ISAAC

INTERNATIONAL

STUDY OF

ASTHMA AND

ALLERGIES IN

CHILDHOOD

NEWSLETTER – JULY 2002

Dear colleagues

As I write this, it is the middle of July, which is mid-winter in Auckland with some very wet days and some beautiful crisp weather. South of Auckland it's been snowing on our North Island mountains and South Island Alps. Others of you will be experiencing mid-summer and will be going on holiday.

Holidays are NOT what we are having at the ISAAC International Data Centre (IIDC) at the present time because Phase Three data and centre reports are "rolling in" and we are expecting a large volume of data.

We are overwhelmed with the enthusiasm in Phase Three - expecting data from over 220 centres from more than 85 countries – about half of these are Phase 3A centres which will allow time trends analysis and the remainder are Phase 3B centres which are newly recruited centres to ISAAC and will result in an expanded world map.

We are pleased that we have received registrations from all these centres, but 53 centres that expressed an interest have not yet registered. The final date for receipt of the Registration document at the IIDC is 15 August 2002.

From the outset we announced that 30 November 2002 is the deadline to receive Phase Three data at the IIDC. We understand from some centres that it will be difficult to meet this deadline. The Steering Committee wishes to include as many centres as possible. If you are a 3A centre, please let your Regional Coordinator know if you expect to be late with your data. If you are a Phase 3B centre we will be extending the deadline to early 2002 – a new deadline will be announced after the September Steering Committee meeting. We need to know as accurately as possible where you are up to, to be able to synchronise a plan to handle the volume of data, resultant work and activity, including completion of the centre reports from the individual centres. Therefore, we would like a precise update now from those centres that have yet to submit their centre report and data.

To update our records I would be grateful if you would complete the table below and return by email to (n.williams@auckland.ac.nz) or facsimile (+64 9 373 7602).

Country Name: .....

Centre Name: .....

Principal Investigator: .....

Projected date of completion of data collection	**Day**		**Mth**		**Year**	200_
Project date of submission of data to IIDC	**Day**		**Mth**		**Year**	200_

REMINDER Data is to be sent to Tadd Clayton (t.clayton@auckland.ac.nz)
Centre Reports to Philippa Ellwood (p.ellwood@auckland.ac.nz)

ISAAC Phase Three appears to be the largest epidemiology study ever undertaken and we are delighted that you are collaborating with us.

This year the ISAAC Steering Committee conference is being held in Stockholm just before European Respiratory Society Annual Congress (ERS). It is my pleasure to invite all ISAAC Collaborators to the ISAAC Collaborators social function being held in Stockholm on 15 September 2002 (please see page 10 for details). We hope it will be convenient for those attending the (ERS) to consider joining the ISAAC Steering Committee and myself at the social function. I realise that some of you may not be able to attend but we will toast you in spirit.

Warm wishes

Innes Asher

On behalf of the ISAAC International Data Centre and Steering Committee

CORRESPONDENCE TO:

Dr Innes Asher
ISAAC International Data Centre
Division of Paediatrics
Faculty of Medical & Health Sciences
University of Auckland
Private Bag 92 019
Auckland
NEW ZEALAND

Ph: 64 9 373 7599 ext 6451
Fax: 64 9 373 7602
Email: mi.asher@auckland.ac.nz
Website http://isaac.auckland.ac.nz

NEWSLETTER CONTENTS

ISAAC PROFILE

ISAAC profile: Dr. med. Erika von Mutius

Erika grew up in Geneva, Switzerland. She then moved to Bavaria, where she attended St. Irmengard Gymnasium in Garmisch. From there she attended the University of Munich Medical School where she completed her internship, residency and was assistant in the Departments of General Practice, Neonatal and Pediatric Intensive Care. She then undertook her pediatric training at University Children's Hospital Munich, Germany followed by Respiratory Pediatric training at the Respiratory Sciences Centre, University of Arizona, Tucson, USA with Professor Fernando Martinez.

She also trained in Clinical Effectiveness at the Harvard School of Public and Health, Boston, USA and graduated in the year 2000 with a Master of Science in Epidemiology.

Erika currently resides in Munich where she is a pediatrician and allergologist. She heads the Asthma and Allergy Department and is also is the Deputy Head of the Outpatient Clinic of the University Children's Hospital (Dr. von Haunerschen Kinderklinik) in Munich.

Erika's research interests include the epidemiology of childhood asthma and allergies with a focus on environmental predictors and gene-environment interactions. She has been involved with numerous multi-centre studies.

Erika has been the recipient of coveted awards from: European Respiratory Society Award for Paediatric Respiratory Research in Europe 1996; Elliot Ellis Lectureship at the 1999 American Academy of Allergy, Asthma and Immunology Annual Meeting and in July 2000 the Award of the Ludwig Maximilians University Munich, Germany, for having written the best doctoral thesis at the university in a 4-year period.

She is an Associate Editor of the European Respiratory Journal and serves as a member on the Editorial Boards of Pediatric Pulmonology, Clinical and Experimental Allergy, Thorax, Sozialpädiatrie, Kinder- und Jugendheilkunde 1997-2000, "Kinder- und Jugendmedizin" and Allergologie.

Erika has also written more than 100 journal articles and review papers and nearly 20 book chapters on a variety of topics in the fields of asthma and allergy.

Erika's international and national scientific membership includes the International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee, European Respiratory Society (ERS), European Academy of Allergology (EAACI), European Society of Pediatric Allergy and Clinical Immunology (ESPACI), German Society of Pediatrics and the American Academy of Allergy, Asthma and Immunology (AAAAI).

As a member of the ISAAC Steering Committee Erika's knowledge of environmental predictors and gene-environment is pivotal to the ISAAC organisation.

Outside of work Erika enjoys outdoor activities such as walking, swimming and skiing. She is a keen follower of the arts, and a lover of classical music. She has travelled extensively and is multi-linguistic with the ability to converse in her native tongue German, French and English.

Kinderklinik der Universität im
Dr von Haunerschen Kinderspital
Lindwurmstrasse 4
München D-80337
GERMANY
Phone: +49-89-5160-2709
Fax: +49 89 5160 4452
Email: Erika.Von.Mutius@helios.med.uni-muenchen.de

ISAAC Phase Three Regional Coordinators

ISAAC Region and Coordinator	Email Address	Facsimile Number
Africa/Anglophone		
Dr Joseph A. Odhiambo	jodhiambo@nairobi.mimcom.net or crdr@todays.co.ke	254 272 9308 or 254 720 030
Africa/Francophone		
Prof Nadia Aït-Khaled	NaitKhaled@iuatld.org or Union@iuatld.org	33 1 4329 9087
America Latin		
Prof Javier Mallol	jmallol@lauca.usach.cl	56 2 331 0375
America North		
Interim arrangement please contact: Prof Richard Beasley	richard.beasley@mrinz.ac.nz	64-4-472 9199
Asia-Pacific & South East Asia		
Dr Chris Lai	keilai@netvigator.com	852 2522 2188
Eastern Mediterranean		
Dr Stephen Montefort	stevemonte@waldonet.net.mt	356 482 800
Europe Western		
Prof Dr Ulrich Keil	keilu@uni-muenster.de	49 251 835 5300
Europe/Northern & Eastern Europe		
Prof Bengt Björkstén	bengt.bjorksten@cfa.ki.se or evi.werendel@imm.ki.se	46 8 32 71 96
India Sub-continent		
Dr Jayant R. Shah	plmlab@jaslokhospital.net or jaslok@vsnl.com	91 22 495 0508
Oceania		
Dr Sunia Foliaki	S.Foliaki@massey.ac.nz	64 4 3800 613

ETHICS. A RECENT EXPERIENCE.

The ISAAC International Data Centre has recently been in correspondence with a Phase One/Three centre in Oceania that has decided to withdraw from ISAAC Phase Three due to an unacceptable response rate.

Their study (13/14 year only) was in progress and 13 schools had already participated with a total of 1646 students being selected. However, the Principal Investigator has informed us that they were only able to achieve a total response rate of 34%. Of course, they were aware that this would exclude them from the international comparison and so decided that they would not continue. In Phase One, using passive consent the response rate was a healthy 90%.

The main issue seemed to be the stringent Ethics Committee requirement for written consent from parents. This additional requirement for the parents of the 13/14 year olds to submit consent before the study took place in the schools has enforced the perception that passive consent is the most effective way in a study like ISAAC to ensure an acceptable response rate.

This raises several issues. Firstly, that we recognise there are different types of research and having an umbrella of ethical rules that govern all research will seriously affect simple questionnaire epidemiological studies such as ISAAC. Clinical trials are the type of research where the participants must be protected by the Ethics Committees and written and informed consent is vital. However more simplistic types of research should not be treated the same way by the Ethics Committees.

The second issue is that for centres that undertook Phase One and who were also undertaking Phase Three, the ideal was to repeat the methodology as closely as possible. If passive consent was used in Phase One, then passive consent should also be used for Phase Three. This is a good argument to put forward to the Ethics Committees in an Ethics application.

We hope that other centres have not had the same experience. We would welcome comment from you in regard to this topic.

Warm regards

Philippa

IIDC Research Manger
p.ellwood@auckland.ac.nz

ISAAC Phase Three Data Entry – Part 2

Epi-Info - Important features you may need to know from Tadd Clayton, IIDC Data Manager

ISAAC NEWSLETTER, APRIL 2002, ISAAC PHASE THREE DATA ENTRY – PART 1

Index

The ISAAC data entry packages have been prepared using a component of Epi-Info. Epi-Info is free epidemiological software provided by the Centers for Disease Control and Prevention (CDC) in Atlanta, Georgia, USA. If you are planning to use one of the ISAAC data entry packages I strongly recommend that you download and install version 6 of Epi-Info if you have not already done so. As I mentioned in the previous article (see the April 2002 newsletter), you should only view your data file using Epi-Info to avoid damaging the file. You will also find it much easier to make any necessary corrections to your data file if you have the full version of Epi-Info installed. Epi-Info is available from:

http://www.cdc.gov/epiinfo/ei6dnjp.htm

Instructions for downloading and installing Epi-Info are also available at that web site.

Duplicate SCHOOL and SERIAL

The previous article described how to carry out double entry of data. As I mentioned then, you need to specify a variable (or variables) which is used to link between the first and second entries of the data. Epi-Info needs this link in order to match the information entered during the second entry with the correct record from the first entry. It is very important that the value of this variable (or combination of variables) is unique for each record in the data file. If two records have the same SERIAL number Epi-Info cannot identify which record should be matched with the information which is to be entered a second time. If records with duplicate values of SERIAL (or SCHOOL and SERIAL) are present in the data file Epi-Info will not proceed with the double entry and will display an error message.

Unfortunately it is as easy to make an error when entering the SERIAL as it is to make a mistake when entering any other item of data. It is therefore quite possible that you will have records with duplicate SERIAL numbers after you have finished the first entry of your data and you will be unable to proceed with the second entry. It can be very difficult to track down duplicate SERIAL numbers in a large data file just by examining the file. If you think you may have a problem with duplicates try using the following small program. To use this program you must be in the ANALYSIS component of Epi-Info (select 'ANALYSIS of data' from the 'Programs' menu). Type the following commands and press the ENTER key at the end of each line:

```
read <filename>
sort school serial
define tempser ####### cumulative
define flag #
if tempser = serial then flag = 1 else flag = 0
tempser = serial
select flag = 1
list school serial
close
```

Duplicate SCHOOL and SERIAL continued

Be sure to replace <filename> with the full name of your data file (e.g. 'C:\isaac\i3full.rec'). You can also save this programme in a file and run it from within Epi-Info. To do this, copy the lines of the programme into a text editor such as Windows Notepad and save it with a name such as 'finddups.pgm'. You run the program from ANALYSIS by typing RUN followed by the full name of the program file and pressing the ENTER key.

The programme generates a list with the record number and SCHOOL and SERIAL numbers of records where the SERIAL number is the same as SERIAL number of the previous record. For example if a data file includes four cases with duplicate SERIAL numbers it might produce the following results:

```
REC  SCHOOL SERIAL
---  ------ -------
 11       1       10
 20       1       18
126       2      112
160       2      148
```

As you can see this shows that records 11, 20, 126 and 160 have the same SCHOOL and SERIAL numbers as previous records in the data set. Unfortunately this programme only shows the second (and subsequent) record with the duplication of SCHOOL and SERIAL. You will have to examine the data file to identify the first record with that SCHOOL and SERIAL number as it may be the first record which needs to be corrected. There are several ways you can achieve this. For example if you use READ in ANALYSIS to examine the file (see above) you can then type SELECT (SCHOOL = <schoolnumber>) AND (SERIAL = <serialnumber>). When you then use UPDATE or BROWSE you will see only records with that combination of SCHOOL and SERIAL numbers.

As I mentioned before, these duplications make it impossible for Epi-Info to identify exactly which record needs to be compared with the new entry when you are carrying out the second entry of the data. To make any corrections to the data file I suggest you follow these instructions:

Start Epi-Info and select 'ANALYSIS of data' from the 'Programs' menu.

1. Type READ followed by the full file name of the data file (e.g. `C:\isaac\i3full.rec`) and press ENTER. You should now see the name of the file across the top of the window (`e.g. Dataset: C:\isaac\i3full (301 recs)`).
2. Type UPDATE and press ENTER. You should now see a screen which resembles a spreadsheet with the variable names across the top, record numbers down the left and data in the middle.
3. Use the arrow keys and the PageUp and PageDown keys to locate the records with the incorrect SERIAL numbers. You can place the cursor on the incorrect value for SERIAL and type over it to enter the correct value. When you then use an arrow key to move out of the cell you will see a message near the bottom of the screen which asks whether you wish to write the change to the disk (i.e. save the change). Press Y to save the change and N if you have made an error and do not wish to save the change.
4. Press the F10 key when you have finished making corrections. Press F10 again to exit ANALYSIS.

I strongly recommend that you make any changes to a copy of the data file so that you always have the original file available in the unlikely event that the changes cause damage to the file. You can make copies using Windows explorer. You can also make copies from within ANALYSIS. The instructions to do this are in the Epi-Info Manual. During the data entry process it is a sensible idea to make regular copies of the data file so that you do not lose too much work if the file becomes damaged.

Duplicate SCHOOL and SERIAL continued

When tracking down and correcting cases of duplicate SCHOOL and SERIAL numbers you should keep in mind that it is possible for more than two records to share the duplicate values. You could therefore make a correction to one of these records but still have a case of duplicate values in the data file. To avoid this problem you should re-run the programme listed above and make any necessary corrections until you no longer find and cases of duplicate SCHOOL and SERIAL numbers.

Deleted Records

When you use the UPDATE (or BROWSE) command in ANALYSIS to view the data file you may occasionally notice records in the data file which are coloured white instead of yellow and have an asterix (e.g. *) next to the record number. This has occurred because you deleted these records during data entry (or at a later time). Rather than immediately deleting records permanently Epi-Info is designed so that the records can be recovered if necessary. When using UPDATE you can do this by positioning the cursor on the record and pressing the F6 key. Once again you will be asked if you wish to save the change when you use an arrow key to move to another record. The deleted records will not affect the double entry process but if you wish to completely remove the deleted records you must use ANALYSIS to create a new version of the file. Instructions to do this are:

Once in ANALYSIS use the READ command (see above) to read in the data file.

1. Type ROUTE <filename> and press ENTER. <filename> is the name you wish to call the new file. It cannot be the same as the old file name. For example you could call the new file '`C:\isaac\i3full02.rec`'. As Epi-Info is an MS-DOS programme it does not recognise long filenames. Filenames must be 8 characters or less before the period or they will appear different in Epi-Info. For example a file called '`isaacdata.rec`' (9 characters before the period) would appear as '`isaacd~1.rec`' in Epi-Info. The original name will not have changed if you view the file in Windows Explorer but Epi-Info will only recognise the file if you use the abbreviated format.
2. Type WRITE RECFILE and press ENTER.

This will create a new file without the deleted records (use READ, BROWSE to check that the deleted records are not present in the new file).

Because Epi-Info does not immediately delete records, there can be some confusion about the total number of records in a data file. For example, if a data file has 3102 records but 3 of the records are marked as deleted, the number you see will be different depending on how you view the file. One way of finding the total number of records is to use the TABLES command in ANALYSIS. If I type TABLES FORM and press ENTER I will receive a table such as:

```
FORM  ¦  Freq  Percent   Cum.
------+----------------------
 9    ¦  3099  100.0%   100.0%
------+----------------------
Total ¦  3099  100.0%
```

This shows me that there are 3099 records (3102 minus the 3 deleted records) in the data file that are coded '09' for the variable FORM. However, if I used the BROWSE or UPDATE command to view the spreadsheet style presentation of the data and press the END key to move to the last record, I will see that the last record is number 3102. Please remember that when you send data to the IIDC, I will export it from Epi-Info. The records that are marked as deleted will not be exported so the total number of observations in the data file that I check may be fewer than you expect if you are not aware of the deleted records.

Data Files

In Epi-Info data is stored in files which end in the suffix '.rec'. The names for the data files in the ISAAC data entry packages are 'isaac3.rec' (core questionnaire), 'envrques.rec' (environmental questionnaire) and 'i3full.rec' (combined questionnaire). Of course you may have changed the names of these files during your data entry. When you come to send your data to the IIDC, it is only the file or files with the data which end in '.rec' that you should send. Please do not send any other files. I also do not need the files 'country.rec' and 'langs.rec' which include a list of countries and languages respectively.

Epi-Info does take some time to get used to but I believe you will find the effort worthwhile as it is a useful tool for epidemiological research and has many capabilities beyond those we are using for ISAAC Phase Three. Please feel free to contact me if you have any problems during your data entry.

Tadd Clayton
IIDC Data Manager
t.clayton@auckland.ac.nz

PHASE THREE DATA DEADLINE

Registered centres that wish to be included in ISAAC Phase Three worldwide publications must provide a complete data set and Centre Report to the IIDC in accordance with our deadline. The data and the Centre Report will then undergo a checking process by the IIDC in conjunction with each centre. A satisfactory data set is one which is prepared according to the Coding and Data Transfer Section of the Phase Three Manual and which has completed the data checking process.

Please see editorial for comment and your feedback

ABSTRACTS

The ecological relationship of tobacco smoking to the prevalence of symptoms of asthma and other atopic diseases in children: The International Study of Asthma and Allergies in Childhood (ISAAC)

Mitchell EA, Stewart AW, on behalf of the ISAAC Phase One Study Group

European Journal of Epidemiology 17: 667-673,2001

Abstract. This study examined the relationship between parental smoking and asthma and other atopic diseases at the ecological level. The prevalence of atopic symptoms in 6-7 and 13-14 year old children was assessed in 91 centres (from 38 countries) and 155 centres (from 56 countries) respectively in the International Study of Asthma and Allergy in Childhood (ISAAC). These symptoms were related to prevalence of tobacco smoking for each country by gender as reported by the World Health Organisation. There was a significant negative association between the prevalence of smoking by men and the prevalence of symptoms of asthma and rhinitis, but not eczema in the 13-14year age group. There was a significant positive relationship between prevalence of smoking by women and prevalence of wheeze in the last 12 months, but not for any other symptoms in the 13-14 year age group. In the 6-7 year age group, there was a significant negative correlation between prevalence of smoking by men and the prevalence of wheeze causing sleep disturbance and a close to significant negative association at the 5% level with the prevalence of wheeze in the last 12 months and rhinitis. Thus, for the countries that are included in this analysis, countries that have high adult male smoking rates have a lower risk of asthma and rhinitis symptoms in children. It should be stressed that this analysis does not involve information on individual exposures and therefore does not contradict the well-established association of active and passive smoking in individuals with the occurrence of asthma symptoms in the same individuals. Rather, it indicates that this well-established individual-level association does not account for the international differences in asthma prevalence, and that other risk factors for asthma must be responsible for the observed international patterns.

Exposure to farming in early life and development of asthma and allergy: a cross-sectional survey

Riedler J, Braun-Fahrländer C, Eder W, Schreuer M, Waser M, Maisch S, Carr D, Schierl R, Nowake D, von Mutius E and ALEX Study Team

Lancet 2002; 358: 1129-33

Background A farming environment protects against development of asthma, hay fever, and atopic sensitisation in children. We aimed to establish whether increased exposure to microbial compounds has to occur early in life to affect maturation of the immune system and thereby reduces risk for development of allergic diseases.

Methods We did a cross-sectional survey in rural areas of Austria, Germany, and Switzerland. 2618 (75%) of 3504 parents of 6-13-year-old children completed a standardised questionnaire on asthma, hay fever, and atopic eczema. Children from farming families, and a random sample of non-farmers' children, who gave consent for blood samples to be obtained for measurements of specific serum IgE antibodies to common allergens were invited to participate (n=901).

Findings Exposure of children younger than 1 year, compared with those aged 1-5 years, to stables and consumption of farm milk was associated with lower frequencies of asthma (1% [3/218] vs 11% [15/138]), hay fever (3% [7] vs 13% [18]), and atopic sensitisation (12% [27] vs 29% [40]). Protection against development of asthma was independent from effect on atopic sensitisation. Continual long-term exposure to stables until age 5 years was associated with the lowest frequencies of asthma (0·8% [1/122]), hay fever (0·8% [1]), and atopic sensitisation (8·2% [10]).

Interpretation: Long-term and early-life exposure to stables and farm milk induces a strong protective effect against development of asthma, hay fever, and atopic sensitisation.

ISAAC International Study of Asthma and Allergies in Childhood

On behalf of the ISAAC Steering Committee I warmly invite all ISAAC Collaborators to share dinner with us.

DATE: 15 September 2002

TIME: 5 pm

VENUE: Restaurant St Erik Hotel,
West Wing,
ERS Congress Centre,
STOCKHOLM.

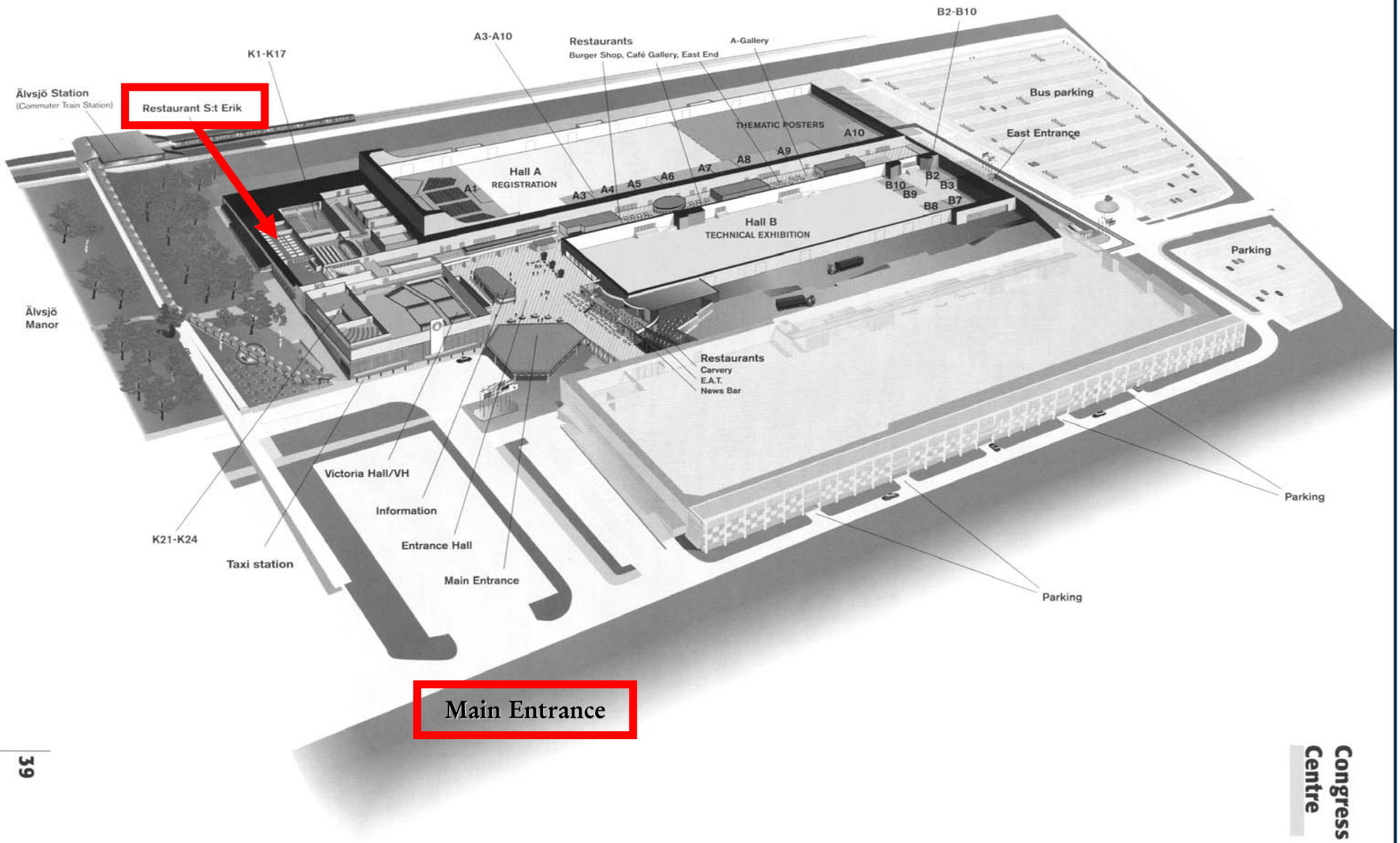
*(Please see attached **ERS_Centre.doc** for map)*

SPONSOR: Pharmacia

Innes Asher, ISAAC Chair

RSVP by
15 August 2002
n.williams@auckland.ac.nz

Dress
Informal


Älvsjö Station
(Commuter Train Station)
Restaurant S:t Erik
K1-K17
A3-A10
Restaurants
Burger Shop, Café Gallery, East End
A-Gallery
B2-B10
Bus parking
East Entrance
THEMATIC POSTERS
A10
A9
A8
A7
A6
A5
A4
A3
A1
Hall A
REGISTRATION
B10
B9
B8
B2
B3
B7
Hall B
TECHNICAL EXHIBITION
Parking
Älvsjö
Manor
Restaurants
Carvery
E.A.T.
News Bar
Victoria Hall/VH
Information
Entrance Hall
Main Entrance
Taxi station
K21-K24
Parking
Parking
Main Entrance