

Japan Environment and Children's Study
International Advisory Board Meeting Report

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Annex

Annex 1: List of IAB members and participants

Annex 2: JECS Fact Sheet

I. JECS International Advisory Board

The Japan Environment and Children's Study (JECS), launched in January 2011 achieved its goal of registering around 100,000 pregnant women in March 2014, and entered its fifth year in 2015. JECS plans to follow-up the children till they reach 13 years of age, and is currently preparing the study protocols to be applied to the children beyond the age of 6 years.

The Ministry of the Environment (MOE) considered it important to gain external advice on the study design and future plans from international experts experienced in similar birth cohort studies and environmental health projects to further improve the quality of the study and proceed to the next stage. For this purpose, the International Advisory Board (IAB) for JECS, consisting of international experts, was established and as its first attempt, the IAB meeting was held at the United Nations University, Tokyo on 14 December 2015.

Ten internationally outstanding experts around the globe were invited to comprise the IAB (Annex 1). Prior to the meeting, the JECS Fact Sheet (Annex 2) and protocols of the Main and Sub-Cohort Studies were sent to the IAB members to provide the details of JECS.

At the IAB meeting, the Director of the JECS Programme Office served as the chair and sought advice from the international experts on the focus points described below based on their expertise. The international experts provided extremely beneficial and valuable advice to promote JECS to the next stage and make JECS further contribute to Japan and the world's public health. We would like to express our utmost gratitude to the experts who joined the meeting.

IAB focus points:

JECS study design and future plans

JECS organisational structure

JECS international collaboration

JECS visibility

II. Recommendations from the International Advisory Board

Overall comments and recommendations

JECS is a unique study that is important not only for Japan but also for the global public health community. The expected results are promising to provide vital information that is applicable to develop legislation and systems which protect and improve the future children's health and

well-being in Japan and other countries. The IAB members believe that the outcome of JECS will reveal critical evidence for environmental effects on children. JECS' research content, study design and sample size are mostly approvable. By collecting data from children during the most important period of their growth, JECS is able to investigate critical windows of the environmental impact on children's health. The quality of the JECS organisation structure is impressive as it has led to internationally outstanding accomplishments, including the large number of recruited participants, high consent and response rates and extensive collection of biological samples during pregnancy. The dedication of the Japanese families to the research should also be underscored as another critical element for the success of the study.

JECS is one of the largest on-going birth cohort studies on children's environmental health in the world. Therefore, it is critical for JECS to sustain the effort for maintaining its quality so that it can be an important reference for future studies. To conduct the study successfully, it is important to receive extensive consultation from external experts and take the strength and advancement of the other studies into account.

Taking account of the paucity of the studies of environmental effects on adolescents' health, JECS should maintain at least part of the cohort for more than 13 years, if all is not possible. It is recommended to extend the planned duration for data analyses, five years after the completion of study data collection, since it seems too short for the massive amount of expected data.

Maintaining a high degree of participant retention is critical for birth cohort studies. Currently JECS keeps the withdrawal rate relatively low (~5%) resulting in over 80% of response rate. However, JECS must examine the reasons for the withdrawals in order to ensure that these withdrawals are not a sign of unaddressed problems, and make any necessary changes to its procedures to prevent the problems from posing negative influence on the progress of the study. Examination of the reasons for the withdrawals would also help JECS find out potential non-response biases.

JECS study design and future plans

Questionnaires

JECS should consider collecting information not only from mothers but also from fathers and teachers as well as children themselves. The participating children of JECS are entering a period of life that is important for development of their language, learning abilities and social-emotional functioning. By expanding the respondents to the questionnaires to school teachers and children themselves, more information on children's abilities and behaviours can be obtained. Information

sources other than family caregivers should be considered at least for data on cognitive development.

To maintain the retention rate and reduce the participants' burden, JECS should consider reducing the frequency of questionnaire administration, for example to once in every two or three years, after the participating children reach age six. The participants may feel tired from too frequent questionnaires and lose motivation to continue the participation. Less frequent questionnaire administration may also reduce logistical workloads at the Regional Centres.

On the contrary, in order to capture the intra-individual variation in environmental exposures, sending questionnaires every six months may not be sufficiently frequent. Shorter and more frequent application of online questionnaires may be beneficial for some exposure sources, such as food consumption and time-location-patterns/time-budget-data in order to reduce recall bias.

JECS should consider developing electronic or web-based questionnaires. Electronic questionnaires may also be advantageous in collecting information from children. Taking account of the well spread use of the mobile phones amongst children and their caregivers these days, the questionnaires could be designed for the mobile use as well. Questionnaires can also be designed in a way that the participating children would feel as if they are playing.

Collection of information on health outcomes

The IAB members recommend paediatricians' examination on as many subjects as possible. Since a nationwide disease registry system is not available in Japan, the planned paediatric examinations around age 6 and 12 on the Main Study will provide objective data that will be important for improving quality of child health assessment.

In the Sub-Cohort Study, obesity and physical inactivity will be important variables which would have a large influence on many outcome variables and so should be investigated in depth.

Collection, storage and analysis of biospecimens

The IAB recommends the collection of biospecimens from children around age 6. Biological samples from children will become important for directly assessing children's exposure levels. Data from chemical analysis on biospecimens and those from questionnaires should be evaluated together. The differences between parental and children's self-reported exposure to environmental stressors revealed by questionnaires should be analysed as well.

The change in the methods of long-term storage of biospecimens should be considered, as

they are important for later analyses. Experience from the German Environmental Specimen Bank can be a good reference.

JECS should consider collecting larger volume of biospecimens. The biospecimen collected in JECS will be a treasure not only for JECS but also for the other studies conducted in future.

Exposure assessment

JECS should pay close attention to other relevant research projects in the selection and measurements of priority contaminants. Collaborations with other international research projects will be helpful in selecting the target chemical substances of the study and avoiding unnecessary effort for development of new methods for measurements and analyses. Utilisation of such information could be beneficial to select target chemicals for JECS and allow comparison of results regarding exposure with those of other studies.

Attention should be given to the differences and errors that can be attributable to timing of or season for the sampling. When the indoor air quality is measured in the Sub-Cohort Study, personal exposure monitoring on randomly selected small-size samples is recommended. In the Sub-Cohort Study, the exposure variables are collected around the children's home, including the indoor chemicals, allergens and the indoor and ambient air quality. Collecting information on time spent in other places such as day care centres, schools and relatives' houses is also suggested. The planned frequency of the home visits may not be sufficient for capturing the intra-individual variation in environmental exposures.

The benefits of the cross-sectional aspects of the Sub-Cohort Study should not be underestimated. The data from the Sub-Cohort Study can possibly become precious resources for developing national exposure factors such as drinking water consumption and use of household chemicals. The Sub-Cohort Study data can also be used to calculate national environmental burden of disease (EBD). Moreover, the data will be vital for developing criteria for appropriate measures for exposure and risk reduction.

Consent/assent from children

JECS should carefully study the need and timing of obtaining informed consent from the participating children themselves. A pilot trial should be conducted to ensure that this process does not jeopardise the long-term continuation of the study participation. The age at which children will

be asked for consent, or assent, should be defined after thorough consideration. The procedures that European countries are taking could be good examples for JECS: They inform children about the study protocols in the course of the studies and take their consent at the age of 18.

Publication of study results and access to data

If the results of the study are not published in a timely manner, the value of the project may decrease. Allowing external researchers to work on the data in collaboration with the JECS study members is recommended. It is important to retrieve a data set from a researcher who is allowed to use it when a collaborative project comes to the end in order to ensure that all the data sets are kept up-to-date.

When setting a rule for giving outside researchers access to biospecimens, it is also essential to consider ways to assess the scientific quality of the proposal and determine which proposals should be given priority for the access, taking account of their limited amount. Preparation of some pre-specified criteria is a useful option.

JECS organisational structure

The IAB recommends more intensive collaboration with the health sector of the government, i.e. the Ministry of Health, Labour and Welfare (MHLW), for the further progress of JECS. Though JECS is the MOE's project with focuses on the effects of chemical substances, the outcome can be applicable to development of the public health practice in much broader areas. Study results may well be useful for the MHLW providing health advisories. The involvement of the MHLW will have wide range of positive effects on outcomes of JECS as well as development of better children's health policy. Thus, the MOE is recommended to cooperate with other Ministries and agencies in Japanese government to further utilise the outcomes of the JECS.

The JECS children will be entering school age. It may be beneficial for JECS to cooperate with school teachers and educational institutions in evaluating children's behaviour, activities and development. In addition to intra-governmental collaboration, the IAB recommends JECS to collaborate with other research projects, professionals and the medical community.

JECS international collaboration

Cooperation with other national birth cohort studies should be explored for both sharing information about study protocols and procedures and harmonisation of methodologies and instruments with

those studies in order for future pooled data analysis. Since JECS and other related birth cohort studies share the common goal which is to identify environmental causes of childhood diseases, the greater the number of participants, the better the research outcomes will be.

Taking account of the achievements made and expected future outcomes from JECS, Japan is now responsible for this unique study that will serve whole humanity. The IAB expects JECS to take the leadership in international collaboration and gain more recognition from international communities.

JECS visibility

The importance of JECS visibility to the public should be strongly emphasised in order to pursuit research outcomes of high quality.

It is important for the Japanese public to recognise the value of maintaining their support for the study. Advertising the research outcomes beyond the public health community, to the taxpayers, is also necessary. Increase in JECS presence in social media through community engagement are also critical and important. Press conferences and supports from celebrities, specialised journalists, eminent doctors, international organisations and non-government organisations should also be explored further. Appearance of the JECS representatives on television and in newspapers is effective as well.