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## **Protocol of the Elfe survey in maternity units**

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## 1 Study population and survey dates

All children born during **4 periods of 4 to 8 days across the year 2011**, in maternity units in metropolitan France listed in the sampling plan were eligible for inclusion in the survey:

- 1st period: children born on 1, 2, 3, 4, April 2011
- 2nd period: children born on 27, 28 June, 1, 2, 3, 4 July 2011
- 3rd period: children born on 27, 28, 29 September, 1, 2, 3, 4 October 2011
- 4th period: children born on 28, 29, 30 November and 1, 2, 3, 4 and 5 December 2011

By recruiting participants over 4 separate periods it was possible to recruit a part of the sample jointly with the INSEE permanent demographic sample (Echantillon Démographique Permanent).

The following **exclusion criteria** were applied:

- birth before 33 weeks of amenorrhoea
- multiple birth of more than two children
- births to parents below age 18 or who were unable to give their informed consent
- families not living in metropolitan France or who planned to move abroad or to the French overseas territories within the next three years.

### **Case of non-French-speaking parents:**

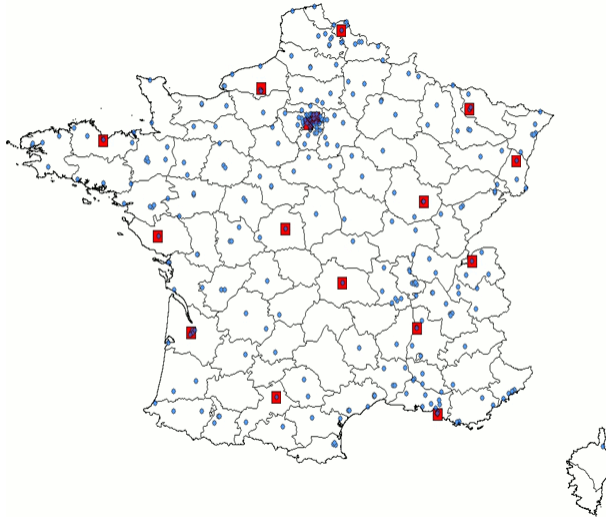
The information brochures and consent forms for inclusion at the maternity unit were translated into three languages (English, Arabic, Turkish) and only newborns with at least one parent able to provide basic information in French on how they could be contacted at a later date were included.

## 2 Maternity units selected for the maternity unit survey

The Elfe survey was conducted on a **random sample of maternity units** in metropolitan France. The maternity units were selected by means of stratified random sampling of maternity units located in France in order to under-sample units with a low expected number of births and hence reduce the costs of deploying personnel and equipment in units with a low recruitment potential. **Details of the sampling plan are given in the report on the weighting of the maternity survey data (<https://www.elfe-france.fr/en/the-research/access-to-data-and-questionnaires/>)** The sample thus obtained included 349 units out of a total of 544. It was representative of the distribution of French maternity units in terms of size, level of medical specialization, geographical location and legal status. However, as the probability of selection varied according to size, the maternity units were given different weights, depending upon the stratum to which they belong, in order to adjust the sample for statistical analysis. A sub-group of maternity units was selected to take part in the collection of biological samples, mainly because of their proximity to a blood sample treatment centre of the French

blood agency (Etablissement français du sang, EFS) (see specific protocol for biological sample collection in maternity units).

### Répartition géographique des maternités (cercles bleus) et des CRB EFS (rectangles rouges) en France métropolitaine



Geographical distribution of maternity units (blue circles) and blood treatment centres (CRB EFS; red rectangles) in metropolitan France.

## 3 Survey in maternity units

### 3.1 Providing information and obtaining consent

This first study phase was undertaken by interviewers, mostly midwives, who had been specially trained for the study and who contacted the mothers during their stay in the maternity unit. The mothers had already been informed about the study via posters and brochures in the maternity units, via the family allowance fund (Caisse d'Allocations Familiales, CAF) and via a letter sent out with the paternity booklet during the fifth month of pregnancy.

The midwife interviewer presented the study and its different phases to the mother in the days following the birth. She handed her an information brochure about the study (Appendix 1) and the consent forms to be signed (Appendix 2), giving the mother time to make up her mind. The first form, to be signed by the mother, concerned data collected in the maternity unit (via questionnaires or from her medical file). The second form concerned data collected during the follow-up period (via phone questionnaires or face-to-face interviews). This second form could be signed by one or other of the two people with parental authority (father or mother).

In addition, so that data could subsequently be collected from the SNIIRAM national health insurance database, the mother was asked in the first form to give her consent for collection of healthcare consumption data recorded by the French social security during her pregnancy, and in the second form, the father or mother were asked to give sent for collection of data on the child's healthcare consumption.

Specific consent was given by the mother for collection of biological samples and their inclusion in the Elfe biobank. Even if the mother consented to data collection in the maternity unit, she could specifically refuse to give biological samples. A distinction was made between use of samples for bioassay and DNA extraction for specific genetic analyses (research fields specified in the consent form). The mother could specifically refuse to authorize the use of her samples for genetic analysis.

## 3.2 Data collection

### 3.2.1 Inclusion in Elfe

Once the mother's consent had been obtained, the midwife interviewer entered the following information into a laptop computer (notebook) used exclusively for the survey:

- **Contact details**

These included the mother's surname and forename, maiden name, address, phone numbers (landline and mobile) and email address; the father's surname and forename, address, phone numbers (landline and mobile) and email address; and lastly, the details of two "contact" people who could be contacted in order to reach the parents if they changed their address or phone numbers without informing us (procedure designed to minimize losses to observation). The notebook was equipped with assisted data entry software to minimize error.

- **Face-to-face questionnaire with the mother**

It includes information on the mother's and father's socio-demographic situation, care during pregnancy, the delivery, drug treatments for psychological problems, tobacco and alcohol consumption and arrangements for the medical follow-up of the child.

- **Data from the medical file**

The medical file contains information on the mother's obstetrical history, previous pathologies, sixth-month blood test results, screening (toxoplasmosis, CMV, hepatitis B, HIV, syphilis) during pregnancy and treatments given if the mother tested positive, pregnancy complications (gestational diabetes, arterial hypertension, etc.), results of first, second and third trimester ultrasound scans (anthropometric measurements of the foetus, complementary examinations, prenatal diagnoses) as well as details of the delivery and the condition of the child at birth (Apgar score, etc.).

Specific case of transferred newborns:

When the infants were transferred to specialized units (neonatal unit, intensive care, surgical unit, etc.) additional information was collected on their hospital stay (type of unit, length of stay, reason for transfer: prematurity, etc.) and their health status.

**Sources:** In order to take advantage of extensive existing experience in questionnaire design acquired through successive perinatal surveys, the “face-to-face” and “obstetrical medical file” questionnaires were based on questionnaires used in national perinatal surveys. This also made it possible to position the Elfe sample with respect to a representative sample of births in France for a wide range of variables (<http://www.drees.sante.gouv.fr/l-enquete-nationale-perinatale.7214.html>)

In addition, the midwife interviewers invited mothers in the maternity unit to complete a **self-administered questionnaire** on their eating habits during the last three months of pregnancy, their use of cosmetics and household products, and their activities and leisure occupations during pregnancy. Mothers were supposed to return the questionnaire to the midwife before leaving the maternity unit. However, a few questionnaires were sent back to us spontaneously by the mothers after they had returned home.

**Sources:**

- *The food frequency questionnaire was based on that of the EDEN survey (eden.vjf.inserm.fr) and modified to include the sensory aspects of the consumption of certain foods by the mother, and additional questions on new foods. It included more than 100 items. A validation survey was conducted by comparison with three 24-hour recalls (one per month during the last three months of pregnancy) on an ad hoc sample of 62 pregnant women. An article is in preparation and the results will be published as soon as possible.*
- *The physical activity questionnaire was translated from an English language questionnaire developed and validated to measure the physical activity of pregnant women (Chasan-Taber L, Schmidt MD, Roberts DE, Hosmer D, Markenson G, Freedson PS. Development and Validation of a Pregnancy Physical Activity Questionnaire. Med Sci Sports Exer 2004 36(10):1750-1760)*
- *Questionnaires on the use of cosmetics and household products: pending*

Last, in wave 4 only, in response to recent publications suggesting that the father's nutritional status before conception may play a role in child development, fathers were invited to complete a **self-administered retrospective questionnaire** on weight changes and diet in the year preceding the pregnancy. For fathers with an Internet connection, a letter was given to mothers stating the purpose of the questionnaire and giving the web address and a personal password.

**Sources:** For the dietary part, the father's questionnaire is a food frequency questionnaire based on the one developed for the mother but with less detailed itemization of the different groups of foods (39 in all).

### 3.2.2 Non-inclusion in Elfe

When the mother refused to take part in the study, a limited amount of data was collected **anonymously**, including information given on the first health certificate established in the week

following birth. All these certificates are processed anonymously by the Direction Générale de la Santé (General health directorate) and include some information from the medical file. In the Elfe study, for all women who refused to take part, certain items of information given on the discharge certificate were recorded anonymously by the midwife interviewers: number of children in the household, educational level, occupation, occupational status, type of delivery (vaginal/caesarean), child's birthweight, body length, head circumference, gestational age, infant transfer to specialized units, presence of a congenital anomaly, and *département* of residence. This information is very important to determine the overall characteristics of non-participants and to compare them with participants via standard perinatal indicators.

### 3.3 Biological samples

In the maternity units concerned, the biological samples were taken in two phases:

- the first phase took place when the woman – who had given her prior consent – was in the delivery room (mother's urine, venous blood sample taken while setting up a blood drip, blood and umbilical cord fragments);
- the second phase took place in the maternity unit in the days following the delivery; with the mother's consent, the Elfe midwife interviewer took a lock of maternal hair, a sample of maternal milk, and samples of the child's meconium and stools taken from nappies.

The collection, preparation and storage of samples for the Elfe project were organized in partnership with the French blood agency (Etablissement Français du Sang, EFS). EFS was chosen because it has a network of blood treatment centres across the whole of France.

As indicated in the project information brochure and in the biobank consent form, the analyses performed for the Elfe study are not part of a personal clinical assessment. Individual results are not sent to respondents, except in cases where they may be used to diagnose a pathology or a need for specific medical treatment. Lead levels in the blood are one such example. If a result is abnormal, the information is given to the mother and to a physician of her choice.

### 3.4 Collection of “environmental” samples in the home

While they were in the maternity unit, consenting mothers were given “dust collectors” in the form of electrostatic cloths made from a non-woven synthetic material, along with an information brochure and instructions for use (Appendix 3). They were asked to open the collector and install it in the child's bedroom as soon as they returned home, preferably in a high position (for example, on top of a wardrobe). After remaining in place for 10 weeks, the dust collector was to be closed and returned by post in a prepaid envelope to the laboratory responsible for its microbiological analysis (fungus, mould, etc.). Mothers were given a reminder during the phone survey at two months: the interviewer asked them if the dust collector had actually been installed, and if the family planned to send it back. A total of 6,317 traps were distributed and 3,217 were analysed (figures as of 30/10/2012).

#### **4 Guarantee of participant anonymity**

Very close attention was paid to the issue of data protection and anonymization. Two requirements were stipulated: first, to separate the name and address files from the file(s) containing collected data; and second, to not create a single database containing all the information collected. To this end, a specific IT platform, PANDORA, was created, whose activation and deactivation are controlled by a data access committee (Comité d'accès aux données, CADE). It provides the necessary links between the individual Elfe participants, the data and the identifiers. This is achieved by applying a new technique that totally "atomizes" the collected data files, making it practically impossible to reassemble them without the necessary authorization and ensuring total traceability of all operations.

#### **5 Authorizations**

The first two phases of the study (survey in maternity unit and at two months) were approved by the CCTIRS and authorized by the French data protection authority (CNIL) (Deliberation no. 2011-081 dated 17 March 2011; authorization no. 910504). They also received the public statistical survey label delivered by the CNIS certification committee (*comité du label*) (visa 2011X716AU). A declaration of biological sample collection was also made to the Ministry of Research following approval by the CCP-Ile de France IX (approval no. CPP-IDF IX -11-024).