Supplementary Information

Article title: Core data elements for pregnancy pharmacovigilance studies using primary source data collection methods: Recommendations from the IMI ConcePTION project

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Online Appendix: Listings of core data element recommendations

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Table 1: Database administrative details

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Pregnancy exposure	The report relates to a confirmed pregnancy (where a woman was carrying a fertilised oocyte, developing embryo or fetus, irrespective of the outcome) with exposure to a medical product	Values: a) Yes, b) No	Yes*	Yes*	Directly reported	Dataset creation	*This may only be relevant for datasets collecting reports of exposures and clinical outcomes in groups which are not necessarily pregnant. For example, in pregnancy registries all cases are exposed but this is not the case in drug registries and spontaneous adverse drug reaction datasets.
Mother case identifier	Unique database identifier for the pregnant woman	Text	NA	NA	Internally generated	Database functionality Dataset creation	Maternal identifiers (e.g. name, date of birth, healthcare system number) and contact details (e.g. address, email, telephone number) will be required for follow-up purposes in prospective data collection systems.
Baby case identifier	Unique database identifier for each offspring record	Text	NA	NA	Internally generated	Database functionality Dataset creation	Infant identifiers (e.g. name, date of birth, healthcare system number) and parental contact details (e.g. name, address, email, telephone number) will be required for follow-up purposes in longer-term prospective data collection systems.
Mother-Baby case link identifier	Common unique identifier linking mother with fetus/fetuses or child/children (same	Text	NA	NA	Internally generated	Database functionality Dataset creation	

	identifier located on both maternal and fetal/offspring records)						
Primary reporter type	Type of reporter providing the information	Values: a) Healthcare professional, b) Other	Yes	Yes	Directly reported	Follow-up/case queries Sub-setting	The primary reporter is assumed to collect information from evolving sources during pregnancy. Additional detail about the type of non-healthcare professional reporter may be required in some data collection instances (example, it may be useful to specifically identify reports from medication users – parents of affected children – or individuals which believe to have been affected by in utero medication exposure).
Primary reporter contact details	Name and contact details for the primary reporter	Value 1: Title Value 2: Name Value 3: Address Value 4 Telephone number Value 5: Email address	Yes	Yes	Directly reported	Follow-up/case queries	Contact details may include postal and/or email address and telephone number.
Initial report date	Date when pregnancy is initially reported to the data collection system	Date (dd/mm/yyyy)	Yes	Yes	Directly reported or internally generated	Derivation (pro/retrospective reporting status) Sub-setting	
Prospective status	Whether the pregnancy was reported prospectively or retrospectively	Values: a) Prospective, b) Retrospective, c) Unknown	Yes	Yes	Directly reported Derived (see notes)	Sub-setting	Prospective - Report of a drug-exposed pregnancy (either during pregnancy or prior to conception) whilst the patient is still pregnant Retrospective - Report of a drug-exposed pregnancy (either during pregnancy or prior to

							conception) after the pregnancy has ended. Where required, alternative definitions of pro/retrospective can be constructed from the information collected about prenatal tests together with the Initial report date and date of end of pregnancy. The collection of additional information (e.g., timing of, type of and findings from prenatal screening) is generally recommended to enable refinement of the prospective definition (e.g., in line with EMA/FDA definitions of pro/retrospective) according to the needs of the research activity. Definitions of prospective status are likely to be different for studies investigating longer-term health and neurodevelopmental outcomes.

Table 2: Maternal/paternal details

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Maternal date of birth	Mother's date of birth	Date (dd/mm/yyyy)	Yes	Yes	Directly reported	Dataset creation Derivation (age at LMP)	Availability depends on local law/data collection and storage permissions.
Maternal age at last menstrual period (LMP)	Mother's age (in years) on the first day of the last menstrual period prior to the pregnancy	Integer	Yes	Yes	Directly reported	Sub-setting Risk factor	Availability depends on local law/data collection and storage permissions.
Household income	The total annual household income (mother and partner before any tax or other deductions).	Value 1: Integer* Value 2: Currency (when >1 country)	No	Yes	Directly reported	Sub-setting Risk factor	An important measure of socioeconomic status. *This may be considered an overly intrusive question for some study participants. Alternative options for collecting the data could be to ask participants to state whether household income is above or below a national or regional average, or alternatively to use income brackets representing quintiles of the national/regional distribution. Post-collection processing to determine if above or below the national average for that country likely required.

							Studies running in a single country with comparable incomes between study subjects could utilize this as a continuous variable or use other markers of socioeconomic status (e.g. residential area). International studies will require standardisation.
Maternal education	Highest level of education achieved by the mother	Options: a) No formal education, b) Primary school (First school/Up to around 11 years)), c) Secondary school (Second school/Up to around 16 years), d) College (Sixth form/Up to around 18 years), e) University (18+ years), f) Unknown	No	Yes	Directly reported	Sub-setting Risk factor	Post collection processing required to determine if above or below the national average for the maternal country. Studies running in a single country could utilize this as a continuous variable. International studies will require standardisation.
Paternal education	Highest level of education achieved by the father	Options: a) No formal education, b) Primary school (First school/Up to around 11 years)), c) Secondary school (Second school/Up to around 16 years), d) College (Sixth form/Up to around 18 years), e) University (18+ years), f) Unknown	No	No	Directly reported	Sub-setting Risk factor	Post collection processing required to determine if above or below the national average for the maternal country. This may not be available in all cases but should still be collected where possible.
Maternal IQ	Intellectual ability of the mother	Value 1: Integer Value 2: Name of measurement tool (free text)	No	No*	Directly reported	Sub-setting Risk factor	* Not essential but highly recommended as an important co-variable risk factor in studies assessing child neurodevelopment.

							Intellectual ability of the mother as measured by a formal, clinically validated tool accepted for measuring adult IQ in the country of data collection. This data should be considered for both educational and cognitive longer term childhood outcomes.
Maternal ethnicity	The ethnicity of the mother	Options (see notes): a) Aboriginal b) Australian, c) American Indian, d) Arab, e) Black/African, f) Central Asian, g) East Asian, h) Hispanic, i) Hawaiian or Pacific Islander, j) Inuit, k) South American l) Native, m) South Asian, n) White, o) Mixed Race, p) Other, q) Unknown	No	No	Directly reported	Sub-setting Risk factor	There are no internationally accepted and validated ethnicity or racial categories which cover all ethnic groups or races around the world. Those proposed in the Recommended data format and suggested values column are thought to represent the most common general terms that are applied when referring to the different ethnicities or races around the world. However, this list should be adapted to ensure any important ethnic/racial differences which exist in the general population where the study is being conducted can be considered in statistical analyses.
Consanguinity	The father of the baby is a first or second degree relative of the mother	Value 1: a) Yes, b) No, c) Unknown If “Yes”, Value 2: Text (details)	No	Yes	Directly reported	Sub-setting Risk factor	Only the categorical response can be used in data sub-setting or as a risk factor statistic. May be useful to improve analysis of infant first year outcomes like growth and congenital anomaly data.

Maternal Height	Height (cm) of the mother at the time of conception	Integer	No*	Yes**	Directly reported	Derivation (BMI) Risk factor	*Important to collect if BMI not collected (for derivation), may also be valuable for assessing birth weight for gestational age using personalised growth charts (see Table 10) Convert from feet and inches, etc. **Relevant to longer term child growth outcomes but not neurodevelopmental outcomes.
Maternal Weight pre-pregnancy	Actual or approximate weight (kg) of the mother at or around the time of conception	Integer	No*	No*	Directly reported	Derivation (BMI)	*Important to collect if BMI not collected (for derivation), may also be valuable for assessing birth weight for gestational age using personalised growth charts (see Table 10) Convert from stones and pounds, etc.
Maternal BMI pre-pregnancy	Maternal BMI at the time of conception (kg/m2)	Integer	Yes	Yes	Derived (Maternal height and maternal weight pre-pregnancy)	Risk factor	
Maternal country of residence	Country in which the mother resides at the time of reporting	Value: ISO 3166 Alpha-2 codes	No	Yes	Directly reported	Sub-setting Population standardisation Risk factor	The diagnosis and assessment of longer-term child outcomes (e.g. neurodevelopment) may differ across regions and countries. Studies running in a single country may wish to utilise data
Smoking in pregnancy	Maternal smoking of	Value 1: a) Yes, b) No, c) Unknown	No*	Yes	Directly reported	Risk factor	*Not essential for data analysis but highly recommended as these are important co-variable risk

	tobacco during pregnancy	If “Yes”, Value 2: Text (details of use, including timing, duration and amounts)					factors Only the categorical response can be used in data sub-setting. Level of nicotine exposure may correlate with longer term outcomes.
Alcohol in pregnancy	Maternal alcohol consumption during pregnancy	Value 1: a) Yes, b) No, c) Unknown If “Yes”, Value 2: Text (details of use, including timing, duration and amounts)	No*	Yes	Directly reported	Risk factor	*Not essential for data analysis but highly recommended as these are important co-variable risk factors Only the categorical response can be used in data sub-setting. Level of alcohol exposure may correlate with longer term outcomes.
Illicit drugs in pregnancy	Maternal recreational drug use in pregnancy (details of drugs, approximate daily amount ingested, duration of use in pregnancy)	Value 1: a) Yes, b) No, c) Unknown If “Yes”, Value 2: Text (details of use, including timing, duration and amounts)	No*	Yes	Directly reported	Risk factor	*Not essential for data analysis but highly recommended as these are important co-variable risk factors Only the categorical response can be used in data sub-setting. Level of exposure may correlate with longer term outcomes.
Folic acid use	Maternal folic acid use in pregnancy	Value 1: a) None, b) Started pre-conception, c) Started first trimester, d) Started after first trimester, e) Unknown If not “None” or "Unknown" – Value 2: a) 400 micrograms (µg), b)	No*	Yes	Directly reported	Risk factor	*Not essential for data analysis but highly recommended as these are important co-variable risk factors Level of folate exposure may be essential for certain longer term outcomes.

		5 mg, c) Other (dose - text)					

Table 3: Pregnancy details

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Date of LMP	Date of the first day of the last menstrual period prior to conception	Date (dd/mm/yyyy)	Yes	Yes	Directly reported	Derivation (Pro-/retrospective reporting status) Derivation (exposure timing) Derivation (gestational age at pregnancy outcome)	This refers to the LMP associated with this pregnancy (not with earlier cycles). LMP is derived as EDD-280 days (please note in early pregnancy, the EDD is derived from LMP, whereas in later pregnancy the EDD can be defined from ultrasound fetal crown-rump length measurements) or (where EDD is unknown) the date of end of pregnancy minus the gestational age at end of pregnancy (in days). International variations exist with regards to updating the EDD (based on ultrasound fetal crown-rump length measurements) during prenatal care. In some locations, these updates may always be applied, whereas in others they may only be appliedd if the EDD is altered by >5 days.
Expected date of delivery (EDD)	Expected date of delivery	Date (dd/mm/yyyy)	Yes	Yes	Directly reported	Derivation (Pro-/retrospective reporting status) Derivation (exposure timing)	The directly reported value may have been based on (e.g.) the date of LMP, results from ultra-sound examinations, the date of embryo transfer (assisted fertilisation). Alternatively, it could be derived from entered dates of LMP based on 280 day gestation length (using the LMP date) or 266 day gestation length

						Derivation (gestational age at pregnancy outcome)	(using estimated date of conception from fetal ultrasound measurements).
Source of directly reported EDD	The final method used to establish the estimated date of delivery	Value 1 - Options: a) LMP, b) Date of embryo transfer, c) Ultrasound results, d) Other (detail) - Text	Yes	Yes	Directly reported	Database management Sub-setting	The EDD may change over the course of the pregnancy (e.g. those based on date of LMP are potentially inaccurate and can be improved upon by ultrasound measurements performed at the end of the first trimester). This detail may be requested during peer-review of study publications, and is a useful statement to add to methods sections to show that any estimated exposure periods are accurate. Clinical calculation of EDD could be based on LMP, Date of embryo transfer (assisted fertilisation), Ultrasound Measurement, or any other obstetric evaluation.
Assisted conception	Assisted conception technique utilised for this pregnancy	Options: a) Yes, b) No, c) Unknown	No	No	Directly reported	Risk factor	
Plurality	Number of fetuses in current pregnancy	Integer	Yes	Yes	Directly reported	Sub-setting	Multiple fetus pregnancies are considered to be at higher risk of several adverse pregnancy/fetal outcomes. Researchers may decide to exclude multiple fetus pregnancies from primary analyses, or conduct sensitivity analyses using the information collected in this variable. Details about the type of multiple pregnancy (e.g. mono-/dichorionic or mono-/diamniotic) my also be valuable when assessing case

							specific risk factors for adverse pregnancy outcome.
Prenatal test(s)	Details of any medical prenatal examination or test performed to investigate fetal wellbeing/medical conditions	Value 1: Date test performed (dd/mm/yyyy) Value 2 (approx. gestational age in days when test was performed): Text Value 3 (Type of prenatal test (see notes): Text Value 4 (Were any congenital anomalies identified) - Options: a) Yes, b) No, c) Unknown If “Yes”, Value 5 (Congenital anomaly details/ findings/ diagnosis): Text If “Yes”, Value 6 (MedDRA/ICD diagnosis code): Text If “Yes”, Value 7 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text	Yes	Yes	Directly reported	Derivation (Pro-/retrospective status) Derivation (Congenital anomaly status)	Values to be reported for each prenatal test performed. Tests to be reported here are only those that have been conducted in a medical setting, social or non-clinical prenatal ultrasound scans should not be described. Value 3 example options for tests include: a) Chorionic Villous Biopsy, b) Amniocentesis, c) Cordocentesis, d) 2d USS, e) 4d USS, f) Maternal blood tests, g) Nuchal translucency, h) Maternal serum (alpha fetal protein etc.), i) Other

Table 4: Maternal medical history details

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Maternal pre-pregnancy medical conditions (history)	Maternal medical conditions present prior to pregnancy	Value 1 - Options: a) Yes, b) No, c) Unknown If “Yes”, Value 2 (MedDRA/ICD diagnosis code): Text If “Yes”, Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text If, “Yes”, Value 4 (Age (in years) at diagnosis): Integer	Yes	Yes*	Directly reported	Study sample demographics Sub-setting Risk factor	Details regarding any pre-existing conditions which may act as risk factors for adverse pregnancy/fetal/infant/childhood outcomes are to be collected. Information may also come from drug indication or concomitant drugs. Examples of important co-morbidities include asthma, autoimmune diseases, cancer, diabetes, epilepsy, hypertension, infection (cytomegalovirus, hepatitis, HIV, herpes simplex, sexually transmitted diseases etc.), neurological conditions (multiple sclerosis etc.), psychiatric illness, organ transplant and thyroid function disorders. *Details regarding maternal mental health are valuable for studies investigating childhood health and neurodevelopmental outcomes, studies investigating these outcomes may benefit from adding separate variables to their data collection forms to ensure this important information is collected

Table 5: Family medical history and obstetric history details

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Family history of congenital anomalies	The presence of any congenital anomaly (major or minor) in any sibling (live born, stillborn or terminated), or the mother or the father of the reference pregnancy, or their immediate/ first degree relatives (grandparents, aunts or uncles of the reference pregnancy)	Value 1 - Options: a) Yes, b) No, c) Unknown If "Yes", Value 2 (MedDRA/ICD diagnosis code): Text If "Yes", Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text If "Yes", Value 4 (record details of anomaly, and relationship to the affected family member): Text	No*	No*	Directly reported	Sub-setting Risk factor Derivation (number of previous pregnancies with congenital anomalies)	*Not essential but highly recommended as an important co-variable risk factor. Only the categorical response can be used in data sub-setting or as a risk factor statistic. May be useful to improve analysis of infant congenital anomaly data.
Relevant family history of genetic conditions	The presence of any genetic condition in a relative thought to be the explanation or of relevance to the abnormalities reported in the reference pregnancy	Value 1 - Options: a) Yes, b) No, c) Unknown If "Yes", Value 2 (MedDRA/ICD diagnosis code): Text	No*	No*	Directly reported	Sub-setting Risk factor	*Not essential but highly recommended as an important co-variable risk factor. Only the categorical response can be used in data sub-setting or as a risk factor statistic. May

		If “Yes”, Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text If “Yes”, Value 4 (record details of the condition(s), and relationship to the affected family member): Text					be useful to improve analysis of infant congenital anomaly data.
Relevant family history of learning disability or of neurodevelopmental disorders	The presence of a learning disability or neurodevelopmental disorder (e.g. attention deficit hyperactivity disorder or autistic spectrum disorder) in a sibling, mother, father or their immediate / first degree relatively (grandparents, aunts or uncles of the reference pregnancy)	Value 1 - Options: a) Yes, b) No, c) Unknown If “Yes”, Value 2 (MedDRA/ICD diagnosis code): Text If “Yes”, Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text If “Yes”, Value 4 (record details of the condition(s), and relationship to the affected family member): Text	No	No*	Directly reported	Sub-setting Risk factor	*Not essential but highly recommended as an important co-variable risk factor. Only the categorical response can be used in data sub-setting or as a risk factor statistic. History of learning disability or neurodevelopmental disorders may be relevant to neurodevelopmental outcomes but less essential for certain childhood health variables.
Relevant family history of diseases with onset in childhood	The present of a health condition which onsets in childhood (<18 years of age)	Value 1 - Options: a) Yes, b) No, c) Unknown	No	No*	Directly reported	Risk factor	*Not essential but highly recommended as an important co-variable risk factor.

		If “Yes”, Value 2 (MedDRA/ICD diagnosis code): Text If “Yes”, Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text If “Yes”, Value 4 (record details of the condition(s), and relationship to the affected family member): Text					Only the categorical response can be used in data sub-setting or as a risk factor statistic. History of health conditions may be relevant to child health conditions but less so to other longer term outcomes (e.g. neurodevelopmental outcomes)
Number of previous pregnancies	Number of previous pregnancies (including non-live births) experienced by the mother only	Integer	No	No	Directly reported	Risk factor	
Number of previous live births	Number of previous live births	Integer	No*	No*	Directly reported	Sub-setting Risk factor	*Not essential but highly recommended as an important co-variable risk factor. May be useful to improve analysis of infant birth weight data Birth order may be particularly relevant for certain developmental outcomes
Number of previous spontaneous abortions	Number of previous spontaneous abortions	Integer	No*	No	Directly reported	Sub-setting Risk factor	*Not essential but highly recommended as an important co-variable risk

							factor. May be useful to improve analysis of miscarriage data
Number of previous induced terminations	Number of previous induced terminations (for any reason)	Integer	No	No	Directly reported	Sub-setting Risk factor	
Number of previous stillbirths	Number of previous stillbirths	Integer	No*	No	Directly reported	Sub-setting Risk factor	*Not essential but highly recommended as an important co-variable risk factor. May be useful to improve analysis of stillbirth data
Number of previous pregnancies with congenital anomalies	Number of previous pregnancies (including non-live births) experienced by the mother which resulted in a fetus or child with congenital anomalies	Integer	No*	No	Directly reported	Sub-setting Risk factor	*Not essential but highly recommended as an important co-variable risk factor. May be useful to improve analysis of infant congenital anomaly data

Table 6: Pregnancy medication exposure details

Each of the following CDE items are to be collected for each maternal medication exposure considered relevant to the reported pregnancy (including preconception exposures up to 6 months prior to pregnancy as standard or longer if relevant; e.g. medications with very long half-lives/conservative labelling recommendations). Multiple start/stop dates should be collected for all medications that are stopped and then restarted.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Drug name(s)	International non-proprietary drug name (i.e. active ingredient(s) of the medicinal product)	Value 1 (name): Text Value 2: ATC code Date (dd/mm/yyyy)	Yes	Yes	Directly reported	Dataset creation Sub-setting/risk factor Derivation (period of exposure: Preconception / Peri-LMP / Trimester 1 / Trimester 2 / Trimester 3)	Includes the drug(s) targeted for investigation and concomitant drugs. Multiple start/stop dates should be collected for all medications that are stopped and then restarted.
Drug start date	Date at which the medication used during pregnancy was started	Date (dd/mm/yyyy)	Yes	Yes	Directly reported	Derivation (period of exposure: Preconception / Peri-LMP / Trimester 1 / Trimester 2 / Trimester 3) Derivation (gestational age at exposure)	Multiple start/stop dates should be collected for all medications that are stopped and then restarted. Start dates are to be recorded for each separate period of use of the drug in the pregnancy under the same record (e.g. Start 1: dd/mm/yyyy, Start 2: dd/mm/yyyy).

						Dataset creation Sub-setting Risk factor	Missing dates should be entered as “missing”.
Drug stop date	Date at which the medication used during pregnancy was stopped	Date (dd/mm/yyyy)	Yes	Yes	Directly reported	Derivation (period of exposure: Preconception / Peri-LMP / Trimester 1 / Trimester 2 / Trimester 3) Derivation (gestational age at exposure) Dataset creation Sub-setting Risk factor	Stop dates are to be recorded for each separate period of use of the drug in the pregnancy under the same record (e.g. Stop 1: dd/mm/yyyy, Stop 2: dd/mm/yyyy). Missing dates should be entered as “missing”.
Drug indication(s)	Specific indication for which the medication was used	Value 1: Text Value 2 (MedDRA/ICD diagnosis code): Text Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text	Yes	Yes	Directly reported	Dataset creation Sub-setting Risk factor	
Peri-LMP exposure	Exposure before LMP in a time period considered relevant to the half-life of the medication under	Options: a) Yes, b) No	Yes	Yes	Directly reported Derived	Dataset creation Sub-setting	“Exposure” relates to the timing when the medication was administered.

	investigation and other concomitant medications (e.g. five half-lives) and/or a time period defined clinically relevant given the expected length of time the medication can produce pharmacodynamics effects				(Drug start/stop dates, Date of LMP)	Risk factor Report statistics	Exposure during this period may be reported directly or defined during data analysis using medication start and stop dates.
Trimester 1 exposure	Exposure occurring in the first trimester (from date of LMP to date of LMP+90 days)	Options: a) Yes, b) No	Yes	Yes	Directly reported Derived (Drug start/stop dates, Date of LMP/EDD)	Dataset creation Sub-setting Risk factor Report statistics	"Exposure" relates to the timing when the medication was administered. Varying definitions of the pregnancy trimesters are available. This document aligns with the UK RCOG definitions. Consequently, trimester 1 is defined to start at the date of LMP, approximately 14 days before conception and therefore covers a period when the fetus may not be exposed directly. Depending on the medication exposure under study, the proposed definition of "first trimester exposure" may be too broad to be considered scientifically relevant for examining malformation risks following in utero medication exposure. For example, medications which are not used to treat a chronic medical condition and may only be used for short time periods may be discontinued between the

							LMP date and the date of conception. Provided these medications have a short half-life, pre-conception exposures probably have limited relevance with regards to malformation risks in the developing fetus. In such cases, the exposure period of interest may need to be adapted so that it more accurately overlaps with the expected period of organogenesis (e.g. from conception - approximately 2 weeks post-LMP - until the end of the tenth week gestational age)
Trimester 2 exposure	Exposure occurring in the second trimester (from date of LMP+91 days to date of LMP+188)	Options: a) Yes, b) No	Yes	Yes	Directly reported Derived (Drug start/stop dates, Date of LMP/EDD)	Dataset creation Sub-setting Risk factor Report statistics	"Exposure" relates to the timing when the medication was administered. Varying definitions of the pregnancy trimesters are available. This document aligns with the UK RCOG definitions.
Trimester 3 exposure	Exposure occurring in the third trimester (from date of LMP+189 days onwards)	Options: a) Yes, b) No	Yes	Yes	Directly reported Derived (Drug start/stop dates, Date of LMP/EDD)	Dataset creation Sub-setting Risk factor Report statistics	"Exposure" relates to the timing when the medication was administered. Varying definitions of the pregnancy trimesters are available. This document aligns with the UK RCOG definitions.

Route of exposure	Route by which the medication is administered	Options: a) Aural, b) Inhalation, c) Ocular, d) Oral, e) IV, f) IM, g) Rectal, h) Topical, i) Vaginal, j) Other (detail) - Text	Yes	Yes	Directly reported	Dataset creation Sub-setting	
Dose per use	Amount of medication administered per use	Value 1: Integer Value 2: Unit (g / mg / mcg / IUs etc.)	Yes	Yes	Directly reported	Dataset creation Sub-setting Risk factor	This detail in combination with time period of use and frequency of use details may be useful for assessing risks associated with daily or cumulative doses.
Frequency of use	Number of times the medication is taken per unit of time	Value 1 (Times taken): Integer Value 2 (Unit of time) – Options: a) day, b) 2-days, c) 3-days, d) week, e) 2-weeks, f) 3-weeks, g) 4-weeks, h) month, i) 2-months, j) 3-months, k) 6-months, l) year, m) Other (detail) - Text	Yes	Yes	Directly reported	Dataset creation Sub-setting Risk factor	This detail in combination with time period of use and dose per use details may be useful for assessing risks associated with daily or cumulative doses

Table 7: Maternal illness and obstetric complication details

Due to the multiplicity of possible medical conditions and measurements of disease activity/severity, it was not considered feasible to provide specific recommendations around the collection of maternal medical conditions arising either during pregnancy or in the post-partum period.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Maternal medical conditions arising in pregnancy	Any maternal medical condition arising during pregnancy	Value 1 (detail): Text Value 2 (MedDRA/ICD diagnosis code): Text Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text Value 4 (gestational age when condition was diagnosed in days): Integer	Yes*	Yes**	Directly reported	Sub-setting Risk factor Report statistics	Value 4 (gestational age when condition was diagnosed in days) is considered an important detail for this data element as it will allow researchers to perform analysis of events occurring at aetiologically relevant time points in the pregnancy. *The importance of maternal medical conditions arising during pregnancy as a co-variable risk factor for adverse pregnancy/infant outcome may vary by the outcome under analysis. **Details regarding maternal mental health are valuable for studies investigating childhood health and neurodevelopmental outcomes, studies investigating these outcomes may benefit from adding separate variables to their data collection forms to ensure this important information is collected.
Maternal post-partum complications	Any maternal complication occurring post-delivery	Value 1 - Options: a) Yes, b) No, c) Unknown	No	Yes	Directly reported	Sub-setting	

		Value 2 (MedDRA/ICD diagnosis code): Text Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text				Risk factor Report statistics	
Maternal death	Death of a woman while pregnant or ≤42 days of the end of the pregnancy (including live/stillbirth delivery, ectopic pregnancy, miscarriage or termination) from any cause related to or aggravated by the pregnancy or its management but not from accidental or incidental causes.	Value 1 - Options: a) Yes, b) No, c) Unknown If “Yes”, Value 2 (date of death): Date (dd/mmm/yyyy) Values 3 (cause of death, MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) - Text	Yes	Yes	Directly reported	Sub-setting Risk factor Report statistics Follow-up	

Table 8: Pregnancy outcome details

The following CDE items should be collected for each fetus in the reported pregnancy.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Pregnancy outcome collection status	Status of pregnancy outcome details reported to the system	Options: a) Outcome known, b) Follow-up pending, c) Lost-to-follow-up, d) Missing	Yes	Yes	Internally generated (derived from reported outcome details)	Dataset creation Follow-up	
Date of end of pregnancy	Date at which the pregnancy completes (for all outcomes).	Date (dd/mm/yyyy)	Yes	Yes	Directly reported Derived (gestational age at end of pregnancy and date of LMP or date of EDD)	Derivation (pro/retrospective status) Derivation (LMP/EDD and subsequently exposure timing) Derivation (gestational age at end of pregnancy)	For live births, this will be the date of delivery (infant date of birth). For terminations/evacuation of retained products of conception, this will be the date the procedure was performed.
Gestational age at end of pregnancy	Gestational age in days (post-LMP) at the time the pregnancy ended	Integer	Yes	Yes	Directly reported Derived (date of end of pregnancy and date of LMP or date of EDD)	Derivation (pro/retrospective status) Derivation (LMP/EDD and subsequently exposure timing)	Calculated as either the time since the first day of the LMP or from prenatal ultrasound scans If necessary, converted from weeks and days (post-LMP) or weeks and days (based on

						Derivation (pre/postmature delivery) Derivation (birth weight for gestational age)	prenatal ultrasound measurements)
Induced termination	Induced abortion (either medical or surgical) of a pregnancy for any reason	Value 1 - Options: a) Yes, b) No, c) Unknown If, “Yes”, Values 2 (reason for termination) - Options: a) Non-medical reason, b) Medical reason (maternal indication), c) Medical reason (fetal indication), d) Other, e) Unknown If “Other”, Value 3 (details): Text	Yes	Yes	Directly reported	Report statistics	
Ectopic pregnancy	Implantation outside of the endometrial cavity (including tubal, cervical, caesarean scar, interstitial, cornual, ovarian, abdominal, hetertopic or of unknown location) confirmed by transvaginal ultrasound.	**Options: a) Yes, b) No, c) Unknown**	Yes	Yes	Directly reported	Report statistics	
Stillbirth	Death of a fetus prior to the complete expulsion or extraction from its mother, after the 22nd	**Options: a) Yes, b) No, c) Unknown**	Yes	Yes	Directly reported	Report statistics	In line with EMA recommendations, this document defines stillbirth as fetal loss >22 completed weeks

	completed week post-LMP (≥154 days) of pregnancy; the death is indicated by the fact that after such separation the fetus does not breathe or show any other evidence of life, such as beating of the heart, pulsation of the umbilical cord or definite movement of voluntary muscles						post-LMP. International definitions of stillbirth vary. Some definitions rely purely on the gestational age at pregnancy loss (varying from 20 weeks post-LMP to 28 weeks post-LMP), others also consider the weight of the fetus at pregnancy loss (e.g. fetal weight >500g required to classify as a stillbirth/intrauterine death). Definitions may require local adaptation. Post-mortem details should be recorded where available.
Spontaneous abortion	Death of a fetus prior to the complete expulsion or extraction from its mother, before the 22nd completed week of pregnancy (≤153 days).	Options: a) Yes, b) No, c) Unknown	Yes	Yes	Directly reported	Report statistics	See notes on stillbirth.
Molar pregnancy	A non-viable product of conception which can be either a 'complete mole' arising after single sperm fertilisation of an ovum lacking genetic material, or a 'partial mole' which arises as a consequence of multi-sperm fertilisation of a healthy ovum. An invasive mole (formerly known as chorioadenoma destruens) is a	Options: a) Yes, b) No, c) Unknown If “Yes”, Value 2 - Options: a) Hydatidiform Mole (complete or partial), b) Invasive Mole, c) Mole of unknown type	Yes	Yes	Directly reported	Report statistics	

	hydatidiform mole that has grown into the muscle layer of the uterus						

Table 9: Delivery details

The following CDE items should be collected for each delivery event in the reported pregnancy (e.g. in rare cases where there is more than one delivery event at different times or where delivery methods vary for each fetus/infant).

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Labour onset	How labour began	Value 1- Options: a) Natural onset, b) Membrane sweep, c) Amniotomy, d) Vaginal prostaglandin tablet, pessary or gel, e) Mifepristone/ misoprostol, f) Other, g) Unknown If "Other", Value 2 (details): Text	No	No	Directly reported	Sub-setting Risk factor	
Mode of delivery	The method by which the fetus was delivered from the mother	Value 1 - Options: a) Spontaneous vaginal delivery (incl. vertex/ breach), b) Assisted vaginal delivery (incl. forceps / ventouse). C) Emergency C-section (post-labour / pre-labour), d) Elective C-section, e) Unknown If "Emergency C-section", Value 2 (details): Text	No*	No*	Directly reported	Sub-setting Risk factor	*Not essential but highly recommended as an important co-variable risk factor.
Maternal delivery complications	Any maternal complications arising as a result of the delivery method during or after delivery	Value 1 - Options: a) Yes, b) No, c) Unknown If "Yes", Value 2 (MedDRA/ICD diagnosis code): Text If "Yes", Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text If "Yes", Value 4 (Timing of complication): Text	No	No	Directly reported	Sub-setting Risk factor	

Table 10: Live/stillborn birth outcome details

The following CDE items should be collected for each live or stillborn infant from the reported pregnancy.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Gestational timing of live/stillborn offspring	Whether a live birth or stillbirth was preterm, full term, or post-term infant	Options: a) Pre-term, b) Full term, c) Post-term, d) Unknown	Yes	Yes	Directly reported Derived (gestational age at end of pregnancy) Derived (date of end of pregnancy and date of LMP or date of EDD)	Report statistics Sub-setting	The directly reported value may be based on the date of LMP or on assessments from prenatal ultrasound scans. Preterm is <37 weeks (<259 days), full-term is ≥37 to <42 weeks (≥259 and <294 days), and post-term is ≥42 weeks (≥294 days).
Infant birth weight	Weight of the offspring at delivery (in grams)	Integer	Yes	Yes	Directly reported	Report statistic Derivation (SGA and LGA) Risk factor (longer term outcomes)	
Infant sex	Sex of the offspring at birth	Options: a) Male, b) Female, c)	Yes	Yes	Directly reported	Report statistics	

		Undetermined, d) Unknown				Derivation (SGA and LGA) Sub-setting Risk factor (longer term outcomes)	
Infant head circumference	Occipito-frontal circumference (i.e. the widest circumference of the skull from the broadest part of the forehead (above the eyebrow and ears) to the most prominent part of the rear of the head), measured using a non-stretchable flexible tape - to be recorded in cms	Integer (in centimeters)	Yes	No*	Directly reported	Report statistics	*Not essential but highly recommended as an important co-variable risk factor. Microcephaly has been associated with a number of congenital infections and medication teratogens. Additionally, microcephaly is classified as a major malformation as per the EUROCAT guidelines. Therefore, this variable, although may not be routinely available, is considered essential for pregnancy/infant outcomes and highly recommended for childhood outcomes.
Infant birth length	Heel to crown (knees flat) measurement of recumbent infant length - to be recorded in cms	Integer (in centimeters)	No	No*	Directly reported	Report statistics	*Not essential but highly recommended as an important co-variable risk factor.
Small for Gestational Age at delivery	An infant born with a birth weight less than the 10th centile on population-level infant birth weight charts	Options: a) Yes, b) No, c) Unknown	Yes	Yes	Directly reported Derived (birth weight, gestational age at delivery, infant	Report statistics	Birth weight for gestational age charts may be customised for various factors including gestational age at delivery as a minimum and additionally maternal BMI, parity and ethnicity, and infant sex.

					sex, national birth weight charts)		Note, that when extracting data, this outcome detail might be collected as adverse events in the baby.
Large for Gestational Age at Delivery	An infant born with a birth weight greater than the 90th centile on population-level infant birth weight charts	Options: a) Yes, b) No, c) Unknown	Yes	Yes	Directly reported Derived (birth weight, gestational age at delivery, infant sex, national birth weight charts)	Report statistics	Birth weight for gestational age charts may be customised for various factors including gestational age at delivery as a minimum and additionally maternal BMI, parity and ethnicity, and infant sex. Alternatively, a resource such as the WHO growth charts or Intergrowth-21 may be utilized, occasionally these are available with local standardisations applied. Note, that when extracting data, this outcome detail might be collected as adverse events in the baby.
Apgar score	Apgar score at set time intervals post-delivery	1-Min Score: Value 1 - Options: a) Known, b) Unknown If “known”, Value 2 (Apgar score, 0-10): Integer 5-Min Score: Value 1 - Options: a) Known, b) Unknown If “known”, Value	No	No	Directly reported	Report statistics	Not relevant for stillbirth outcomes (using the definition of stillbirth in these recommendations). Apgar is a clinical scoring system used to establish the clinical status of the newborn at one and five minutes post-delivery, and every additional five minutes until 20 minutes in infants with ongoing Apgar scores <7. The scoring system comprises five components investigating: Appearance (skin colour), Pulse (heart rate), Grimace (reflexes), Activity (muscle tone) and

		2 (Apgar score, 0-10): Integer 10-Min Score: Value 1 - Options: a) Known, b) Unknown If “known”, Value 2 (Apgar score, 0-10): Integer 15-Min Score: Value 1 - Options: a) Known, b) Unknown If “known”, Value 2 (Apgar score, 0-10): Integer 20-Min Score: Value 1 - Options: a) Known, b) Unknown If “known”, Value 2 (Apgar score, 0-10): Integer					Respiration (respiration rate). Scores of between 0 and 2 are provided for each component depending on the clinical features of the newborn, providing summary scores of between 0 and 10. Scores of 7-10 are reassuring, 4-6 moderately abnormal, and 0-3 as low. Whilst these scores are important early markers of neonatal status, there is no clear association with longer term outcomes.

Table 11: Live born neonatal/infant outcome details

The following CDE items should be collected for each live born infant from the reported pregnancy.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Complications in the first year of life	Any complication experienced in the first year of life	Value 1 - Options: a) Yes, b) No, c) Unknown If "Yes", Value 2 (MedDRA/ICD diagnosis code): Text If "Yes", Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 4 (record additional details of the complication not covered by the coding system): Text Value 5 (did the complication occur in the neonatal period) - Options: a) Yes, b) No, c) Unknown	Yes	Yes	Directly reported	Report statistics	Note that this element should contain data relating to neonatal complications (complications arising from birth until the end of 27th day after birth, i.e. first 28 days of life).
Postnatal death of live born infant	Details of the death of a live born infant	Value 1 - Options: a) Yes, b) No, c) Unknown If "Yes", Value 2 (date of death): Date	Yes	Yes	Directly reported	Report statistics Follow-up	Age at death categories include infant death where the offspring dies in the first year after birth, or childhood death where the offspring dies beyond the first year

		(dd/mmm/yyyy) If “Yes”, Value 3 (MedDRA/ICD cause of death code): Text If “Yes”, Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 5 (record additional details of the complication not covered by the coding system): Text Values 6 (age at death category) - Options: a) Infant death, b) Child death, c) Unknown If “Infant death”, Values 7 (neonatal death) - Options: a) Yes, b) No, c) Unknown					after birth. Neonatal deaths are a sub-category of infant death where the offspring dies after birth but before the end of 27th day after birth, i.e. within the first 28 days of life. It is recommended to record age at death in days for children <1 month old, record in months for children <2 years old and years in children ≥2 years. Post-mortem details should be recorded where available.
Product/disease-specific outcomes	Offspring outcomes specific to the investigated medicinal product	Value 1 - Options: a) Yes, b) No If “Yes”, Value 2 (MedDRA/ICD diagnosis code): Text If “Yes”, Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text	Yes*	Yes*	Directly reported	Report statistics	*Only essential these details are collected when these outcomes are to be described in the study report statistics. Examples may include measures of immune function in the offspring of those exposed to immunosuppressant in utero.

		Value 4 (record additional details of the complication not covered by the coding system): Text Values 5 (age at diagnosis): Integer					

Table 12: Malformation details

The following CDE items should be completed for each fetus in the reported pregnancy.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Congenital anomaly	Presence of any structural/morphological, functional or biochemical anomaly(ies) in the fetus that occur during intrauterine life and can be identified prenatally, at birth or later in life	Options: a). Yes, b) No, c) Unknown	Yes	Yes	Directly reported	Report statistics	
Details of all congenital anomaly(ies)	Details of the anomaly(ies) present in the exposed fetus	Value 1 (diagnosis: free text in accordance with coded diagnostic term(s)): Text Value 2 (MedDRA/ICD diagnosis code): Text Value 3 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 4 (age at diagnosis): Text	Yes	Yes	Directly reported	Report statistics Sub-setting	These fields will be empty where no anomalies are described. It is important to confirm the details through postnatal examination or investigation, or post-mortem. Record details for each anomaly separately.

Infant malformation case classification	Classification of status of a fetus / infant case with an anomaly(ies) based on a hierarchy of observed events	Options: a) Genetic malformation case, b) Major malformation case (non-genetic), c) NOS malformation case (non-genetic), d) Minor malformation case (non-genetic).	Yes	Yes	Reported Derived (based on reported details and classification system)	Report statistics Sub-setting	**It is strongly recommended that this element is completed by an expert committee.** **Classifications should only be undertaken by experienced researchers/clinicians.** **For statistics reporting purposes it is the fetus or infant that is categorized not each individual malformation.** **Cases are categorised according to the following hierarchical logic:** **1. Does the baby have any structural malformation events or birth defects (i.e., non-functional/biochemical anomalies)?** **2: (if yes) Does the baby have any genetic/cytogentic malformation events?** **2a: (if yes) classify case as genetic malformation case** **2b: (if no) classify case per EUROCAT as: - Major malformation case** **if the fetus has a malformation but there are insufficient details to allow the classification, then classify as: - NOS malformation case** **if not major or NOS, then classify as: - Minor malformation**

							case **Each congenital malformation event is judged by experienced adjudicators (qualified paediatrician, clinical geneticist, teratologist, paediatric neurologist, nephrologist, toxicologist, or clinical pharmacologist), according to the EUROCAT guidance.** **In fetuses/infants with more than one malformation, the case categorisation is determined by the presence of any anomaly meeting the criteria of the highest-ranking category in the following hierarchy: Genetic malformation > Major malformation (non-genetic)> Unspecified malformation (NOS (non-genetic); not otherwise specified) > Minor malformation (non-genetic).**

Table 13: Longer-term child health outcome details

It is recognised that not all child longer-term outcomes will be able to be covered by a single study but the domains listed here should be covered by a set of complementary studies, which together build up a comprehensive evidence-base. It is also noted that individual measurements of offspring health and development will not be sufficient to detect nor exclude associations between in utero medication exposure and adverse health or neurodevelopmental outcomes; rather data should be collected regularly throughout childhood.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Infant/child medical problems	Has the infant/child had any medical problems since birth.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Values 2 (date of diagnosis): Date (dd/mmm/yyyy) Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail): Text Value 5 (additional relevant details not covered by coding system): Text	Yes	Yes	Directly reported	Report statistics	These details should be recorded for every medical problem experienced during infancy or childhood. Child health is very complex and numerous conditions may present. For the purposes of the CDE recommendations, it was not considered practical to include a listing of all possible conditions. If researchers are aware of any specific conditions related to either an exposure or outcome of interest, these should also be included specifically. There may also be benefit in including detail on condition severity.
Infant/child specialist visit	Has the child required any specialist reviews?	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 - Options: a) Paediatrician, b) Nutritionist, c) Clinical Geneticist, d) Ophthalmologist, e) Child	Yes	Yes	Directly reported	Report statistics	There are considerable international variations in healthcare utilisation practices. In some countries, access to a specialist may be routine, whereas in others, specialist review may be reserved for more severe conditions. As such, there may be variation in the

		Development Centre, f) Audiologist, g) Physiotherapist, h) Speech Therapist, i) Occupational Therapist, j) Psychologist, k) Neurologist, l) Other If Other, Value 3 (details): Text					suitability of this data variable to identify signals of infant/childhood health or neurodevelopmental concerns. In countries where routine specialist access is observed, researchers may wish to limit the collection of this data element to non-standard clinical interactions (if possible).
Infant/child medication	Child medication use.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (medication name): Text Value 3 (ATC code): Text Value 4 (indication): Text Value 5 (MedDRA/ICD diagnosis code): Text Value 6 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 7 (date started): Date (dd/mm/yyyy) Value 8 (date stopped if applicable): Date (dd/mm/yyyy)	Yes	Yes	Directly reported	Report statistics Risk factor	
Infant/child professional concerns	Report of any developmental concerns raised by professionals.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (details): Text	Yes	Yes	Directly reported	Report statistics	It may be educational or health professional who raise concerns.

Infant/child vision difficulties	Difficulties with child vision.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (details): Text Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 5 (difficulties confirmed by an eye test) - Options: a) Yes, b) No, c) Unknown	Yes	Yes	Directly Reported	Report statistics	
Infant/child hearing difficulties	Difficulties with child hearing.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (details): Text Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 5 (difficulties confirmed by a hearing test) - Options: a) Yes, b) No, c) Unknown	Yes	Yes	Directly Reported	Report statistics	
Infant/child toileting difficulties	Does the child have any frequent difficulties with the	Value 1 - Options: a) Yes, b) No, c) Unknown	Yes	Yes	Directly Reported	Report statistics	

	passing of urine or opening of their bowels?	If Yes, Value 2 (details): Text Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text					
Infant/child eczema/ skin conditions	Diagnosis of eczema or other skin conditions.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (details): Text Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 5 (details of any investigations): Text	Yes	Yes	Directly Reported	Report statistics	
Infant/child asthma/ respiratory conditions	Diagnosis of asthma or other respiratory conditions.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (details): Text Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text	Yes	Yes	Directly Reported	Report statistics	

		Value 5 (details of any investigations): Text					
Infant/child congenital heart disease	Diagnosis of congenital heart disease.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (details): Text Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 5 (details of any investigations): Text	Yes	Yes	Directly Reported	Report statistics	
Infant/child food allergies	Diagnosis of food allergies.	Value 1 - Options: a) Yes, b) No, c) Unknown If Yes, Value 2 (details): Text Value 3 (MedDRA/ICD diagnosis code): Text Value 4 (Coding system) - Options: a) MedDRA, b) ICD10, c) Other (detail) – Text Value 5 (details of any investigations): Text	Yes	Yes	Directly Reported	Report statistics	

Table 14: Longer-term child neurodevelopmental outcome details

It is recognised that not all child longer-term outcomes will be able to be covered by a single study but the domains listed here should be covered by a set of complementary studies, which together build up a comprehensive evidence-base. It is also noted that individual measurements of offspring health and development will not be sufficient to detect nor exclude associations between in utero medication exposure and adverse health or neurodevelopmental outcomes; rather data should be collected regularly throughout childhood.

CDE Item	Definition	Recommended data format and suggested values	Essential to collect when studying pregnancy and infant outcomes	Essential to collect when studying longer term childhood outcomes	Source	Purpose	Notes
Child cognitive functioning	The expected developmental level within the area of cognitive functioning varies by the age of the child. This should be measured via age appropriate assessment using either 1. parental completed questionnaires 2. through direct research / clinical assessment of the child or 3. Diagnoses of deficits (e.g. intellectual disability). 4. Attainment of key milestones.	Will depend on the method of collection	Yes	Yes	Directly reported	Report statistics	Includes functioning in the areas of intelligence, memory, attention and executive functioning.
Child motor functioning	The expected developmental level within the area of motor functioning varies by the age of the child. This should be measured via age appropriate assessment using either 1. parental completed questionnaires 2. though direct researcher assessment of the child or 3. Diagnoses of deficits relating to motor development/ functioning (e.g. dyspraxia). 4. Attainment of key milestones.	Will depend on the method of collection	Yes	Yes	Directly reported	Report statistics	
Child language functioning	The expected developmental level within the area of language functioning varies by the age of the child. This should be measured via age appropriate assessment using either 1. parental completed questionnaires 2. through direct research / clinical assessment of the	Will depend on the method of collection	Yes	Yes	Directly reported	Report statistics	Attainment of cognitive milestones can be used but due to normal variation in attainment times and cross-cultural differences,

	child or 3. Diagnoses of deficits (e.g. language delay or disability). 4. Attainment of key milestones.						standardized questionnaire or assessments are more valid.
Child social functioning	The expected level of social functioning varies by the age of the child. This should be measured via age appropriate assessment using either 1. parental completed questionnaires 2. though direct researcher assessment of the child or 3. Diagnoses of deficits relating to social development/functioning (e.g. autism spectrum disorder). 4. Attainment of key milestones.	Will depend on the method of collection	Yes	Yes	Directly reported	Report statistics	
Child behaviour and emotional functioning	The expected level of behaviour and emotional varies by the age of the child. This should be measured via age-appropriate assessment using either 1. parental completed questionnaires 2. though direct researcher assessment of the child or 3. Diagnoses of deficits relating to behavioural or emotional regulation difficulties (e.g. attention deficit hyperactivity disorder, depression). 4. Attainment of key milestones.	Will depend on the method of collection	Yes	Yes	Directly reported	Report statistics	