Filing of pregnancies in Argus

Scope

This instruction describes how to enter pregnancy information in Argus for the following report types:
Spontaneous, **Literature**, **Solicited** and **Clinical trial**

The overall requirements for processing data in Argus are outlined in Q040018.

For trial identification (ID): NN1250-4300, please refer to the Clinical Trial Study Description on SharePoint for the specific guidance on how to perform Argus case entry.

Applies to

This instruction applies to all Argus case handlers, who perform case entry and verification of individual case safety reports (ICSRs) in Argus.

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Age Groups and Report Types

In this instruction, the term **'child'** is used as an umbrella term to describe the following three age groups (also see section 'Definitions'):

- Neonate (from 0 to 27 completed days);
- Infant (from 28 days to 23 completed months);
- Child (from 2 years to 11 completed years)

Handling of personal data in pregnancy cases: all personal data must be handled in accordance with Q171710, Q040018 and Q145488. Please refer to section 6 Analysis Tab for examples.

In this instruction, **Spontaneous** and **Literature** have the same colour-coding, as they follow the same process for case handling.

Clinical trial and **Solicited** (only non-interventional studies): For information on which forms are to be completed, refer to the appropriate protocol or agreement and Q110034. For further information on reporting **Clinical trial** cases, see Q110034.

1 How Many Cases to Create in Argus

For all cases where there is both a parent and a foetus/child case, the cases must be linked, except in trial ID: NN1250-4300 where cases should only be linked if medically relevant.
Ensure case numbers of the linked cases are entered in the additional information tab under 'reference ID' and case numbers are in the narrative (see reference Q145488 for linking cases).

In this instruction, the term **'exposure'** will be used to cover one or more of the following events capturing drug exposure:

- 'Maternal exposure during pregnancy'
- 'Paternal drug exposure'
- 'Drug exposure in utero'
- 'Drug exposure via breast milk'
- 'Exposure via father'

Other terms reflecting pregnancy are available and can be used on a case-by-case basis. For example, in cases where the patient was not exposed to the product during pregnancy.

Spontaneous, Literature and **Solicited**:
Enter adverse events (AEs) and the 'exposure' event in the same case if it is the same patient. Create separate cases to capture 'parent' and 'child' events. If the parent has more than one pregnancy, create separate cases for each pregnancy.

For further information on reporting **Spontaneous and Literature** cases, see reference Q112556.

Clinical trials (not dedicated pregnancy trials/studies):

Create a case with the 'exposure' event.

- If an AE occurs to the mother during the same pregnancy, this event can be added to the existing exposure case. Medical judgement should be used in determining whether to add the new event to the existing exposure case.

- For trials using the EDC-Argus interface where the option to draw an ISIR is available: If additional parental AEs occur, and are reported on a separate SIF, there is the option to reject the file on the E2B pending list and use the ISIR to update the existing exposure case (if deemed medically relevant). The relevant notification report should be combined with the ISIR.

- For trials using the EDC-Argus interface where the option to draw an ISIR is not available: If additional parental AEs arise, and are reported on a separate Safety Information Form (SIF), create a separate case for the AE (do **NOT** create another 'exposure' event).

- Ensure that all related cases are linked using the reference ID – World Wide Unique Identifier format (see section 8 Additional Information Tab).

- If an AE occurs to the foetus/child, create a separate foetus/child case, code both the AE and 'Drug exposure in Utero/Drug exposure via breast milk/Exposure via father' or another term if none of the above are appropriate, and link the case to the parent case.

- Please note, if Novo Nordisk (NN) replacement/treatment medication is given during pregnancy (or breastfeeding if a child case has been created), create a separate spontaneous case capturing the NN registered product and link the cases using the reference ID –Worldwide Unique Identifier format, see reference Q185964.

Clinical trials (dedicated pregnancy trials/studies):

- For information on which events to be captured, please refer to trial protocol.

- In trial ID: NN1250-4300, spontaneous cases need only be created if there is a clear allegation by the investigator to a Novo Nordisk product.

For further information on reporting **clinical trial** cases, see reference Q110034.

1.1 Maternal/Foetus/Child Exposure

The below table provides an overview of how many events and how many cases to create in Argus and event seriousness.

Note: the event 'Maternal exposure during pregnancy' can be changed to a more suitable 'exposure' term if deemed appropriate.

In dedicated pregnancy trials/studies, 'exposure' events are not required to be created in Argus. For these studies, please refer to study protocol and Clinical Trial/

Study Description on SharePoint for guidance on how many events and how many cases to create in Argus.

Maternal/Foetus/Child Exposure		
Event	**Number of Cases**	**Seriousness of event**
Pregnancy, no associated AEs in the mother, foetus, or child Event: • 'Maternal exposure during pregnancy''	1 'mother' case This applies to both prospective and retrospective cases	Non-serious
Induced abortion Events: • Induced abortion is captured as a SAE, only if reported as SAE • 'Maternal exposure during pregnancy'	1 'mother' case	Non-serious or as evaluated case-by-case (refer to trial protocol). If the induced abortion is due to a serious adverse event (SAE) for the mother, then the induced abortion event is serious
Spontaneous abortion (miscarriage) Events: • Spontaneous abortion as reported • 'Maternal exposure during pregnancy'	1 'mother' case	Spontaneous abortion is serious Maternal exposure during pregnancy is non-serious
Foetal death/stillbirth without information on defects Events: • Foetal death/stillbirth as reported • 'Maternal exposure during pregnancy'	1 'mother' case	Foetal death/stillbirth is serious, and reported outcome refers to the mother Maternal exposure during pregnancy is non-serious

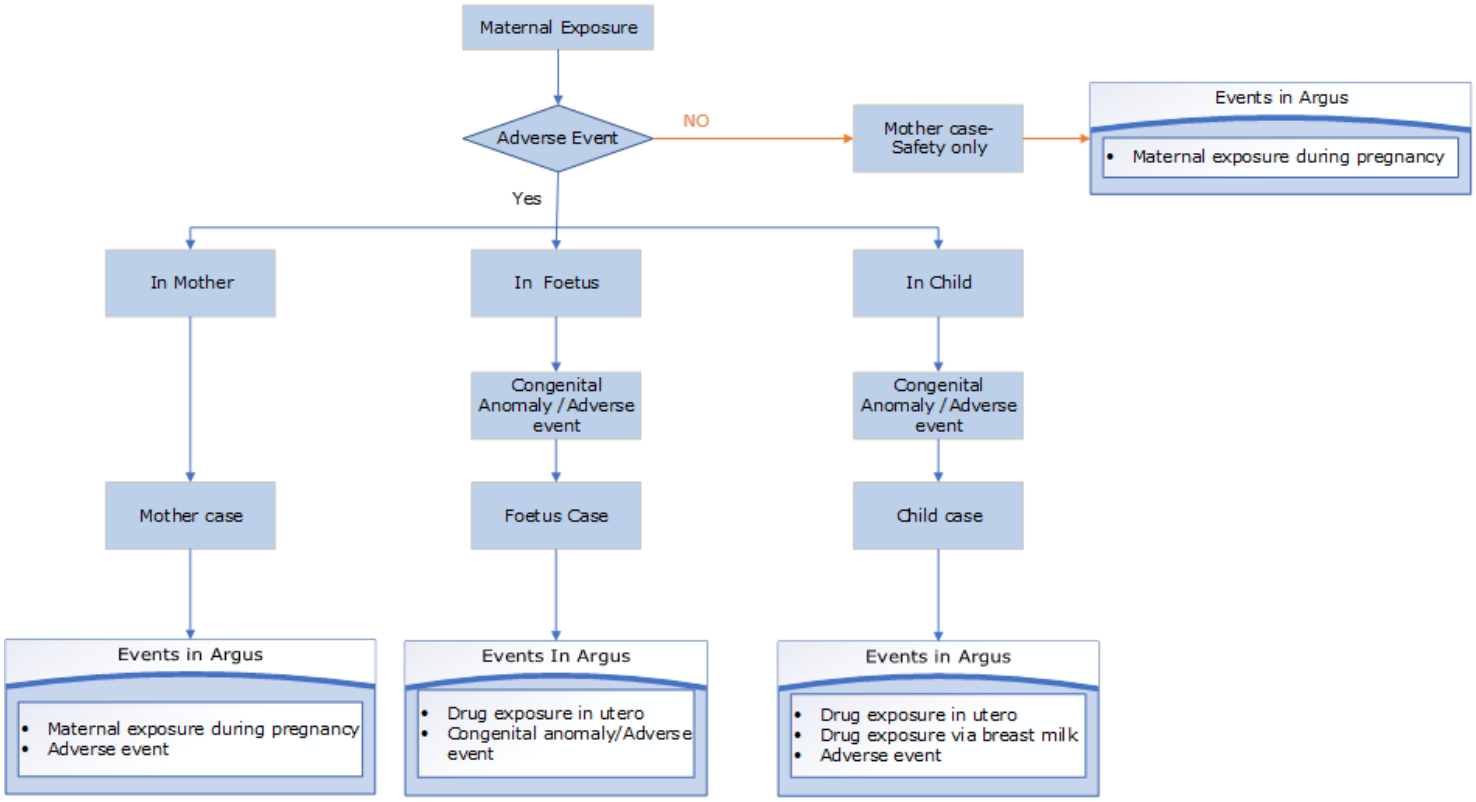
Maternal/Foetus/Child Exposure		
Event	**Number of Cases**	**Seriousness of event**
Foetus with congenital anomalies or AEs Event in <u>mother</u> case: • 'Maternal exposure during pregnancy'	*1 'mother' case dependent on report type	Maternal exposure during pregnancy is non-serious
Events in <u>foetus</u> case: • Congenital anomaly(ies) or AEs as reported • 'Drug exposure in utero'	1 'foetus' case	Seriousness criterion 'Congenital anomaly' if congenital anomalies reported Evaluate seriousness of AEs case-by-case Drug exposure in utero is non-serious
Child with congenital anomalies, developmental delay or AEs Event in <u>mother</u> case: • 'Maternal exposure during pregnancy'	*1 'mother' case dependent on report type	Non-serious. Maternal exposure during pregnancy is non-serious
Events in <u>child</u> case: • Congenital anomaly/ anomalies or developmental delay/AEs as reported • 'Drug exposure in utero' • If applicable, 'Drug exposure via breast milk'	1 'child' case	Seriousness criterion: 'Congenital anomaly' if congenital anomalies reported For developmental delay use 'Medically significant' Evaluate seriousness of AEs case-by-case Exposure events are non-serious
Pre-term delivery Events in <u>mother</u> case: • If applicable/ reported event capturing pre-term delivery	1 'mother' case	Pre-term delivery occurring before 37 completed gestational weeks may represent a serious complication for the mother, therefore evaluate seriousness case-by-case

Maternal/Foetus/Child Exposure		
Event	**Number of Cases**	**Seriousness of event**
• 'Maternal exposure during pregnancy'		Maternal exposure during pregnancy is non-serious
Events in <u>child</u> case: • If applicable/reported event capturing premature baby • 'Drug exposure in utero' • If applicable: 'Drug exposure via breast milk'	1 'child' case	Pre-term birth occurring before 37 completed gestational weeks may represent a serious complication for the child, therefore evaluate seriousness case-by-case Drug exposure in utero is non-serious
Twins /multiple births Events in <u>mother</u> case: • If applicable/reported any SAEs • 'Maternal exposure during pregnancy' Events in <u>foetus/child</u> case: • If applicable/ reported events capturing abnormalities or AEs • 'Drug exposure in utero' • If applicable: 'Drug exposure via breast milk'	*1 mother case dependent on report type	• Evaluate seriousness of 'mother' case case-by-case • Exposure events are non-serious • If foetus/child cases are required, create one case for each twin

*** For retrospective reports of foetus/child with congenital anomalies or AEs, creation of a separate 'mother' case may not be required if no exposure information for mother is reported. Please refer to local requirements in Whom and When.**

In clinical trials, please refer to trial protocol for information on events which require reporting.

The below flow chart can be used to assist in determining how many events and how many cases to create in Argus.



1.2 Paternal Exposure

Paternal Exposure		
Event	**Number of Cases**	**Seriousness**
No AEs in mother, foetus or child Event: • 'Paternal drug exposure'	1 'paternal' case	Non-serious
Foetus with congenital anomalies Event: • 'Paternal drug exposure'	1 'paternal' case	Non-serious

Paternal Exposure		
Event	**Number of Cases**	**Seriousness**
Events in foetus case: • Congenital anomaly or congenital anomalies as reported • 'Exposure via father'	1 'foetus' case	Serious, 'Congenital anomaly' Exposure via father is non-serious
For all other events, follow the instructions in section 1.1 Maternal/Foetus/Child Exposure, but create 'father' cases instead. **The term 'Exposure via father' must be used in foetus/child cases instead of 'Drug exposure in utero'.**		

Paternal 'exposure' events are only reported in clinical trials where there is a requirement for the use of contraception in male subjects and when the pregnancy outcome is abnormal (refer to trial protocol and reference Q110034).

1.3 Foetus/Child Only

In order to identify foetus/child only cases where no mother/father case exists, the 'Child Only Case' check box (see Figure 1), on the Patient tab is to be ticked. If this value is ticked, the pregnancy button is accessible from the Parent tab only, and not through the Patient tab (See section 3 Patient Tab).

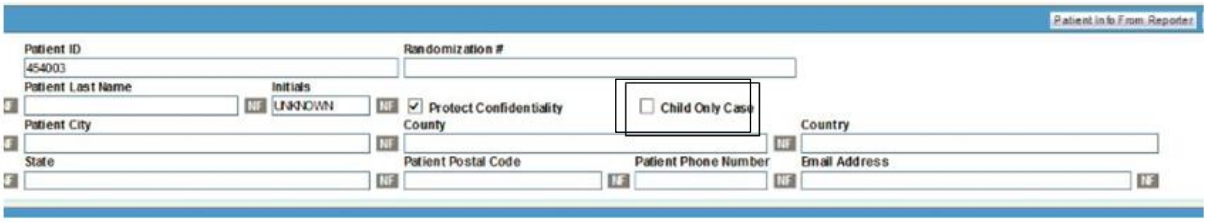


Figure 1. Child only check box.

2 General Tab

Include the classification 'Pregnancy' on the General Tab (Figure 2) to any cases related to exposure of a foetus/child, via either parent, to a marketed product or an Investigational Medicinal Product (IMP).

Note that the 'Pregnancy' classification must be added to any additional cases which are linked to drug exposure cases including linked child cases.

Also, include the classification 'Non-expedited' if the case is not required to be submitted at any point in time – neither on an expedited basis nor when the case is ready for closure, see reference Q145488. E.g.: non-serious ' exposure' cases where no additional serious adverse events have been reported.

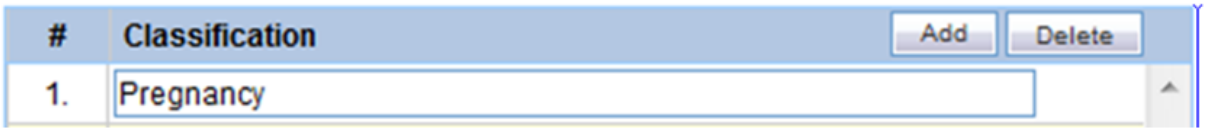


Figure 2. General Tab.

Use the same report type for foetus/child cases as is used for the mother or father case.

3 Patient Tab

Patient Identification	
What	**How**

Patient Identification in foetus and child cases	**Spontaneous and Literature:**
	• Use Patient Initials field
	  ○ Maternal Exposure
	  ○ Use mother's **initials** followed by a capital **'X' (for example MTX)**
	  ○ Paternal Exposure
	  Use father's **initials** followed by a capital **'Y' (for example SJY)**

	Solicited:
	• Use the Patient ID field only if the foetus/child has a **Subject ID**
	• Use the Initials field if there is no **Subject ID** for the foetus/child
	  ○ Maternal Exposure
	  ▪ Use mother's initials followed by a capital **'X' (for example MTX)**
	  ○ Paternal Exposure
	  ▪ Use father's initials followed by a capital **'Y' (for example SJY)**

	Clinical trial:
	• Use the Patient ID field
	  ○ Maternal Exposure
	  ▪ Use mother's **Subject ID** followed by a capital **'X' (for example 113002X)**
	  ○ Paternal Exposure
	  ▪ Use father's **Subject ID** followed by a capital **'Y' (for example 154004Y)**

If the only patient identifier in a case is 'foetus'	• **Enter 'UNK' in the initials box (do not use the nullflavor (NF) field).**
For multiple foetus/child cases (twins, triplets etc.)	• Follow the instructions above for Patient Identification in foetus and child cases • Enter a number **1**, **2** or **3**… after the **'X'** or **'Y'** to identify each foetus/child (for example in a spontaneous case: MTX1 or in a clinical trial: 113002X1)

Patient Identification	
What	**How**
If no mother/father case exists	• Tick the box 'child only case' (see section 1.3 Foetus/Child Only)
For EDC pregnancy studies	• Follow the foetus/child ID specified in the protocol

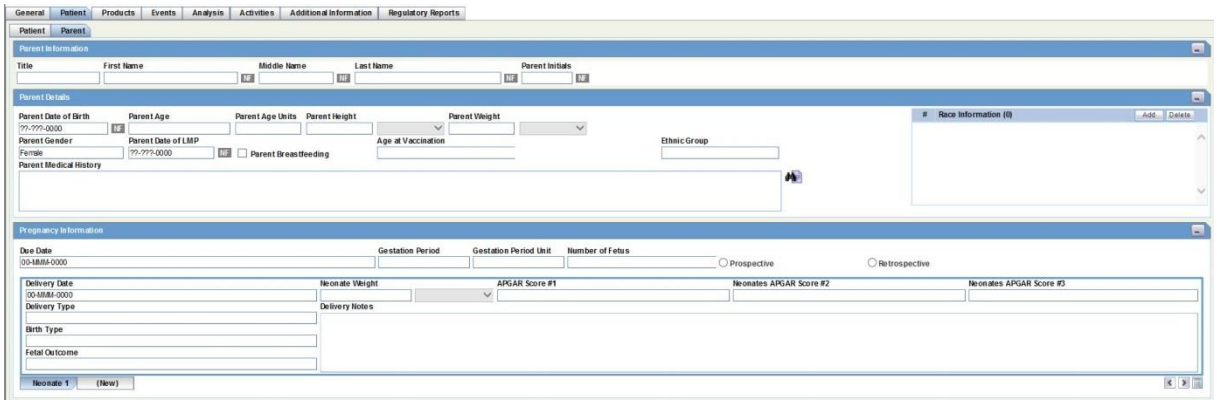


Figure 3. Pregnancy Information field, and Neonate tabs.

Patient Details	
What	**How**
Date of LMP	• Enter first day of last menstrual period (LMP) ○ Partial dates can be entered (e.g.: ??-JUL-2016) ○ Leave blank if no information is provided ○ Do not populate the nullflavor (NF) (not in use)
Patient Age Group	• If the age group is not auto-populated, select the applicable age group manually (see section: Definitions)
Breastfeeding	• Tick box, if applicable

Patient Information on Patient and Parent Tabs	
What	**How**
Title, First Name, Middle Name, Last Name	• Leave fields blank

Patient Details on Patient and Parent Tabs	
What	**How**
Age at Vaccination	• Leave field blank

Patient Details on Patient and Parent Tabs	
What	**How**
Race Information	• Select patient's race information from drop-down list • If race information for the foetus/child is not reported, leave field blank

Parent Tab	
Who	**What**
Paternal exposure cases	• Report the father as the 'Patient' and enter the mother as the 'Parent' in order to access the pregnancy information box. Mother's medical history can be added here • **Note:** Auto-generated narratives combine the patient and parent medical histories. Manually separate the medical histories in the narrative
Foetus/child cases	• Report the medical information (for example medical history and relevant tests) of the parent who was exposed to the product • If both maternal and paternal information is reported: o Enter the information of the parent who was exposed on the Parent tab and in the narrative o Enter the information of the parent who wasn't exposed in the narrative • If applicable add any relevant laboratory data related to the parent who was exposed as free text in the field 'Parent medical history' in the Parent information box (see Figure 4) If parent initials and date of birth are not available, activate the Nullflavor (NF) field

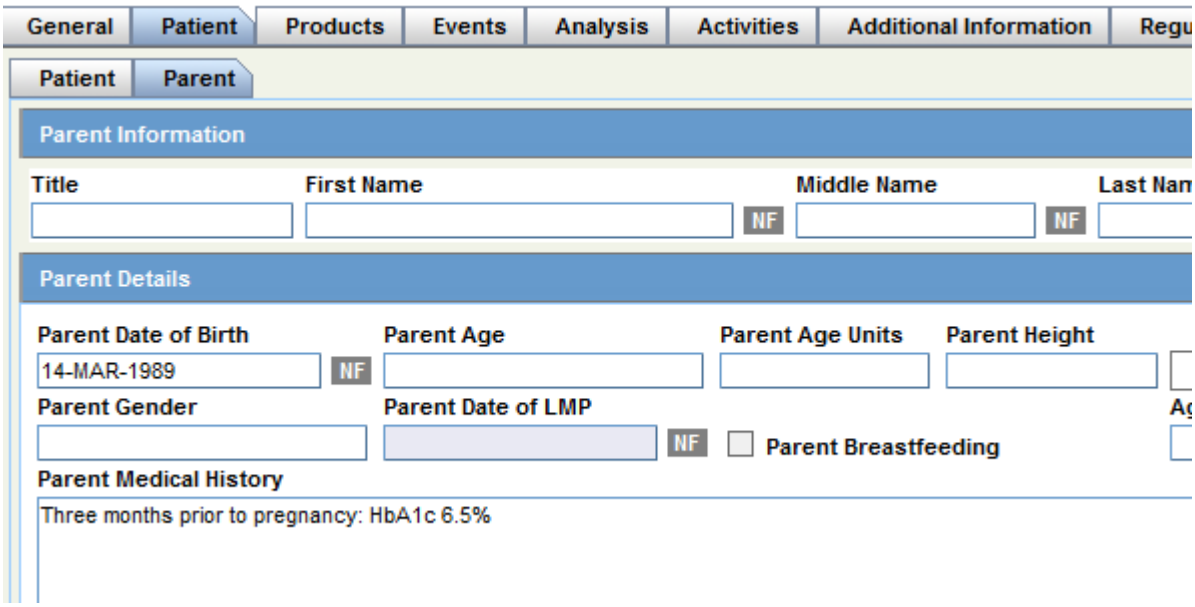


Figure 4. Parent medical history

Pregnancy Information Box*	
Field	**Enter**
Pregnant	• Choose 'Yes' under the 'Pregnant' field, then the Pregnancy Information box appears, see figure 3
Due Date	• Automatically calculated from LMP • Enter manually if a due date is reported and not automatically calculated

Gestational Age at Onset	• Number of weeks of pregnancy at the time of the AE
	  • Automatically calculated from LMP (note: field will remain blank if 'exposure' event has the same onset as date of first day of LMP or if 'exposure' event is the only event in the case)
	  • Enter manually if reported and not automatically calculated
	  • Leave blank if not reported or automatically calculated
	  • Option to choose days or months instead of weeks if applicable

Gestational Age Unit	• Weeks. Option to choose days or months if applicable
Number of Foetuses	• Enter number of foetuses

Type of Report	• Prospective or Retrospective (see section 'Definitions')
	  ○ In prospective cases, capture any (historical) pregnancy(ies) in the case narrative and medical history section if found relevant.
	  ○ For literature surveillance of single cases capture the pregnancy (which is most often retrospective), see reference Q141681.

Pregnancy Information Box*	
Field	**Enter**
Delivery Date	• Enter the date of pregnancy outcome (birth, termination, etc.)
Neonate Weight	• Enter the weight in grams
Apgar Scores	• Scores are generally taken at 1 and 5 minutes after birth, and in the event of a difficult resuscitation, the Apgar score may be done again at 10, 15, and 20 minutes after birth • If there are no time indications and: o There is only one score reported, enter it in the first field o There are 2 scores reported, enter them in fields 1 and 2 • Note: Apgar scores must not be coded as laboratory tests on the Patient tab
Delivery Type	• Select from the drop-down list • Do **NOT** use values ending with "." ("Normal."and "Abnormal.") - these are invalid terms which cannot be removed as they have been used on old cases
Foetal Outcome	• Select from drop-down list • **Note:** This field does not have to reflect the verbatim reported. Select the most accurate term
Birth Type	• Select from drop-down list
Delivery notes	• Enter relevant data not captured in the Pregnancy Information box (e.g. head circumference) • Leave blank, if no relevant data
Neonate Tabs	• Create a Pregnancy Information box for each foetus/child (see Figure 3)

* If the information is not reported, these fields can remain blank.

Note: The neonate information in the pregnancy information section is not captured in 'case details/revisions' in pregnancy cases that were migrated from Argus 4.2 to Argus 5.1 (go live date 29-AUG-2011). Neonate information in previous case versions can be accessed via: 'Utilities - Logs – Audit Log', or 'Case Action - Case Revisions – Revision History'.

4 Products Tab

For all report types, product details must reflect the parent's dosage regimen (both parent and foetus/child cases).

For Parent Cases	
Field	**Event**
Action Taken	• Action taken refers to the primary AE. See reference Q145488. • If a subsequent AE is reported into an existing drug exposure case, the Action Taken must reflect the primary event • **Note:** In **Clinical trial** cases, if the only event is 'Maternal Exposure During Pregnancy' and the patient was taking the trial product at the time of pregnancy confirmation, enter Action Taken as 'Product Discontinued'
Gestation Period at Exposure	• Enter the gestational age in weeks when exposure to suspected product started • If not reported, leave blank
Gestation Period at Exposure Units	• Enter 'weeks' (see box above) • If not reported, leave blank

For Foetus/Child Cases	
Field	**Enter**
Route of administration	• Transplacental • Transmammary • Unknown (paternal exposure) **Note:** If the foetus was exposed during pregnancy, and the same child was exposed via breast milk after delivery, create 2 dosage regimens to reflect both transplacental and transmammary exposure
Action Taken	• Use medical judgement to assess action taken if not specifically reported. • In child cases, action taken is not applicable for transplacental exposure, however use medical judgement to assess action taken for transmammary exposure.

5 Event Tab

For all report types:

Event Tab	
What	**How**
If pregnancy is the only event reported (no AEs in the parent or the foetus/child)	• Code 'Maternal exposure during pregnancy', 'Paternal drug exposure' or another term if none of the above are appropriate

Event Tab **What**	**How**
	• In dedicated pregnancy trials/studies' (both **Clinical trial** and **Solicited**), 'exposure' events are not captured. This also applies if there are SAEs in a case
If an AE is reported during the pregnancy (not applicable in dedicated pregnancy trials/studies)	• Add the AE to the existing exposure case • Capture the AE as the primary event, and the exposure event as secondary • NB: in **Clinical trial** cases, if more than one SIF is reported and a new case is created because there is no option to use an ISIR: Only one 'exposure' event is required, which must be captured in the primary case

Onset Date/Time for 'exposure' events	• If suspected product was started **prior to** first day of LMP, enter the first day of LMP as onset date
	  ○ Estimated conception date (calculated from ultrasound scan) can also be used if this is reported
	  ○ A partial date may be entered
	• If suspected product was started **after** first day of LMP, enter the start date of the suspected product as the onset date
	• If suspected product has already been stopped prior to first day of LMP or estimated day of conception, the selected AE term and product's half-life should be considered when selecting onset date.

Outcome and event stop date for Clinical trial 'exposure' events	• If trial product was discontinued before pregnancy outcome, enter outcome as 'Recovered' and event stop date must reflect last date on trial product • If trial product was not discontinued, enter outcome as 'Not recovered' and update to 'Recovered' when there is an outcome (e.g.: neonate is born). Event stop date must reflect date of pregnancy outcome • If the patient was not exposed to trial product at the time of estimated conception or first date of LMP, enter outcome as 'Not recovered' and update to 'Recovered' when there is an outcome (eg.: neonate is born). Event stop date must reflect date of pregnancy outcome

Event Tab	
What	**How**
	• If patient is lost to follow-up, enter outcome as 'Unknown'
Outcome and event stop date for **Spontaneous, Literature** and **Solicited** 'exposure' events	• If suspected product was discontinued before pregnancy outcome, enter outcome as 'Recovered' and event stop date must reflect last date on suspected product • If suspected product was not discontinued, enter outcome as 'Not recovered' and update to 'Recovered' when there is an outcome (e.g.: neonate is born). Event stop date must reflect date of pregnancy outcome • If the outcome is not reported and it is unknown whether the suspected product was stopped or not, enter 'Not Reported' • If the patient was not exposed to the suspected product at the time of estimated conception or first day of LMP, enter outcome as 'Not recovered' and update to 'Recovered' when there is an outcome (e.g.: neonate is born). Event stop date must reflect date of pregnancy outcome • If patient is lost to follow-up, enter outcome as 'Unknown'
AE reported in a **foetus/child**	• Code the AE • Code 'Drug exposure in utero', 'Drug exposure via breast milk' and/or 'Exposure via father' as applicable, as a secondary event

5.1 Event Assessment Tab

The table below outlines causality for all 'exposure' events.

Causality Assessment	
What	**How**
Clinical trial and **Solicited**	• Assess NN causality as 'Unlikely'
Spontaneous and Literature	• Assess NN causality as 'Reportable'
Investigator/ Reporter causality	• Enter as 'Unknown' because NN does not require a causality from Investigators or Reporters • Refer to Analysis Tab for entry in the narrative (section 6)

NN Listedness	
What	**How**
For all report types	• For all 'exposure' events, select 'Listed'

6 Analysis Tab

6.1 Narrative

For all report types, an auto-generated narrative must be created.
Auto-generated narratives must be amended manually to protect patient confidentiality.
The following information must be included in the narrative if reported:

- Date patient was confirmed to be pregnant
- Information on the number of foetuses
- Date of the first day of the LMP and/or date of conception as per ultrasound
- Time of exposure to product, e.g. trimester or if exposed only prior to pregnancy, length of time prior to pregnancy

Clinical trials: When performing case entry of SAEs related to pregnancy, check in electronic data capture (EDC) whether there are any non-serious AEs related to the pregnancy (e.g.: events occurring around the pregnancy period). If there are, these should be mentioned in the case narrative.

Medical History	
What	**How**

Paternal case	• Enter the mother's medical history on the Parent tab
	  • The auto-generated narrative currently combines the patient and parent medical histories
	  • Separate the paternal and maternal medical histories

Foetus/Child case	• Enter the medical history of the parent exposed to the product on the Parent tab
	  • The auto-generated narrative currently combines the patient and parent medical histories
	  ○ Separate the foetus/child and parent medical histories
	  • If information from both parents has been reported, enter the medical history of the parent who was not exposed manually in the narrative

Patient age group	
What	**How**
Foetus/child case	• Use the correct age group term for the foetus/child in the narrative (for age group definitions, see section 'Definitions')

Outcome **What**	**How**

Live Birth, with or without abnormalities	When applicable, add information regarding:
	• Complications during pregnancy
	• **Do NOT enter the delivery date in the narrative:** use the gestational weeks
	  ○ For example, in 'Mother' cases: 'In gestational week XX, the patient gave birth to a neonate with a birth weight of XX grams and a birth length of XX centimetres'
	• If pregnancy outcome date is entered as the Event Stop Date (i.e. if the suspected product was continued during pregnancy)
	  ○ This date will appear on the auto-generated narratives, and must **NOT** be deleted as we are required to have an event outcome date
	• If there is an abnormal outcome:
	  ○ Briefly describe the event in the narrative of the parent case
	  ▪ For example: 'The neonate was born with congenital abnormalities See Argus case XXXXXX for details')
	  ○ Details of the abnormal outcome must be in the narrative of the foetus/child case
	  ○ Use date of the AE diagnosis **NOT** birth date
	  ▪ For example: 'On XX-XXX-XXXX, the patient was diagnosed with Down's syndrome…'
	  ○ Parent and foetus/child cases must be linked*****. See reference Q145488

Not a live birth	• Date of loss of pregnancy • Information on cause/foetal abnormalities, if available, see Maternal Form 2 and Paternal Form in the case report forms (CRF) standards*:* https://novonordisk.sharepoint.com/sites/standlib/DCIStdLib/Forms/Public%20Quick%20Access.aspx?viewid=b75ffd6c%2D529f%2D4f48%2Db98f%2D509244c8db75
For all exposure cases	• For Reporters/Investigator's causality, state 'Not Applicable' in the narrative (see Section 5.1 Event Assessment Tab) for causality reported on the Event Assessment tab)

* In trial ID: NN1250-4300: Cases need only be linked if medically relevant

Date of birth (DOB)	
What	**How**
DOB in child cases	• **Do NOT enter the child's DOB in the narrative** • For cases where the event onset is the same as the patient's DOB, please be aware that the auto-generated narrative needs

Date of birth (DOB)	
What	**How**
	to be slightly rephrased. E.g.: 'At a gestational age of 36 weeks and 1 day, the patient was born prematurely by caesarean section.' • For **Spontaneous and literature and Solicited** cases, remember to remove the DOB from the narrative top text. E.g.: 'This non-serious case from Italy was reported by a consumer as "premature delivery" (delete the 'beginning on' date and instead report the gestational weeks in the body of the narrative)

Narrative Top text	
What	**How**
Top text in foetus/child cases	• Auto-generated narrative top text needs to be updated to clearly state who is the subject and by which route trial product(s) received

6.2 Reporter Comment

Alternative aetiology is not applicable in non-serious 'exposure' cases where the only event captured is an ‘exposure’ event.

7 Activities Tab

What	**How**
For ‘exposure’ cases where pregnancy outcome has not been reported	• For all report types: Create an action item with a due date approximately 6 weeks after the expected date of delivery to request pregnancy outcome and health status of infant at 1 month of age • For **Spontaneous and Literature** cases, see reference Q151835 for suggested queries • For **Clinical Trial** cases, refer to trial protocol, and reference Q110034 for forms to request • For **Solicited** cases, refer to protocol and reference Q151835 for suggested queries

8 Additional Information Tab

What	How
When there is both a parent case and a foetus/child case: • Case related to the same pregnancy • Additional AEs related to the pregnancy	• Link the cases, see reference Q145488 • Provide references on the Additional Info tab ○ Reference type – E2B linked report (see Figure 5) ○ Reference ID – World Wide Unique Identifier format (see Figure 5) ○ Describe the linked cases in the narrative (see section 6 Analysis Tab) ○ Example of reference note: Linked mother case

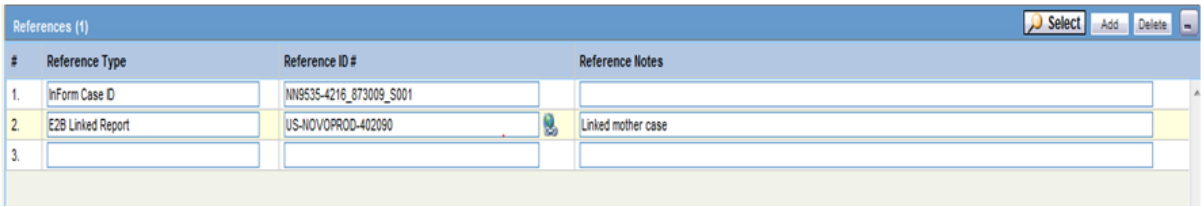


Figure 5. Linked cases.

Definitions

This list contains definitions of abbreviations and terms used in this document.

Term	Definition
AE	Adverse event
Age group	Age group definitions: • Neonate: 0 to 27 completed days • Infant: 28 days to 23 completed months • Child: 2 years to 11 completed years Please also see the definition of the term 'Child' used in this instruction
APGAR score	An assessment made at 1, 5 and 10 minutes after birth measuring **A**ppearance (skin colour), **P**ulse (heart rate), **G**rimace (reflex irritability), **A**ctivity (muscle tone) and **R**espiration (breathing). Apgar scores range from zero to ten. An Apgar score of 10 means an infant is in the best possible condition.
Child	For the purposes of this instruction, the term **'child'** is used as an umbrella term to describe the following three age groups: • Neonate (from 0 to 27 completed days); • Infant (from 28 days to 23 completed months); • Child (from 2 years to 11 completed years)
Congenital anomaly	Morphological, functional and/or biochemical developmental disturbance in the embryo or foetus whether detected at birth or not. The term congenital anomaly is broad and includes congenital abnormalities, foetopathies, genetic diseases with early onset, developmental delay, etc.
Developmental delay	Developmental delay refers to children who experience significant variation in the achievement of expected milestones for their actual or adjusted age.
Ectopic pregnancy	Pregnancy occurring outside of the uterus. See Spontaneous abortion/miscarriage.
EDC	Electronic data capture system used in NN interventional clinical trials
Full term-birth	From 37 to less than 42 completed weeks
ICSR	Individual case safety report
LMP	Last menstrual period (the patient’s first day of the last menstrual period)

Term	Definition
Normal / abnormal delivery	Normal delivery can be both caesarean and vaginal as long as the delivery was not complicated. For example, all pre-planned caesarean sections are considered normal and enter 'caesarean' as delivery type. Abnormal delivery is delivery with complications that required acute measures. For example, acute caesarean section or a vaginal delivery requiring a larger episiotomy.
Post-term birth	42 completed gestational weeks or more
Pre-term delivery	Delivery less than 37 completed gestational weeks (‘premature baby’ must be reported as an SAE if it fulfils one of the seriousness criteria, for example, hospitalisation/prolonged hospitalisation)
Primary event	A term which provides clinically significant information about the context in which the reported events must be evaluated and captured appropriately considering reporting requirements
Prospective data in pregnancy cases	Data acquired prior to the knowledge of the pregnancy outcome, or prior to the detection of a congenital malformation.
Retrospective data in pregnancy cases	Data acquired after the pregnancy outcome is known, or after the detection of congenital malformations
SIF	Safety Information Form
Spontaneous abortion/miscarriage	Early foetal death, before 20 completed weeks of gestation, comprises ectopic pregnancy and miscarriage
Stillbirth	Late foetal death, after 20 completed weeks of gestation, is known as stillbirth
Termination (Induced/ elective abortion)	Artificial interruption of pregnancy
Trimester’s definition	First: from first day of LMP until end of gestational week 12 + 6 days Second: gestational week 13-27+ 6 days Third: gestational week 28 until delivery
World Wide Unique Identifier	A unique number which indicates the country of occurrence, the company or authority that submitted the ICSR, and a report number US-NOVOPROD-270525

Reference on SharePoint

Content	Link	Path
For trial identification (ID) NN1250-4300: Clinical Trial Study Description for specific guidance on how to perform Argus case entry	https://novonordisk.sharepoint.com/sites/GlobalSafety-teamsite/Safety%20Operations%20Site/Clinical%20TrialStudy%20description/Forms/AllItems.aspx	SharePoint – Organisation – R&D - R&D Areas – MARS – MARS AREAS – Global Safety - Global Safety Team site – Safety Operations – Case Handling – Clinical Trial/ Study Description
Dedicated pregnancy trials/studies: Study protocol and Clinical Trial/Study Description for guidance on how many events and how many cases to create in Argus.	Protocols are located in Veevavault at https:login.veevavault.com Link to Clinical Trial/Study Description https://novonordisk.sharepoint.com/sites/GlobalSafety-teamsite/Safety%20Operations%20Site/Clinical%20TrialStudy%20description/Forms/AllItems.aspx	SharePoint – Organisation – R&D - R&D Areas – MARS – MARS AREAS – Global Safety - Global Safety Team site – Safety Operations – Case Handling – Clinical Trial/ Study Description
Maternal Form 2 and Paternal Form: Case report forms (CRF) standards	https://novonordisk.sharepoint.com/sites/standlib/DCIStdLib/Forms/Public%20Quick%20Access.aspx?viewid=b75ffd6c%2D529f%2D4f48%2Db98f%2D509244c8db75	In SharePoint browser type 'stand/' (Clinical Data Standards) go to Quick links – Data Collection & Management – Global CRF Standards & Templates

Document Approvals

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