



european surveillance of
congenital anomalies

**Special Report: Sources of Information on Medication Use in
Pregnancy**

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Sources of Information on Medication Use in Pregnancy

**WP9 Medication During Pregnancy Report
Joint Action on EUROCAT**

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Introduction

With 43 registries in 23 different countries, EUROCAT surveys over 1.7 million births per year. This is now equal to 29% of the European birth population in any one year. Since most registries collect data on maternal drug use during the first trimester, EUROCAT is highly valuable as a database for pharmacovigilance studies. However, the various registries have different methods of data collection and processing. And since the quality of the data may differ between the registries, it is not always possible to pool data from them for broader studies. In this report we describe the sources of information on maternal medication use employed by the registries which contributed medication data to the EUROCAT central database for congenital anomaly cases born between 2004-2010.

Methods

The sources of information on maternal medication use, as recorded by the registries that contributed medication data to the central database, were collected on the basis of a questionnaire filled in by the following 19 registries:

- Belgium, Antwerp
- Belgium, Hainaut-Namur
- Croatia, Zagreb
- Denmark, Odense
- France, Paris
- Germany, Mainz
- Germany, Saxony-Anhalt
- Ireland, Cork & Kerry
- Italy, Emilia Romagna
- Italy, Tuscany
- Malta
- Netherlands, Northern Netherlands
- Norway
- Poland
- Poland, Wielkopolska
- Spain, Basque country
- Switzerland, Vaud
- UK, Wales
- Ukraine

The questionnaire is attached in appendix 1. It focused on the different sources of information for maternal medication use that were used by the registries and how the registries defined 'unknown medication use' and 'no medication use' in the EUROCAT Data Management Program (EDMP). The EDMP is the software program used to upload data from the registries' own software programs; it performs quality checks before the data is added to the EUROCAT central database.

Sources of medication use

We defined two major sources of information on medication use in pregnancy: ‘medical files’ and ‘registry- based data collection methods’. Medical files can be categorized into: medical files from maternal healthcare providers in relation to pregnancy; medical files from healthcare providers of the child, and medical files from maternal healthcare providers not in relation to pregnancy. The healthcare providers have recorded the data on maternal medication use in their medical files. Registry-based data collection methods can be categorized into: interviews by the registry staff and questionnaires (sent out by the registry). In these circumstances the information is provided directly by the mother and not via a healthcare provider. A scheme of the information sources is shown in the figure 1.

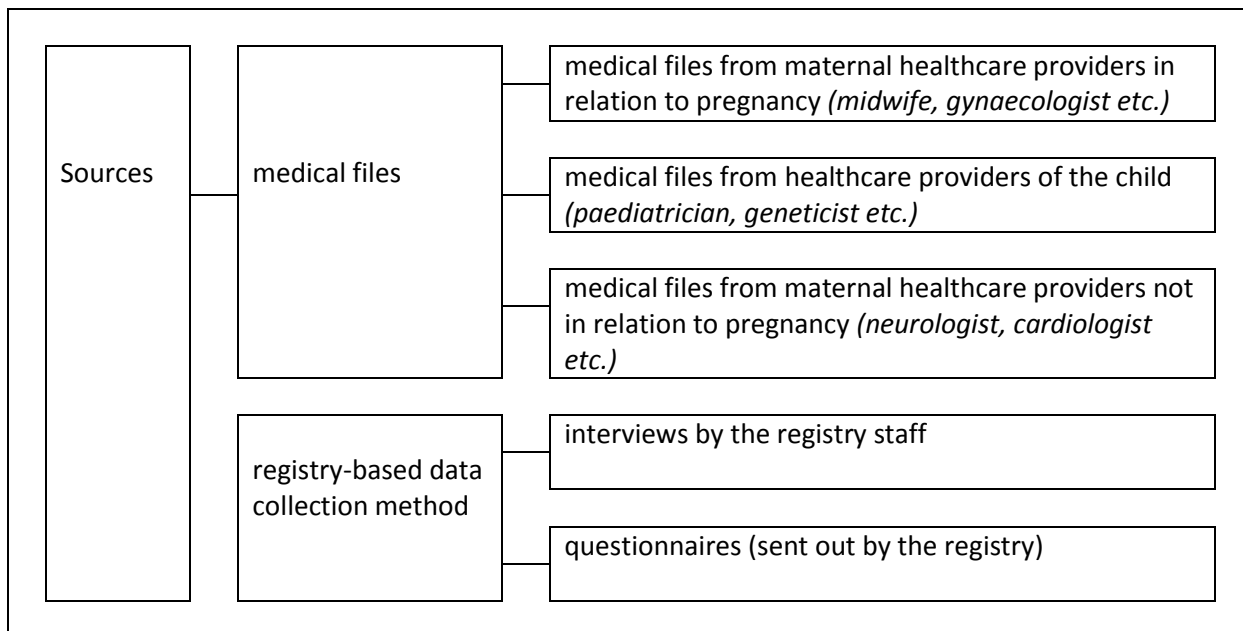


Figure 1: scheme of sources of information

For each of the five sources we asked what type of medication was usually recorded (chronic medication/ medication for short time use/ pregnancy-related medication/ Over The Counter drugs[OTC]), and with what frequency records were made (standard/sometimes/never recorded). In addition, we asked whether the records were based on prescriptions or actual use as confirmed by the mother; whether the information was based on specific questions or ‘open’ input from the mother; how the data collection took place, and for what kind of birth types this source was available.

We further asked in which situations the registry recorded maternal medication use as ‘unknown’, ‘no drugs taken’ or when the registry left the medication variable empty on the basis of multiple choice options.

Results

We collected information on the sources that provided information on maternal medication use to 19 registries, which then contribute the medication data to the central EUROCAT database.

Table 1 shows that all registries, except Tuscany, used at least one type of 'medical file' as a source and 16% (3/19) of the registries used at least one type of 'registry-based data collection method'. 21 % (4/19) of the registries only used one source. Paris, Cork & Kerry and Norway only used medical files from maternal healthcare providers in relation to pregnancy as a source. Tuscany only used a questionnaire as a source. 58 % (11/19) of the registries used two sources and 21 % (4/19) of the registries used three or more sources. Of the registries using three or more sources, Emilia Romagna used medical files from maternal healthcare providers in relation to pregnancy, medical files from health care providers of the child, and medical files from maternal healthcare providers not in relation to pregnancy. Hainaut-Namur used medical files from maternal healthcare providers in relation to pregnancy, medical files from health care providers of the child, and questionnaires sent out by the registry. Mainz used medical files from maternal healthcare providers in relation to pregnancy, medical files from health care providers of the child and medical files from maternal healthcare providers not in relation to pregnancy. Northern Netherlands used medical files from maternal healthcare providers in relation to pregnancy, medical files from health care providers of the child, medical files from maternal healthcare providers not in relation to pregnancy, interviews by the registry staff and questionnaires sent out by the registry.

Medical files from maternal healthcare providers in relation to pregnancy were the most commonly used sources 95% (18/19); this was followed by medical files from health care providers of the child: 79%(15/19). 79% (15/19) of the registries used at least medical files from at least two sources- maternal healthcare providers in relation to pregnancy and medical files from health care providers of the child.

Table 1 Sources of information on maternal medication use

	Medical files			Registry based data collection method	
	from maternal healthcare providers in relation to pregnancy ¹	from health care providers of the child ²	from maternal healthcare providers not in relation to pregnancy	interviews by the registry staff	questionnaires (sent out by the registry)
Belgium, Antwerp	X	X	-	-	-
Belgium, Hainaut-Namur	X	X	-	-	X
Croatia, Zagreb	X	X	-	-	-
Denmark, Odense	X	X	-	-	-
France, Paris	X	-	-	-	-
Germany, Mainz	X	X	X	-	-
Germany, Saxony-Anhalt	X	X	-	-	-
Ireland, Cork & Kerry	X	-	-	-	-
Italy, Emilia Romagna	X	X	X ³	-	-
Italy, Tuscany	-	-	-	-	X
Malta	X	X	-	-	-
Netherlands, Northern Netherlands	X	X	X ⁴	X	X ⁵
Norway	X	-	-	-	-
Poland	X	X	-	-	-
Poland, Wielkopolska	X	X	-	-	-
Spain, Basque country	X	X	-	-	-
Switzerland, Vaud	X	X	-	-	-
UK, Wales	X	X	-	-	-
Ukraine	X	X	-	-	-
Number of registries in total: 19	18	15	3	1	3

¹ includes midwife, obstetrician, gynaecologist, delivery units, General Practitioner [GP], pregnancy pass

² includes paediatrician, neonatologist, geneticist, paediatric cardiologist, paediatric neurologist, paediatric surgeon

³ Emilia Romagna Prescription Database, in which prescriptions are recorded irrespective of pregnancy status

⁴ pharmacy data, which are recorded irrespective of pregnancy status

⁵ maternal medication use of specific drugs (folic acid, multivitamins, vaccinations anaesthetics, insulins, other medication in relation to Diabetes Mellitus) is a standard item in the questionnaire

Medical files from maternal healthcare providers in relation to pregnancy

18 registries used medical files from maternal healthcare providers in relation to pregnancy as a source.

83% (15/18) of the registries indicate that chronic medications were usually recorded. For pregnancy-related medications, medications for short term use and OTC medications the rates were 78% (14/18), 50% (9/18) and 44% (8/18), respectively.

For 67% (12/18) of the registries using these sources, they indicated that they were aware whether actually used medications, prescribed medications or a combination of both were recorded in the medical file; whether the recording was based on specific questions of the health care provider, open input from the mother or a combination of both.

Half the registries, 42 % (5/12), recorded prescribed and actually used medication based on this source. The others recorded only prescribed medication or only actually used medication: 8% (1/12) and 50% (6/12), respectively.

A majority, 56% (10/18), of sources contained prospective information, but retrospective information or a combination was also possible: 17% (3/18) and 28% (5/18), respectively. All the sources were available for live births and still births. The sources used by the registries of Emilia Romagna, Poland and Wielkopolska (17% (3/18)) were only available for live births and still births. The sources used by the registries of Saxony-Anhalt, Cork & Kerry¹, Malta² and Norway (22% (4/18)) were available for live births, still births and fetal deaths. The sources used by the registries of Antwerp, Hainaut-Namur, Zagreb, Odense, Paris, Mainz, Northern Netherlands, Basque country, Vaud, Wales and Ukraine (61% (11/18)) contained information on live births, still births, foetal deaths and Terminations of Pregnancy for Fetal Anomaly (TOPFAs).

Medical files from health care providers of the child

15 registries used *medical files from health care providers of the child* as a source. 67% (10/15) of the registries indicate that chronic medications were usually recorded. For pregnancy-related medications, medications for short term use and OTC medications the rates were 40% (6/15), 33% (5/15) and 27% (4/15), respectively.

For 67% (10/15) of the sources, it was known how the health care provider obtained the information on medication. 'Knowing how the health care provider obtained information' means that the registry knows whether the record was for actually used medications, prescribed medications or a combination of both; whether the record was based on specific questions by the health care provider, open input from the mother or a combination of both.

A majority of registries, 70% (7/10), recorded actually used medication based on this source: the others recorded prescribed and actually used medication: 30% (3/10).

All information in these sources 100%(15/15) was retrospectively recorded

Medical files from maternal healthcare providers not in relation to pregnancy

Three registries used *medical files from maternal healthcare providers not in relation to pregnancy* as a source: Emilia Romagna, Mainz and Northern Netherlands. Emilia Romagna used the Emilia Romagna Prescription Database, which contained information on dispensed medications prescribed by General Practitioners. OTC and other medications prescribed in private clinics or dispensed by the hospital were not available. Mainz used several sources of information, like hospital data, which contain information on prescribed and actually used medication, Northern Netherlands asked the mother's permission to obtain their pharmacy records from their community pharmacy. These records contained information on all prescribed medications, except those prescribed in private clinics. OTC medication was sometimes

¹ TOPFA is illegal in Ireland

² TOPFA is illegal in Malta

recorded. The actual use was verified in a telephone interview with the mother (see interviews by the registry staff).

All sources recorded data prospectively and the data was available for all types of births. However, since for Emilia Romagna the data on women who appear in the certificate of assistance at birth were only retrieved, it was only possible to link live births and still births and not foetal deaths and TOPFAs.

Interviews by the registry staff

Only the Northern Netherlands used interviews by the registry staff as a source of information. During the interview, unclear answers in the questionnaire (see *Questionnaires (sent out by the registry)*) could be clarified, the actual use of prescribed medication according to the pharmacy record was verified and, in addition, there was a list of physical complaints to verify the mother's use of OTC during pregnancy. The interview always took place after the birth and was carried out for all types of births.

Questionnaires(sent out by the registry)

Three registries used questionnaires (sent out by the registry) as a source of information: Hainaut-Namur, Tuscany and Northern Netherlands.

For Hainaut-Namur, the use of chronic medication and pregnancy-related medication was usually recorded. The use of medication for short term use was sometimes recorded, but the use of OTC drugs was never recorded. For Tuscany, the use of chronic medication, medication for short term use, pregnancy-related medication and OTC drugs was usually recorded. The questions asked were open questions. For the Northern Netherlands, only the use of specific medications (folic acid, multivitamins, vaccinations anaesthetics, insulins, other medication in relation to diabetes) was a standard item in their questionnaire.

For Hainaut-Namur and the Northern Netherlands the questionnaires were sent out after birth and this was done for all types of birth. For Tuscany the questionnaire was not sent out by the registry, but the mother answered after birth or termination to the single questions in presence of medical professional who completed the questionnaire at that moment. Since the questionnaire was set up with the aim of data collection for the registry, it was classified as registry-based data collection method.

Discrepancies among sources

If more than one source was used, discrepancies concerning the prescription or use of medication were sometimes found, which needed to be resolved. The registries had different solutions to this problem: some made a distinction between the sources in accuracy (differences in prioritising of the sources); some verified the information (for example, by contacting the sources), and some chose the most likely option.

Information on medication use sent to Central Registry

The information on medication use is sent to the Central Registry in Ulster, where all the information is collected. Table 2 shows that 68.4% (13/19) of the registries sent information on medication use only based on the first trimester, whereas 31.6% (6/19) of the registries sent information based on the whole pregnancy.

Table 2 Information on medication use sent to Central Registry

	Only based on first trimester	Based on whole pregnancy
Belgium, Antwerp	X ¹	
Belgium, Hainaut-Namur		X
Croatia, Zagreb		X
Denmark, Odense	X	
France, Paris	X	
Germany, Mainz	X	
Germany, Saxony-Anhalt	X	
Ireland, Cork & Kerry	X	
Italy, Emilia Romagna		X
Italy, Tuscany	X	
Malta	X	
Netherlands, Northern Netherlands	X	
Norway		X
Poland		X
Poland, Wielkopolska		X
Spain, Basque country	X	
Switzerland, Vaud	X	
UK, Wales	X	
Ukraine	X	
Total:19	13	6

¹ If a drug wasn't taken in the first trimester but the onset was later we mention the drug in the "general remarks" field

Definitions of values used in EDMP for 'blank', 'drug use not known', and 'no drugs taken'

In EDMP up to five items can be notified regarding medication use. 'Drugs1' is the first item regarding drug use in EDMP which can be filled. The EUROCAT coding guide specifies that the ATC code for the drug used should be entered in this field. Where no drug is used a "0" (zero) is entered in the field; where drug use is not known, a "9" is entered. For some EUROCAT case records, the field is not filled in at all and remains 'blank'.

Table 3 shows the proportion (%) of cases in EDMP for Drugs1 with respect to 'drug taken', 'blank', 'drug use not known', and 'no drugs taken' for the years 2004-2010. From this table it is clear that registries do not always follow the instructions. Therefore in table 4 the details of the definitions of values used in EDMP for Drugs1 with respect to 'blank', 'drug use not known', and 'no drugs taken' are represented as used by the registries.

Table 3 Details of the average proportion (%) of cases in EDMP for Drugs1 with respect to ‘drug taken’, ‘blank’, ‘drug use not known’ and ‘no drugs taken’ for the years 2004-2010.

	Drug taken (inclusive a single letter, or a one or two number code and vitamins and minerals) (%)	No drugs taken “0” (%)	Unknown “9” (%)	Blank (%)
Belgium, Antwerp	6.0	8.3	40.5	45.3
Belgium, Hainaut-Namur	*1.7	*0.2	*0.0	*98.1
Croatia, Zagreb	13.2	0.1	2.4	84.3
Denmark, Odense	17.7	68.2	2.0	12.1
France, Paris	10.3	83.5	6.3	0.0
Germany, Mainz	70.4	0.0	0.0	29.6
Germany, Saxony-Anhalt	14.3	5.4	59.3	21.0
Ireland, Cork & Kerry	19.9	54.2	11.1	14.8
Italy, Emilia Romagna	33.8	23.4	42.8	0.0
Italy, Tuscany	13.2	4.1	14.0	68.8
Malta	23.0	73.8	2.3	0.9
Netherlands, Northern Netherlands	46.8	41.4	9.4	2.4
Norway	22.4	59.5	18.0	0.0
Poland	51.8	17.9	19.1	11.2
Poland, Wielkopolska	43.3	19.7	34.6	2.3
Spain, Basque country	7.7	45.1	2.4	44.8
Switzerland, Vaud ¹	14.4	59.8	25.5	0.2
UK, Wales	15.6	37.3	47.0	0.0
Ukraine	3.8	14.5	1.2	80.4
average	31.9	32.0	23.5	12.8

** based on the years 2004-2005*

Table 4 Details of the definitions of values used in EDMP for 'blank', 'drug use not known' and 'no drugs taken'.

	Definition of 'blank'					Definition of 'drug use not known'			Definition of 'no drugs taken'	
	Not enough sources of drug use for the mother can be found	The sources are found, but no mention of a drug having been taken in the first trimester can be found	Mention of a drug but the information is illegible or non-specific	"Drugs1" is never left blank	No drugs taken	Not enough sources of drug use for the mother can be found	The sources have been found, but no mention of a drug having been taken in the first trimester can be found	Mention of a drug but the information is illegible or non-specific	Record found that states the woman took no drug in the first trimester	No mention of any drug in the sources consulted can be found
Belgium, Antwerp	X		X			X		X	X	
Belgium, Hainaut-Namur	X	X	X			X			X	X
Croatia, Zagreb	X					X			X	
Denmark, Odense		X				X	X		X	
France, Paris				X		X	X	X		X
Germany, Mainz*		X			X					
Germany, Saxony-Anhalt				X		X	X	X	X	X
Ireland, Cork & Kerry				X		X	X	X	X	
Italy, Emilia Romagna		X					X		X	
Italy, Tuscany	X						X		X	
Malta	X					X				X
Northern Netherlands				X		X	X		X	X
Norway		X					X		X	
Poland				X		X	X	X	X	
Poland, Wielkopolska				X		X	X	X	X	
Spain, Basque country				X		X		X	X	X
Switzerland, Vaud				X			X		X	
UK, Wales				X		X		X	X	X
Ukraine	X						X		X	
total	6	5	2	9	1	13	13	8	17	8

From table 4 it is clear that there were large differences between the 19 registries. These should be kept in mind when compiling and analyzing data.

Most of the registries never left Drugs1 blank. When left blank, it usually meant that it was unknown if a medication was taken because not enough sources were found or the sources did not mention any drugs taken. Mainz defined blank as 'no drugs taken'.

For the definition of 'drug use not known' half of the registries applied more than one definition. More than half of the registries applied '*Not enough sources of drug use for the mother can be found*'. More than half of the registries applied '*The sources have been found, but no mention of a drug having been taken in the first trimester can be found*'. Less than half of the registries applied '*Mention of a drug but the information is illegible or non-specific*'.

For the definition of 'no drugs taken' about three-quarters of the registries applied one definition. For most registries '*Record found that states the woman took no drug in the first trimester*' was applicable. The table shows that 'No mention of any drug taken in the sources consulted' is interpreted differently between registries as either 'no drugs taken' or 'unknown drug use'.

Discussion

All registries, except Tuscany, used at least one type of 'medical file' as a source, whereas just three registries used a 'registry-based data collection method' as a source to collect data on maternal medication use. Most registries used one or two sources, while four registries used three or more sources. Medical files from maternal healthcare providers in relation to pregnancy, such as midwives and gynaecologists, were most commonly used as a source, followed by medical files from health care providers of the child. More than half of the registries used both sources. According to the registries, chronic and pregnancy-related medication use were usually recorded, although medication for short term use and OTC medication were less well recorded. Other recording aspects varied among the sources and the registries and they also have different ways of resolving discrepancies among their sources.

Medical files were most commonly used to collect information on maternal medication use. These files were readily available for most registries and the information on maternal medication use was frequently prospectively recorded. However, it was not always clear from these files if all the information on medication use was complete.

The registry-based data collection methods, such as interviews conducted by the registry staff and questionnaires (sent out by the registry), provided information on actually used medication. However, the information could be subject to bias; recall bias due to the time between the birth and the interview or questionnaire; bias due to respondents providing the socially desirable answer; and bias due to a poor response rate. Furthermore, these methods are time-consuming and higher costs are involved.

The completeness of registrations regarding medication use and the kind of medication recorded differed per registry and source of information. Some registries provided information on all kinds of medications, including OTC drugs, while others only had information on chronic medication use and medication used during pregnancy. Another important aspect is that some registries recorded the actual use, while others only recorded the prescribed use. The time of data collection and the types of births for which they took record also play a role in the

information their database holds. When using EUROCAT information for further studies, researchers must keep in mind how the registries obtained their information and should take this into account in their analyses and in drawing conclusions.

Conclusion

Most registries used one or two sources to obtain information on maternal medication use. The medical files from maternal health care providers in relation to pregnancy were most commonly used. There were differences between the registries and the sources of information they used to compile their records. When performing further studies, it is important for researchers to keep in mind how the registries obtained their information and to take this into account.

For EUROMedicAT WP3 and JOINT ACTION WP9 we are working on an overview of used sources for maternal medication use in pregnancy. We would like to map which sources are used and what kind of information these sources provide.

For the sources we distinguish 'Medical files as source for maternal medication use in pregnancy' and 'Specific data collection methods by registry'.

Medical files can be made by maternal care givers (think of midwife/obstetric/ gynecologist etc.), but also by care givers of the child (think of pediatrician, clinical geneticist etc.).

Specific data collection methods can be interviews by a registry employee, questionnaires sent out by the registry etc.

For different kind of medication (Chronic medication/ medication for short time use/ pregnancy related medication/ OTC) we would like to know whether medication use is standard/ sometimes/ never recorded. Besides, we would like to know whether the records are based on prescriptions or actual use; whether the information is based on questions or 'open' input by the mother; in which way the data collection takes place and for what kind of birth types this source is available.

In addition, we would like to map the definitions of values filled in in EDMP for 'blank', 'drug use not known' and 'no drugs taken'.

In the past, Janneke Jentink interviewed some registry leaders about data collection methods; Anthony Wemakor sent out questionnaires and during the Eurocat meeting in Budapest Marian Bakker and Hao Wang asked the present registry leaders to complete a questionnaire as well. Our idea is to combine and verify this information and to complement, where necessary.

Therefore, we designed a questionnaire and filled it out, as far as possible. Our question to you is whether you can verify the entered questions and complete where necessary.

If you are unsure which box applies best to your situation, please don't tick a box, but mention it in the comment/ explanation section underneath.

Medical files as source for maternal medication use in pregnancy

- Medical files from obstetric care giver (midwife/obstetric/ gynecologist)
- Medical files from caregivers of the child (for instance pediatrician, clinical geneticist etc.)
- Other sources (specified..)

Specific data collection methods by registry

- Interview with mother by registry
- Questionnaire by registry
- Other sources (specified..)

Definitions of values filled in in EDMP

Medical files as source for maternal medication use in pregnancy

- **Medical files from obstetric care giver (midwife/obstetric/ gynecologist)**

- ☐ Applicable, please continue with the questions on this source
☐ Not applicable, please continue with the next source

Please specify which care giver:

The first questions are on the types of medication which could be recorded.

1. *Chronic medication** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of *chronic drugs*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

2. *Medication for short time use** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of medication for short time use, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

3. *Pregnancy related medication** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of *pregnancy related medication*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

4. *OTC medication** is

- ☐ standard

- ☐ sometimes
☐ never
recorded.

Comments:

* *OTC medication* is medication which is available Over the Counter, so without prescription.

The next questions are on the procedures on obtaining information on medication.

5. Do you know how the caregiver obtains information on medication use in pregnancy?
☐ yes, please go to question 6
☐ no, please go to question 10

Comments:

6. Prescriptions of medication can be recorded, but the actual use of medication can be registered as well. How does this information source handle this?
☐ Only prescribed medication is
☐ Only actually used medication is
☐ Prescribed and actually used medication are recorded.

Comments:

7. The recorded medication is in response to
☐ specific questions asked by the caregiver, please go to question 8
☐ 'open' input by the mother, please go to question 10
☐ specific questions asked by the caregiver and 'open' input by the mother, please go to question 8

Comments:

8. The questions asked by the caregiver are
☐ open
☐ closed
☐ open and closed.

Comments:

9. The caregiver asks for
(please tick all those which apply)
☐ specific drug groups
☐ specific drugs
☐ variable/ not clear

Comments:

Medication use can be recorded during one moment in or the whole pregnancy (prospective) and after pregnancy (retrospective). How does this information source handle this?

10. Data collection takes place in a
- ☐ retrospective (recorded after pregnancy)
 - ☐ prospective (recorded during pregnancy)
 - ☐ retrospective and prospective

Comments:

Does this information source contain information on medication use for all types of birth?

11. This source is available for
(please tick all those which apply)

- ☐ live births
- ☐ still births
- ☐ fetal death
- ☐ TOPFAs

Comments:

12. Did this reporting method change over time?
- ☐ yes, please specify
 - ☐ no

Comments:

- Medical files from caregivers of the child (for instance pediatrician, clinical geneticist etc.)

☐ Applicable, please continue with the questions on this source

☐ Not applicable, please continue with the next source

Please specify which care giver:

The first questions are on the types of medication which could be recorded.

1. *Chronic medication** is

☐ standard

☐ sometimes

☐ never

recorded.

Comments:

* For examples of *chronic drugs*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

2. *Medication for short time use** is

☐ standard

☐ sometimes

☐ never

recorded.

Comments:

* For examples of medication for short time use, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

3. *Pregnancy related medication** is

☐ standard

☐ sometimes

☐ never

recorded.

Comments:

* For examples of *pregnancy related medication*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

4. *OTC medication** is

☐ standard

☐ sometimes

☐ never
recorded.

Comments:

* *OTC medication* is medication which is available Over the Counter, so without prescription.

The next questions are on the procedures on obtaining information on medication.

5. Do you know how the caregiver obtains information on medication use in pregnancy?
- ☐ yes, please go to question 6
- ☐ no, please go to question 10

Comments:

6. Prescriptions of medication can be recorded, but the actual use of medication can be registered as well. How does this information source handle this?
- ☐ Only prescribed medication is
- ☐ Only actually used medication is
- ☐ Prescribed and actually used medication are recorded.

Comments:

7. The recorded medication is in response to
- ☐ specific questions asked by the caregiver, please go to question 8
- ☐ 'open' input by the mother, please go to question 10
- ☐ specific questions asked by the caregiver and 'open' input by the mother, please go to question 8

Comments:

8. The questions asked by the caregiver are
- ☐ open
- ☐ closed
- ☐ open and closed.

Comments:

9. The caregiver asks for
(please tick all those which apply)
- ☐ specific drug groups
- ☐ specific drugs
- ☐ variable/ not clear

Comments:

Medication use can be recorded during one moment in or the whole pregnancy (prospective) and after pregnancy (retrospective). How does this information source handle this?

10. Data collection takes place in a
- ☐ retrospective (recorded after pregnancy)
 - ☐ prospective (recorded during pregnancy)
 - ☐ retrospective and prospective

Comments:

Does this information source contain information on medication use for all types of birth?

11. This source is available for
(please tick all those which apply)

- ☐ live births
- ☐ still births
- ☐ fetal death
- ☐ TOPFAs

Comments:

12. Did this reporting method change over time?
- ☐ yes, please specify
 - ☐ no

Comments:

- **Other sources (specified..)**

- ☐ Applicable, please continue with the questions on this source
- ☐ Not applicable, please continue with the next source

Please specify which care giver:

The first questions are on the types of medication which could be recorded.

1. *Chronic medication** is

- ☐ standard
- ☐ sometimes
- ☐ never
- recorded.

Comments:

* For examples of *chronic drugs*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

2. *Medication for short time use** is

- ☐ standard
- ☐ sometimes
- ☐ never
- recorded.

Comments:

* For examples of medication for short time use, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

3. *Pregnancy related medication** is

- ☐ standard
- ☐ sometimes
- ☐ never
- recorded.

Comments:

* For examples of *pregnancy related medication*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

4. *OTC medication** is

- ☐ standard
- ☐ sometimes
- ☐ never

recorded.

Comments:

* *OTC medication* is medication which is available Over the Counter, so without prescription.

The next questions are on the procedures on obtaining information on medication.

5. Do you know how the caregiver obtains information on medication use in pregnancy?

- ☐ yes, please go to question 6
- ☐ no, please go to question 10

Comments:

6. Prescriptions of medication can be recorded, but the actual use of medication can be registered as well. How does this information source handle this?

- ☐ Only prescribed medication is
- ☐ Only actually used medication is
- ☐ Prescribed and actually used medication are recorded.

Comments:

7. The recorded medication is in response to

- ☐ specific questions asked by the caregiver, please go to question 8
- ☐ 'open' input by the mother, please go to question 10
- ☐ specific questions asked by the caregiver and 'open' input by the mother, please go to question 8

Comments:

8. The questions asked by the caregiver are

- ☐ open
- ☐ closed
- ☐ open and closed.

Comments:

9. The caregiver asks for
(please tick all those which apply)

- ☐ specific drug groups
- ☐ specific drugs
- ☐ variable/ not clear

Comments:

Medication use can be recorded during one moment in or the whole pregnancy (prospective) and after pregnancy (retrospective). How does this information source handle this?

10. Data collection takes place in a
- ☐ retrospective (recorded after pregnancy)
 - ☐ prospective (recorded during pregnancy)
 - ☐ retrospective and prospective

Comments:

Does this information source contain information on medication use for all types of birth?

11. This source is available for
(please tick all those which apply)

- ☐ live births
- ☐ still births
- ☐ fetal death
- ☐ TOPFAs

Comments:

12. Did this reporting method change over time?

- ☐ yes, please specify
- ☐ no

Comments:

Specific data collection methods by registry

- **Interview with mother by registry**

- ☐ Applicable, please continue with the questions on this source
☐ Not applicable, please continue with the next source

The first questions are on the types of medication which could be recorded.

1. *Chronic medication** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of *chronic drugs*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

2. *Medication for short time use** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of medication for short time use, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

3. *Pregnancy related medication** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of *pregnancy related medication*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

4. *OTC medication** is

- ☐ standard
☐ sometimes
☐ never

recorded.

Comments:

* *OTC medication* is medication which is available Over the Counter, so without prescription.

The next questions are on the procedures on obtaining information on medication.

5. Prescriptions of medication can be recorded, but the actually use of medication can be registered as well. How does this information source handle this?

- ☐ Only prescribed medication is
- ☐ Only actually used medication is
- ☐ Prescribed and actually used medication are recorded.

Comments:

6. The recorded medication is in response to

- ☐ specific questions asked by the registry employee, please go to question 7
- ☐ 'open' input by the mother please go to question 9
- ☐ specific questions asked by the registry employee and 'open' input by the mother, please go to question 7

Comments:

7. The questions asked by the registry employee are

- ☐ open
- ☐ closed
- ☐ open and closed.

Comments:

8. The registry employee asks for
(please tick all those which apply)

- ☐ specific drug groups
- ☐ specific drugs
- ☐ variable/ not clear

Comments:

Medication use can be recorded during one moment in or the whole pregnancy (prospective) and after pregnancy (retrospective). How does this information source handle this?

9. Data collection takes place in a

- ☐ retrospective (recorded after pregnancy)
- ☐ prospective (recorded during pregnancy)

☐ retrospective and prospective

Comments:

Does this information source contain information on medication use for all types of birth?

10. This source is available for
(please tick all those which apply)

- ☐ live births
- ☐ still births
- ☐ fetal death
- ☐ TOPFAs

Comments:

11. Did this reporting method change over time?

- ☐ yes, please specify
- ☐ no

Comments:

- **Questionnaire by registry**

- ☐ Applicable, please continue with the questions on this source
☐ Not applicable, please continue with the next source

The first questions are on the types of medication which could be recorded.

1. *Chronic medication** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of *chronic drugs*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

2. *Medication for short time use** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* For examples of medication for short time use, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

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- ☐ standard
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☐ never
recorded.

Comments:

* For examples of *pregnancy related medication*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

4. *OTC medication** is

- ☐ standard
☐ sometimes
☐ never
recorded.

Comments:

* *OTC medication* is medication which is available Over the Counter, so without prescription.

The next questions are on the procedures on obtaining information on medication.

5. Prescriptions of medication can be recorded, but the actually use of medication can be registered as well. How does this information source handle this?

- ☐ Only prescribed medication is
- ☐ Only actually used medication is
- ☐ Prescribed and actually used medication are recorded.

Comments:

6. The recorded medication is in response to

- ☐ specific questions asked in the questionnaire, please go to question 7
- ☐ 'open' input by the mother please go to question 9
- ☐ specific questions asked in the questionnaire and 'open' input by the mother. please go to question 7

Comments:

7. The questions asked in the questionnaire are

- ☐ open
- ☐ closed
- ☐ open and closed.

Comments:

8. In the questionnaire is asked for
(please tick all those which apply)

- ☐ specific drug groups
- ☐ specific drugs
- ☐ variable/ not clear

Comments:

Medication use can be recorded during one moment in or the whole pregnancy (prospective) and after pregnancy (retrospective). How does this information source handle this?

9. Data collection takes place in a

- ☐ retrospective (recorded after pregnancy)
- ☐ prospective (recorded during pregnancy)
- ☐ retrospective and prospective

Comments:

Does this information source contain information on medication use for all types of birth?

10. This source is available for
(please tick all those which apply)

- ☐ live births
- ☐ still births
- ☐ fetal death
- ☐ TOPFAs

Comments:

11. Did this reporting method change over time?

- ☐ yes, please specify
- ☐ no

Comments:

- **Other sources (specified..)**

- ☐ Applicable, please continue with the questions on this source
- ☐ Not applicable, please continue with the next source

Please describe the source

The first questions are on the types of medication which could be recorded.

1. *Chronic medication** is

- ☐ standard
- ☐ sometimes
- ☐ never
- recorded.

Comments:

* For examples of *chronic drugs*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

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- ☐ standard
- ☐ sometimes
- ☐ never
- recorded.

Comments:

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- ☐ standard
- ☐ sometimes
- ☐ never
- recorded.

Comments:

* For examples of *pregnancy related medication*, please check Table 1 of Bakker M, Jentink J, Vroom F et al. Drug prescription patterns before, during and after pregnancy for chronic, occasional and pregnancy-related drugs in the Netherlands. *BJOG* 2006; 113: 559-5

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Comments:

* *OTC medication* is medication which is available Over the Counter, so without prescription.

The next questions are on the procedures on obtaining information on medication.

5. Prescriptions of medication can be recorded, but the actually use of medication can be registered as well. How does this information source handle this?

- ☐ Only prescribed medication is
- ☐ Only actually used medication is
- ☐ Prescribed and actually used medication are recorded.

Comments:

6. The recorded medication is in response to

- ☐ specific questions asked in the source, please go to question 7
- ☐ 'open' input by the mother please go to question 9
- ☐ specific questions asked in the source and 'open' input by the mother, please go to question 7

Comments:

7. The questions asked in the source are

- ☐ open
- ☐ closed
- ☐ open and closed.

Comments:

8. In the source is asked for
(please tick all those which apply)

- ☐ specific drug groups
- ☐ specific drugs
- ☐ variable/ not clear

Comments:

Medication use can be recorded during one moment in or the whole pregnancy (prospective) and after pregnancy (retrospective). How does this information source handle this?

9. Data collection takes place in a

- ☐ retrospective (recorded after pregnancy)
- ☐ prospective (recorded during pregnancy)

☐ retrospective and prospective

Comments:

Does this information source contain information on medication use for all types of birth?

10. This source is available for
(please tick all those which apply)

- ☐ live births
- ☐ still births
- ☐ fetal death
- ☐ TOPFAs

Comments:

11. Did this reporting method change over time?

- ☐ yes, please specify
- ☐ no

Comments:

General:

If more than one source of information used, how does the registry solve the discrepancies?

Definitions of values filled in in EDMP

The last part of the questionnaire is on the definitions you handle of values filled in in EDMP, namely: 'blank'; 'drug use not known' and 'no drugs taken'.

Could you please specify which applies/ apply to your registry?
(please tick all those which apply)

Definition of 'blank'	<input type="checkbox"/> <i>When I cannot find enough of the sources of drug use for the mother</i> <input type="checkbox"/> <i>When I have found the sources but I cannot find any mention of a drug having been taken in the first trimester</i> <input type="checkbox"/> <i>When there is mention of a drug but the information is illegible or non-specific</i> <input type="checkbox"/> <i>Other, specify</i> <input type="checkbox"/> <i>I never leave "Drugs1" blank</i>
Definition of 'drug use not known'	<input type="checkbox"/> <i>When I cannot find enough of the sources of drug use for the mother</i> <input type="checkbox"/> <i>When I have found the sources but I cannot find any mention of a drug having been taken in the first trimester</i> <input type="checkbox"/> <i>When there is mention of a drug but the information is illegible or non-specific</i> <input type="checkbox"/> <i>Other, specify</i>
Definition of 'no drugs taken'	<input type="checkbox"/> <i>When I find a record that states the woman took no drug in the first trimester</i> <input type="checkbox"/> <i>When I find no mention of any drug in the sources that I consult</i> <input type="checkbox"/> <i>Never because we cannot be sure of our sources</i> <input type="checkbox"/> <i>Other, specify</i>

Comments: