harm suffered by participants

***(Operational standard paragraphs 87–95)***

*(Refer also to Appendix 3 of the Guidelines (NAFG-2009-v1).)*

C1. Will participants be treated by, or at the direction of, a registered health professional as part of the research? (Treatment includes screening, diagnosis, for definitions see the Guidelines (NAFG-2009-v1) pages 11-13.) ☑ Yes ☐ No

If **no**, go to section D. If **yes**, please answer questions C2–C5.4.

C2. Is the research being carried out principally for the benefit of a manufacturer or distributor of the drug or item in respect of which the research is taking place? ☐ Yes ☑ No

C2.1 If the answer to C2 is **yes**, please complete **Statutory Declaration Form B** and answer questions C3–C5.4.

C2.2 If the answer to C2 is **no,** please complete **Statutory Declaration Form A** and go to section D.

Depending on all the circumstances, the minimum cover that is likely to be acceptable to the ethics committee is that provided under ACC. In any case, all exclusions to compensation must be clearly and explicitly set out in the participant information sheet, including those that may be described in C5.

C3. Is the manufacturer/distributor's agreement to provide compensation in accordance with the RMI attached? ☐ Yes ☐ No

C4. Has the manufacturer or distributor agreed to cover any injury/adverse consequence resulting from participation in this research? ☐ Yes ☐ No

C4.1 If no, what qualifications have been specified for cover?

C4.2 **Limiting the type of compensation**

C4.2.1 Has the manufacturer or distributor excluded any type of compensation, for example, pain and suffering, loss of earnings, loss of earning capacity, funeral costs, dependents' allowances or any other financial loss or expenses? ☐ Yes ☐ No

C4.2.2 If yes, please state what is excluded. (Include in the compensation statement on the information sheet)

C5. **Limiting liability – exclusion clauses**

C5.1 Has the manufacturer or distributor limited or excluded liability if the injury is attributable to the negligence of someone other than the manufacturer or distributor (such as negligence by the investigator, research staff, the hospital or institution, or the participant)? ☐ Yes ☐ No

C5.2 Has the manufacturer or distributor limited or excluded liability if the if the injury resulted from a significant deviation from the study protocol by someone other than the manufacturer or distributor? ☐ Yes ☐ No

C5.3 Is evidence of the following indemnity insurance attached?

Sponsor ☐ Yes ☐ No

If yes to either C5.1 or C5.2;

Hospital/institution ☐ Yes ☐ No

Investigator ☐ Yes ☐ No

C5.4 Is company liability limited in any other way? ☐ Yes ☐ No

If **yes**, please specify.

## D. Privacy and confidentiality *(Operational standard paragraphs 48–56)*

| | | |
|---|---|---|
| D1. | How will potential participants be identified? | Potential participants will be initially identified from the hospital medical records based on the inclusion / exclusion criteria. |
| D2. | How will participants be recruited (for example, advertisements, notices)? | Participants will be recruited during their index hospital admission with lower respiratory infection at Kidz First children's hospital. If a child is admitted and is discharged from hospital prior to the research staff discussing the study with the family/whaanau the research staff will phone the parent/legal guardian to provide them with the study information and will offer a home visit to explain the study if the parent/legal guardian is interested in participating, and to obtain consent if appropriate. |
| D3. | Where will potential participants be approached (for example, outpatient clinic)? If appropriate, describe by type (for example, students). | Once inclusion / exclusion criteria are checked from medical records potential participant's parents or legal guardians will be contacted by investigator or research nurse and be invited to participate. |
| D4. | Who will make the initial approach to potential participants? | The family/whaanau of prospective participants will be approached by the research nurse involved in the study and the study information given to them. |

NB: Do not include information on storage and use of tissue samples and related information in the following questions. That is covered separately under Part 5.

| | | |
|---|---|---|
| D5. | How will data, including audio- and videotapes, be handled and stored to safeguard confidentiality (both during and after completion of the research project)? | Patient records/study documents will only be handled by study staff. Throughout the study, information will be collected and stored in such a way as to maintain participant's confidentiality. For the duration of the study, all study related documentation will be securely stored, with controlled access by study staff. All electronic data will be password protected and only study staff will have access to these files. Results of this study will be presented in an annoymised fashion. |
| D6. | What will be done with the raw data when the study is finished? | The study information will be archived for age of majority plus 10 years at a secure off-site storage facility. It will then be marked for destruction this is undertaken by the secure storage facility as per the contract with CMDHB. |
| D7. | How long will the data from the study be kept, and who will be responsible for their safe keeping? (Health information relating to an identifiable individual must be retained for at least 10 years, or in the case of a child, 10 years from the age of 16.) | Essential documents and data will be retained for at least 15 years from the completion of the study. |

| | | |
|---|---|---|
| D8. | Name those who will have access to the raw data, participant information and/or clinical records during, or after, the study? | Study staff and any regulatory agencies (e.g Ethics Committee). |
| D9. | Describe any arrangements to make results available to participants, including whether they will be offered their audio- or videotapes. | There are no audio or video tapes used in this study. A summary of results of the study will be offered to the families of the participants after completion of the analysis of the data. |

## E. Informed consent *(Operational standard paragraphs 28–43)*

A participant's informed consent should be obtained in writing, unless the procedures are not experimental and there are good reasons for not requiring written consent. If consent is not to be obtained in writing, the justification should be given and the circumstances under which consent is obtained should be recorded. Attach a copy of the information sheet and consent form provided to participants.

| | | |
|---|---|---|
| E1. | By whom, and how, will the project be explained to potential participants? | The principal investigator or enrolling research nurse will explain the project face-to-face after the family of the participant has had sufficient time to read the information sheet in advance. |
| E2. | When and where will the explanation be given? | The project will be explained in person by the investigator or appropriate delegate at the index hospital admission. |
| E3. | Will a competent interpreter be available, if required? | ✓ Yes ☐ No |
| | If **no**, why not? | |
| E4. | How much time will be allowed for the potential participant to decide about taking part in the project? | As long as the family needs to make a fully informed decision. |
| E5. | In what form (written, or oral) will consent be obtained? If oral consent only, state reasons. | All consents will be in written format. |
| E6. | If recordings are made, will participants be offered the opportunity to edit the transcripts of the recordings? | ☐ Yes **N/A** No |
| E7. | Will data or other information be stored for use in a different study for which ethics committee approval would be required? | ☐ Yes ✓ No |

E7.1 If **yes**, please explain how.

E8. Is there any special relationship between the participants and the researchers (for example, doctor/patient, student/teacher)?

Doctor/Patient

E9. Will there be any financial cost to the participant, for example, travel and parking costs? If so, will such cost be reimbursed? (Refer to the Guidelines (NAFG-2009-v1).)

Each participant will be provided with either a $20 petrol voucher or a taxi chit to ensure any transport costs can be covered by the families/whaanau to allow them to attend each clinic visit.

E10. Will any payments be made to participants, or will they gain materially in other ways from participating in this project? ☐ Yes ☑ No

E10.1 If **yes**, please supply details.

## F. Cultural and social responsibility *(Operational standard paragraphs 73–82)*

Section F enshrines two fundamental principles. They are:

i. Culturally safe research practice: Research involving participants from specific ethnic or socially identified groups (even when small numbers from each group are involved) must involve those participant groups in the research process as full participants. Where a particular ethnic or socially identified group is the principal subject of the research, there must be engagement with appropriate parties, and this process must be outlined in the application.

ii. If the research is in an area of health inequalities, then the researcher must demonstrate how the research will contribute to achieving equity of outcomes for those population groups most in need within the public good health system.

F1. Have you read the HRC booklet *Guidelines for Researchers on Health Research Involving Māori*? ☑ Yes ☐ No

### Relevance and responsiveness to Māori

F2. **All health research conducted in Aotearoa New Zealand is of relevance to Māori**. How relevant is a decision to be made by Māori. The researcher must be able to articulate the context and the relevance of the proposed research to Māori and the possible consequences for Māori health outcomes, and generally, the greater the degree of relevance to Māori, the greater the expectation of participation of Māori and hence consultation expectations.

F2.1 Given your approach to sampling, what are the anticipated numbers of Māori participants?

This research will be carried out in a hospital in the Counties Manukau region where a significant percentage of the children/study participants are of Maaori ethnicity. From 2000 to 2006 the average admission rate to Kidz First Children's Hospital for LRI admissions per year was 1541 children, 449 (29%) of those admissions are children of Maaori ethnicity. LRI significantly impacts the Maaori paediatric population.

F2.2 What is the incidence among Māori of the health issue/disability relevant to the study?

In 2000-2004 respiratory diseases in Maaori children were the first to third most common reason for the admission to hospital in the age groups < 1 year, 1-4 years, 5-14 years and 15-24 years of age. Hospital admission of infants for bronchiolitis was twice as common in Maaori and for pneumonia was 73% higher in females and 59% higher in males than in non-Maaori. From this we would estimate between 20 and 30% of participants would be Maaori i.e. 80 to 120 individual participants.

F3. Please explain how this research will contribute to improving Māori health outcomes and reducing health inequalities for Māori.

Early intervention to prevent the development of ongoing respiratory disease would have clear benefits for the Maaori population of South Auckland and New Zealand, and help reduce the gap in respiratory health currently observed between Maaori and their Pakeha counterparts. The early intervention involves the application of a standard of health care for infants that are known to be at high risk of developing chronic respiratory disease. The intervention involves engaging with whaanau through the provision of enhanced primary and sometimes secondary/tertiary health care. This engagement of whaanau will be aided through a Maaori community health worker who is working with the research team and who will work along side any recruited Maaori participants throughout the duration of the study. The holistic model of care is utilising a wellness approach where issues will be addressed to improve whānau ora.

F4. Describe the process by which Māori have been engaged in the conception and design of the proposed research. Please identify the group/s with which consultation has taken place and outline their stated view about the proposed research. Please attach their letter/s of support for this specific research project.

Henare Mason (Arawa/Tuhoe) has offered himself as an advisor and co-investigator to the research study, he will continue to provide advice throughout the duration of the study through to dissemination of study results. Henare is a member of the CMDHB Maaori Research Review Committee (MRRC), the clinical trial research unit for Uniservices at Auckland University, and is the Chair of the Tamaki PHO.

A formal letter of consultation will also be provided to the committee by the CMDHB Maaori Research Review Committee (MRRC).

F4.1 Describe any ongoing involvement the group(s) consulted have in the project.

As stated above, Henare Mason will continue to provide advice throughout the duration of the study through to dissemination of study results.

F4.2 Describe how information will be disseminated to participants and the group(s) consulted during and at the conclusion of the research project.

Maaori will be informed of the findings through a variety of networks.

- Results of the study will be sent to individual participants.
- The results will be formally presented to the Maaori Research Review Committee (MRRC) and the Maaori health governance group (POU) CMDHB.
- We will seek input from the MRRC on appropriate Maaori community Hui meetings to present the findings at the end of the study. Maaori providers PHO's and community providers that are involved in the study will be offered both written and oral presentations of the research findings at the end of the study. A newsletter informing key stakeholders of study progress and relevant issues will be circulated every six months.
- Health professionals including Maaori health services will be targeted in the presentation of the results to hospital and community health services.
- We will utilise media such as national radio and TV with Maaori media streams. Results of the study will be offered to the Ministry of Health.
- Results will be published in peer-reviewed journals and presented at both national and international conferences.

## Responsiveness to ethnic peoples

F5. What other ethnic groups will be participating in this research based on your sampling frame (for example, Pacific peoples or Asian peoples)?

People from all ethnic backgrounds will be approached for involvement in the study. Counties Manukau region have significant morbidity from lower respiratory infection and the highest hospitalisation rate in New Zealand (Craig 2006). In particular this impacts on the Maaori and Pacific children in this region. At Kidz First children's hospital Pacific children make up 57% and Maaori children are 29% of the total LRI admissions. This research is therefore of particular significance for Pacific children and their families. From this we would estimate between 50 and 60% of participants would be Pacific i.e 200 to 240 individual participants. In addition to a Maaori community health worker we will also be employing a Pacific community health worker to work with any pacific families who participate in this research study. We have also sought advice from Dr Teuila Percival a well respected Samoan paediatrician who has many years experience working with the Pacific community both in South Auckland and in Samoa. She is a co-investigator on this study and is vice president of the Pasifika Medical Association.

F5.1 Are there any aspects of the research based on participation or the relevance of the research to specific ethnic groups that might raise specific cultural issues? ☑ Yes ☐ No

If **yes**, please outline.
If **no**, go to F6.

It is predicted that high proportion of Pacific families will participate in this research study. It is imperative that we engage with these families to ensure they have good understanding of the study and the processes involved.

F5.2 How can this research contribute to reducing inequalities for ethnic peoples in the New Zealand health system?

Early intervention to prevent the development of ongoing respiratory disease would have clear benefits for the pacific population of South Auckland and New Zealand, and help reduce the gap in respiratory health currently observed between Pacific and their Pakeha counterparts. The early intervention involves the application of a standard of health care for infants that are known to be at high risk of developing chronic respiratory disease.

F5.3 Describe what consultation has taken place with specific ethnic group(s) prior to the project's development and attach evidence of their support.

Liaison with the Pasifika Medical Association through Dr Teuila Percival.

F5.4 Describe any ongoing involvement the group(s) consulted have in the project.

Dr Teuila Percival is a co-investigator on this trial so will have continual liaison throughout the project. A final report will be collated and provided to the Pacific Health Cultural Unit at CMDHB and the Pasifika Medical Association.

F5.5 Describe how you intend to disseminate information to participants and the group(s) consulted at the end of the project.

The participants of this study will have the option within the consent form to request a copy of the study results. Written and/or oral presentations to Pacific health groups will be offered.

## Responsiveness to other peoples of interest

F6. Are there any aspects of the research based on participation or the relevance of the research to specific peoples of interest that might raise specific issues for such communities (for example, for prisoners, people with disabilities, people with diverse sexual identities)?

☐ Yes ☑ No

If **yes**, please outline.
If **no**, go to F7.

F6.1 How can this research contribute to reducing inequalities for other peoples of interest in the New Zealand health system?

F6.2 Describe what consultation has taken place with specific peoples of interest group(s) prior to the project's development and attach evidence of their support.

F6.3 Describe any ongoing involvement the group(s) consulted have in the project.

F6.4 Describe how you intend to disseminate information to participants and the group(s) consulted at the end of the project.

F7. Will the study drug/treatment continue to be available to the participant after the study ends?

☐ Yes ☑ No

F7.1 If **yes**, will there be a cost, and how will this be met?

| | | |
|---|---|---|
| F7.2 | If **no**, why not? | Full evaluation of the intervention will be required at 24 months to assess whether any benefit has been observed. If benefit has been observed and the results are statistically significant then engagement with CMDHB and PHO's will be necessary before the programme could be continued as standard care. |
| F7.3 | If there was a placebo arm, what will happen to these participants at the end of the study? | N/A |

***Note: This information needs to be included in the information sheet.***

# Part 3: General

Describe and discuss any ethical issues arising from this project, other than those already dealt with in your answers above.

Nil else.

**Thank you for your assistance in helping us assess your project fully.**

Please now complete:

- the declarations (Part 4). If there is more than one site, include a declaration for each site.

If applicable complete:

- a Registered Drug Form
- Form A or B
- Part 5
- Part 6
- Part 7
- Part 8

Attach:

- Checklist to ensure all relevant documents are attached. Incomplete applications will not be reviewed.

# Part 5: Use of Human Tissue

To be completed if the research involves collection of human tissue.
(See guidelines page 28 for definition.)

| | | |
|---|---|---|
| 1.1 | Provide details, eg, type, number of samples, total volume to be obtained. | Blood samples will be collected by using a heel prick for children < 12 months and finger prick for children > 12 months.<br><br>Vitamin D test - 0.5 mls required<br><br>Iron test - 0.6 mls required<br><br>Intervention Group will have 2 blood tests; at baseline and 24 month visits.<br><br>Non-intervention Group will have 1 blood test, at the 24 month visit. |
| 1.2 | Will consent, or has consent, been obtained? If yes, proceed to 1.6 | ☑ Yes ☐ No |
| 1.3 | If consent is not able to be obtained for use of tissue, how consistent is the proposed use of tissue with the original consent for the use of the tissue? | N/A |
| 1.4 | State reasons why informed consent cannot be obtained or why it would not be desirable or possible to do so. | N/A |
| 1.5 | State the public good associated with continuing the research without the consent of the individual. | N/A |
| 1.6 | How was or will the tissue be obtained (including frequency and scope of consent that was or will be given)? | With consent, a nurse, doctor or appropriate staff member trained in phlebotomy will obtain blood samples via finger prick at visit 1 and final visit for group 1 and at final visit for group 2.. |
| 1.7 | What are the current use(s) of the tissue and any intended or foreseeable future uses of that tissue (including the scope of consent that was or will be given) and why is it necessary? | With consent, blood samples will be taken to measure full blood count, iron and vitamin D levels |
| 1.8 | If access is to be granted to third parties, how will that be done? | NA |

| | |
|---|---|
| 1.9 How will tissue be stored, eg, identified/ de-identified/anonymised, length of time, means of storage and labelling, security, the responsible individual or organisation? | Local hospital samples will be identified with the participant name and hospital number – information (results) required for the study will be transcribed, by the site study nurse, into the participant's anonymised case report form. Following analysis the samples will be destroyed per local laboratory approved standard operating procedures. |
| 1.10 How will the tissue be disposed or returned? | Samples will be destroyed at the end of the analysis in accordance with accredited laboratory guidelines and regulatory regulations. |
| 1.11 Is genetic analysis to be carried out (see also Part 6)? | NA |
| 1.12 Can the participant request the tissue to be withdrawn from the research? If so, how and at what point? | Participants may withdraw their sample/s anytime by informing the Investigator. |
| 1.13 Will personal and health information or sensitive information be linked to the tissue? If yes, are procedures in place to recontact participants or their clinician to provide clinically relevant information if it arises. | Samples are identified by an allocation number only. The test results will be linked to the participant's health information for the purpose of conducting statistical efficacy and safety analysis required by the trial. |
| 1.14 What safeguards will be in place to ensure that the tissue will not be vulnerable to unethical use. | All parties involved with sample handling/ analysis are aware of ethical standards with regard to dealing with human tissue samples. Laboratories are contracted to do specific analyses only, and are accredited and GLP compliant. |

2. If there any additional safeguards in place not covered in 1.1–1.14 above please give details.

An integral part of the informed consent process is that the participant understands that the samples collected during the study are for research purposes only.

Participants are made aware during the consent process that they can withdraw from the study at any time.

3. Will the human tissue involved in the research project be stored for later use in a future study? If yes, please give details. ☐ Yes ☒ No

Is this covered by distinct informed consent? ☐ Yes ☐ No

4. Will any human tissue samples or the information derived from them go out of New Zealand? ☐ Yes ☒ No
If yes, complete the following questions.

4.1 If so to what organisation/s and how will they be transferred?

4.2 What governance structures, procedures and processes does this organisation have to ensure the participant's choices are respected ie storage facilities, control of access, appropriate disposal methods?

4.3 How will tissue be stored, eg, identified/de-identified/anonymised, length of time, means of storage and labelling, security, the responsible individual or organisation?
(If different from 1.9.)

4.4 How long will the tissue and/or data be stored and what will happen at the end of this time?

4.5 If identified tissue and/or data is stored, will participants be able to request that their tissue be returned to New Zealand or request confirmation that their tissue and related information has been destroyed?

4.6 What appropriate ethical safeguards will be in place?

4.7 Will all future use of the tissue and the information derived from it be subject to review by an ethics committee approved by the New Zealand Health Research Council of New Zealand? ☐ Yes ☐ No

If **no**, provide confirmation from the organisation storing the tissue or the information derived from it,that it has protocols in place to ensure that any future use will have ethical and scientific review by a committee or institutional review board that conforms to the International Ethical Guidelines for Biomedical Research Involving Human Subjects (Council for International Organizations of Medical Sciences and World Health Organization 2002).

# Part 8:
# When a Participant is Unable to Make an Informed Choice

To be completed when one or more participants in a project will likely not be able to make an informed choice about whether to take part. **Do not complete this section if all participants in the study are competent to make an informed choice and give informed consent themselves**. Refer to the Guidelines for information about children in research.

1. Will any of the participants have a person with them who is available and entitled to make an informed choice on their behalf if they themselves are unable to do so? ☑ Yes ☐ No

   **If yes**, that person can make a proxy informed choice for the potential participant. Include an appropriate consent form for that person legally entitled. (Note: Where possible the incompetent person should also orally consent to the level of his or her understanding.)

   **If no**, complete sections 1.1 and 1.2.

   1.1 Is there any person interested in the potential participant's welfare who knows the participant (eg, family member/friend/whānau) and is willing and available to express a view as to what the potential participant would choose were he or she competent and fully informed about the study. ☐ Yes ☐ No

   **If yes**, include an information sheet for the family member/friend/whānau statement as per page 24.

   Please note: if it is appropriate that there be wider consultation with family, then this should be encouraged.

   1.2 Explain why it is not possible for a potential participant to make an informed choice and why it is not possible for a proxy choice to be made or for a person interested in the potential participant's welfare to state what the participant would choose if he or she was competent and fully informed.

2. What would be the risks to the participants of taking part in this study?

The risks have been outlined in the main ethics application.
All participants will be 2 years of age or younger. Parent or legal guardian will sign consent form prior to any study procedures.

We believe this study caries minimal psychological risk, the demographic and clinical information collected for this study will only be obtained following informed consent being obtained from each parent/legal guardian involved. Support will be offered to all families/whanau from the research team in particular our Community Health Workers.

Physical Risk: Each child will have a chest x-ray taken at the 24 month clinic visit and the intervention will also have one taken during the initial phases of the study. These x-rays will only be undertaken where consent is obtained.

3. Could the research be carried out on people who are able to consent? ☐ Yes ☑ No

4. Explain why approval is being sought to use this participant/population/patient group.

Currently there is little data available on the long-term health outcomes of children who have a severe lower respiratory infection in the first two years of life in Counties Manukau.

5. What is the potential health interest for the group of patients/population of which the participant would be a member?

Developing knowledge of the long-term health outcomes for young children who have had a severe lower respiratory infection in the first two years of life may lead to the recognition of future development of programmes and services to combat chronic respiratory illness in this vulnerable population group.

# Information Sheet for Parents and Legal Guardians

# Healthy Lungs

**You and your child are invited to be part of a research study at Kidz First Children's Hospital and Community Health.**

**The lead study investigators are:**
Dr Adrian Trenholme, Paediatrician and Dr Catherine Byrnes Paediatric Respiratory Specialist Phone (09) 2760000 extension 7016

***Why are we doing this study?***

In Counties Manukau, we have very high rates of chronic lung disease in children. We are looking at ways of keeping children healthy. The health programme we use for children with cystic fibrosis is working well and we want to see if it will work for children without cystic fibrosis but who have had a lung infection. Taking part in this research is entirely voluntary (your choice). If you do not wish to take part in this study, it will not affect any future health care or treatment your child receives from health care providers.

***Who is been invited to partake in this study?***

We are approaching you because a child in your care is under two years old and has been admitted to Kidz First children's hospital with a lung infection; such as pneumonia or bronchiolitis. The research study is called *'Healthy Lungs'*. We are expecting approximately 400 children and their families to be involved in this study.

***What would this require from you?***

We need to compare two groups of children; ***group one*** will receive the new health programme and ***group two*** will receive the same care they would receive if not in this study. We don't know if the health programme will work. If you decided to take part in this study, your child will be in group 1 **OR** group 2. Both groups will be

seen at two years after their child's hospital admission and their health will be assessed by a specialist paediatric doctor.

***Which group will my child be allocated to?***

We don't know whether your child will be in group 1 or group 2. The group they go into will be chosen randomly (like the 'flip of a coin'). Your child will have an equal chance of being in either group and you will not be able to choose which group you would like to be in.

***What will happen with each group?***

Both groups of children will receive their usual care from their family doctor, practice nurse, and plunket nurse/tamariki ora nurse. Medical information will be collected from your child's family doctor visits and from hospitals on hospital admissions.

**Group One**

This group of children will be seen by the research team including; a doctor or nurse practitioner (who is an expert children's nurse who can prescribe medicines) a nurse and a community health worker. The clinic visits will occur at month one after study enrolment, at month three and then every three months and as required for two years, in a community clinic located in Manurewa, Mangere or Otara. Each clinic visit will last between 30 minutes to 1 hour. At this visit, each child will be examined by the doctor or nurse practitioner and nurse and offered assistance with things that they think are necessary to keep your child healthy.

**Group Two**

This group of children will be contacted by telephone or in person by the research community health workers every three months to record any illnesses your child has had, including visits they may have had to your family doctor (GP) and any other health professionals. We would like to track your child's health for two years.

**Both Groups**

Both groups of children will be seen at two years from the start of the research study. At this time, your child will be fully examined by a specialist children's doctor and will have a chest x-ray and blood test if you consent. At this time if your child is

found to have any health problem they will be referred to the appropriate health care service for any treatment they require.

***Confidentiality***

All of the information about your child will be kept confidential. This means that only the research team know about your child's medical conditions and family situation. Information will be kept in a locked filing cabinet in a locked office.

***Are there any risks if I choose to participate?***

The medical examinations will be carried out by trained health providers (doctors, nurse practitioner, nurses and community health workers). If you consent to having a blood test there is a possibility of some bruising at the site where the blood is taken from. There is also some risk with the chest-x-ray please refer to the next section about chest x-rays.

***The chest x-ray***

We would like to take a chest x-ray (a picture) of your child's lungs. A chest x-ray makes images of the heart, lungs, airway, blood vessels and the bones of the spine and chest. An x-ray (radiograph) is a medical test that helps physicians diagnose medical conditions. Radiography involves exposing a part of the body to a dose of ionizing radiation to produce pictures of the inside of the body. This does mean that your child will have a small amount of radiation exposure. This exposure has been assessed as a negligible (small amount). We are exposed to radiation everyday and this chest x-ray has been assessed as being equivalent to only 2.4 days background radiation. This procedure is not painful however, your child may experience some discomfort and may become upset for a short period because they have to stay very still for the picture. The chest x-ray will only take a very short time approximately five minutes.

The chest x-ray is an important part of this research study. To enable you and your child to take part in this study we will ask that you give consent for your child to have a chest x-ray at the 24 month visit, the doctor may recommend an earlier chest x-ray if they think it is required during the study.

***The blood test***

With your permission, we would like to take up to two blood tests for this research study. You can still take part in the research but refuse to have the blood test. If your child is allocated to group two we would like to take one blood tests at the end of the study at the 24 month clinic visit. If your child is allocated to group one we would like to take two blood tests; one at the beginning, and one at the end of the research study. The blood test will be obtained by a 'finger prick' a single needle prick to the finger and blood is dripped in to a test tube for testing; there is a possibility of some bruising where the blood is taken from. After testing the blood sample will be destroyed.

***Will my child benefit from being in this study?***

Your child will receive a full examination by a specialist children's doctor two years after their hospital admission. However the main benefit of the study will be in providing information on how best to reduce lung disease in children in the future..

***What will happen to the information collected for the study?***

The information will be recorded and then analysed by the researchers. This information will then be kept in a secure place. All identifiable information to your child will be removed from the information. No research participants' names will appear on any material produced as a result of this research. The results of the study will be reported to groups in the Counties Manukau area and in international journals. A report on the result will be sent to you after the study is completed and analysed if you would like to receive them. The chest x-ray will be taken by an accredited radiology service.

***Can I leave the study?***

Your participation in this study is voluntary (your choice). If you choose not to let your child join, they will still receive the same care that they would normally receive. If your child does join the study and if, for any reason and at any time, you wish to stop your child's participation in the study, you are free to do so at any time without giving any reason. Your decision to have your child leave the study will have no effect on your child's future care or treatment by doctors.

***Accident Compensation (ACC)***

'In the unlikely event of a physical injury as a result of your participation in this study, you may be covered by ACC under the Injury Prevention, Rehabilitation, and Compensation Act 2001. ACC cover is not automatic, and your case will need to be assessed by ACC according to the provisions of the Injury Prevention, Rehabilitation, and Compensation Act 2001. If your claim is accepted by ACC, you still might not get any compensation. This depends on a number of factors, such as whether you are an earner or non-earner. ACC usually provides only partial reimbursement of costs and expenses, and there may be no lump sum compensation payable. There is no cover for mental injury unless it is a result of physical injury. If you have ACC cover, generally this will affect your right to sue the investigators. 'If you have any questions about ACC, contact your nearest ACC office or the investigator.
'You are also advised to check whether participation in this study would affect any indemnity cover you have or are considering, such as medical insurance, life insurance and superannuation.'

***Who do I ask if I have any questions regarding this research study?***

Please feel free to ask any questions you have of the research staff that gave you this form. You can also contact the study investigators whose contact details are given below if you want to discuss anything now or during the study. We encourage you to discuss this with your family before you decide whether you want to take part in the study. If you have any queries or concerns regarding your rights as a participant in this study, you may wish to contact an independent health and disability advocate:

Free phone: 0800 555 050
Free fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz'

Please feel free to ask any questions you might have about the study before, during and, after completing the study visits. Taking part in this research is entirely voluntary (your choice). If you wish to discuss this study with the Maaori Support Group at Middlemore Hospital, you can contact them as follows:

Te Kaahui Ora
Phone :( 09) 262 9546 or
Private Bag 94052
South Auckland Mail Centre
Manukau
Auckland
New Zealand

This study has received ethical approval from the Northern X Regional Ethics committee reference ***(Ref number to be inserted)***

**The study investigators are:**

Dr Adrian Trenholme, Paediatrician Ph: 2760044 ext 7016

Dr Catherine Byrnes, Paediatric respiratory specialist

Ph: (09) 3078989 extension 5471

## Consent Form

# Healthy Lungs

| | | | |
|---|---|---|---|
| English | I wish to have an interpreter | Yes | No |
| Deaf | I wish to have a NZ sign language interpreter | Yes | No |
| Maaori | E hiahia ana ahau ki tetahi kaiwhaka Maaori/kaiwhaka pakeha korero | Ae | Kao |
| Cook Island Māori | Ka inangaro au i tetai tangata uri reo | Ae | Kare |
| Fijian | Au gadreva me dua e vakadewa vosa vei au | Io | Sega |
| Niuean | Fia manako au ke fakaaoga e taha tagata fakahokohoko kupu | E | Nakai |
| Sāmoan | Ou te mana'o ia i ai se fa'amatala upu | Ioe | Leai |
| Tokelaun | Ko au e fofou ki he tino ke fakaliliu te gagana Peletania ki na gagana o na motu o te Pahefika | Ioe | Leai |
| Tongan | Oku ou fiema'u ha fakatonulea | Io | Ikai |

**By signing this consent form, I agree to the following:**

| | |
|---|---|
| I have read and understand the Information Sheet dated 23rd August 2010 and I know whom to contact if I have any questions about the study. | |
| I understand that my child will be randomly allocated to either group one or group two. | |
| I have received a copy of the Information Sheet and will receive a signed copy of this consent form to keep. I understand that the original will remain on file with the study doctor. | |
| I have had an opportunity to use whaanau support or a friend to help me ask questions and discuss the study. I am satisfied with the answers I have been given. | |
| I understand that my child's participation is voluntary and that I am free to withdraw my child at any time, without giving a reason, without my child's medical care or legal rights being affected. | |
| I give permission for the research team informing my GP of my participation in this research study and to request medical information regarding my child that is relevant to their health. | |
| I consent to my child having up to two chest x-rays. | |
| I consent to my child having a blood test/s<br>If they are allocated to group one this will be two blood tests if they are allocated to group two this will be one blood test (please circle your option) | Yes<br><br>No |

*At the completion of this study, I would like to receive a summary of the study results*

YES_____ NO_____

## Consent Form

# Healthy Lungs

| | |
|---|---|
| Name of Child _____<br><br>Parent/Legal Guardian signature _____<br><br>Parent/ Legal Guardian Name<br>(Print name) _____ | Date_____ |

| | |
|---|---|
| Signature of person who conducted informed consent discussion<br>Signature _____<br><br>Print name _____ | Date_____<br><br>Time_____ |

| | |
|---|---|
| By signing and dating the consent form, I (the translator) attest that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the Parent/Legal Guardian, and that informed consent was freely given by the Parent/Legal Guardian. | |
| Signature of translator (if used) _____<br><br>Print name _____ | Date_____ |

**A3.1.0 Study Design continued from A3.1**

**Control Group (n=200)**
These children will receive an initial assessment in hospital and then current 'usual care' in South Auckland. Usual care consists of GP review for family directed health concerns, well child and immunisation visits. Referral to paediatric services will be undertaken if there are clinical concerns and then primary, secondary and tertiary health care adopted as necessary. The children and their families will be contacted regularly by the Community Health Worker (by phone or in person) to maintain contact and to review primary and secondary health care contacts, medication use. They will be reviewed in clinic two years following their index admission with severe lower respiratory infection and will be assessed in the same way outlined for the intervention group.

**Intervention Group (n=200)**
These children will receive an adapted programme based on the Cystic Fibrosis model of care for early childhood. The essence of this model of care is for regular review from infancy, early detection of deviation from normal health and early intervention to prevent ongoing disease or irreversible damage occurring. The key to success for this project is the engagement, support and rigorous follow up for children and their families. The Community Health Worker/s has a central role in this process alongside the practice nurses and study respiratory nurse and experienced local GPs, in addition to secondary paediatric and tertiary respiratory teams. Co-ordination will be undertaken by the study respiratory nurse who works alongside the clinic nurse and will undertake follow up in the community of any non-attenders with assistance from the Community Health Worker/s.

**24 month outcome visit (Both Groups)**
At 24 months clinical history, examination, blood tests where consent obtained (Full blood count, iron studies, vitamin levels) and chest x-ray will be undertaken. Abnormality on any findings will be addressed in both groups. This includes utilising any of the interventions programmes outlined above, continued paediatrician review or referral to respiratory paediatric care as appropriate. With persistent changes on chests x-ray, prolonged symptoms or chest deformity +/- clubbing further respiratory investigations are likely to be warranted including broncoscopy, broncholavage and chest CT scans. These investigations would be undertaken earlier as part of the study than would otherwise be available to children with these persisting symptoms and signs.

**Intervention includes:**

- Antibiotic therapy for LRI or wet cough - an action plan for the treatment of respiratory infections will be developed with the family and copied to the identified primary care practitioners
- Chest physiotherapy - education and demonstration by the study nurse or physiotherapist
- Asthma therapy - according to Paediatric Society NZ Asthma Guidelines
- Smoking cessation education for family members
- Immunisation with routine, Influenza and Pneumococcal vaccines where indicated
- Nutritional support to optimise growth
- Dental assessment where necessary
- Community Health worker engagement
- Routine clinical management of co-morbidities e.g. gastro-oesophageal reflux
- Referral to other appropriate medical/social/financial services.
- Rigorous follow up of all interventions to ensure family engagement in response