EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 June 2014

EudraCT Results – XML Guidance

XML format for CT results.

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Contents

1. About this document

1.1. Disclaimer

Please note that the XML schemas used by EudraCT for clinical trial results may still be subject to changes. Those changes, if any, are however to address possible defects and would be expected to have minor impact.

1.2. Purpose

This document aims at providing an overview of the use of XML file exchange between the clinical trial sponsors and the EMA EudraCT Results system.

1.3. Scope of the document

This document focuses on the data exchange aspect and process. It does not cover the following aspects:

1. The description of the logical model of clinical trial results, as implemented by EudraCT.
2. A description of the XML standard (see [REF-1].)
3. The design and architecture of systems operated by sponsors in order to create XML messages based on the EudraCT XML schema; this can be a system based on a bespoke application or acquired from a supplier.

2. Definitions, acronyms and abbreviations

Controlled Term	An element of structured and predefined information
CT	Clinical Trial
Data Provider	A party providing data to EudraCT
Data Provider System	A system designed for the creation of data to be consumed by EudraCT; it is controlled by a Data Provider
EDQM	European Directorate for the Quality of Medicines & Healthcare
EUTCT	European Union Telematics Controlled Terms
MAH	Marketing Authorisation Holder
PIP Addressee	Paediatric Investigation Plan addressee
XML	Extensible Markup Language
XSD	XML Schema Definition

3. Data message exchange

The exchange of data messages is an alternative way for data providers to submit their data to EudraCT. Data providers can indeed submit their data with the Web UI, with XML message upload or a combination of Web UI and XML message.

EudraCT provides a two way exchange model where the data provider can submit data to EudraCT by XML message as well as retrieving an XML message from EudraCT.

Data providers can take advantage of this exchange to build systems to produce XML messages ready for upload to EudraCT or to work offline on an XML message previously downloaded from EudraCT.

3.1. Message download

An authenticated and authorised data provider can download, via the Web UI, the XML representation of the result set for any assigned CT; the message can be saved locally as a file for further use.

This XML representation contains all the data for the CT results stored in EudraCT at the time of download.

3.2. Message upload

An authenticated and authorised data provider can upload, via the Web UI, the XML representation of the result set for any assigned CT.

There are some important points to note regarding the upload process:

- The data uploaded as XML message go through a validation process. The validation process uses a set of rules described in section 5.
- If the data violates any rules, the system will report information on those violations; it is the responsibility of the data provider to address these violations and to submit the corrected version of the message.
- If no violations are reported against the data in the XML message, EudraCT considers the data correct and usable.
- EudraCT does not save the data automatically upon successful upload; it is the responsibility of the data provider to save the data as an explicit step.
- When the data is saved, it overwrites the values previously saved in the database, just as if it was entered through the Web UI and then saved.

Please note that finalising and posting the result data always requires performing manual actions in the Web UI, indeed result data cannot be submitted and posted in a fully automated way.

3.2.1. Adverse events

The data for adverse events can be uploaded either as part of the result set or separately. The upload process follows same kind of validation as the full result set and EudraCT overwrites the previously saved averse events with the uploaded version.

If the adverse events section is uploaded separately, the other sections of the result data are however preserved.

4. Controlled terms

A controlled term is an element of structured information. The information contains a number of well-defined attributes which help computer systems to consume and manipulate them without any ambiguity.

EudraCT makes use of controlled terms wherever possible in order to guarantee a high level of coherence between systems exchanging data messages and their use is mandatory wherever indicated in the XML schema.

These terms are typically gathered into logical lists known as controlled term lists; these lists are maintained by 3 sources of terms:

4.1. EUTCT

EUTCT (see [REF-4]) is a source for the following lists of terms used in EudraCT Results:

1. Country
2. Medical Dictionary For Regulatory Activities (MedDRA)

4.1.1. Concepts

The European Union Telematics Controlled Terms (EUTCT) System is a Community repository and provider of controlled terms in multiple languages for the on-going exchange of data between information systems and applications.

A term in EUTCT has the following attributes:

1. **Identifier**: this is an agreed European identifier, a sequential 12-digit number unique across all controlled term lists in EUTCT.
2. **Name**: this is the official full name of the controlled term in English.
3. **Short name**: the first or principle shortened, acronym or abbreviated name of the Controlled Term.
4. **Status**: The status of the controlled term in the controlled term list. The status can be one of the following five values: *Current*, *Provisional*, *Non-Current*, *Nullified* and *Under Consultation*.
5. **Revision number**: a number representing how many times the controlled term has been revised.

Example:

In the trial information section, the data provider is requested to indicate the number of subjects per country. In this case, the country must be sourced from EUTCT.

Let Belgium be this country:

Attribute	Value
Identifier:	100000000337
Name:	Kingdom of Belgium
Short name:	Belgium
Status:	Current

Revision number: 6

4.1.2. Accessing EUTCT terms

The homepage of the EUTCT system is http://eutct.ema.europa.eu.

The controlled terms maintained in EUTCT are available to guest users at http://eutct.ema.europa.eu/eutct/showAvailableListsDisplay.do?guestuser=true. The entry point is a table of controlled term lists which are themselves modelled as controlled terms. The actual terms to use are in their respective controlled term list.

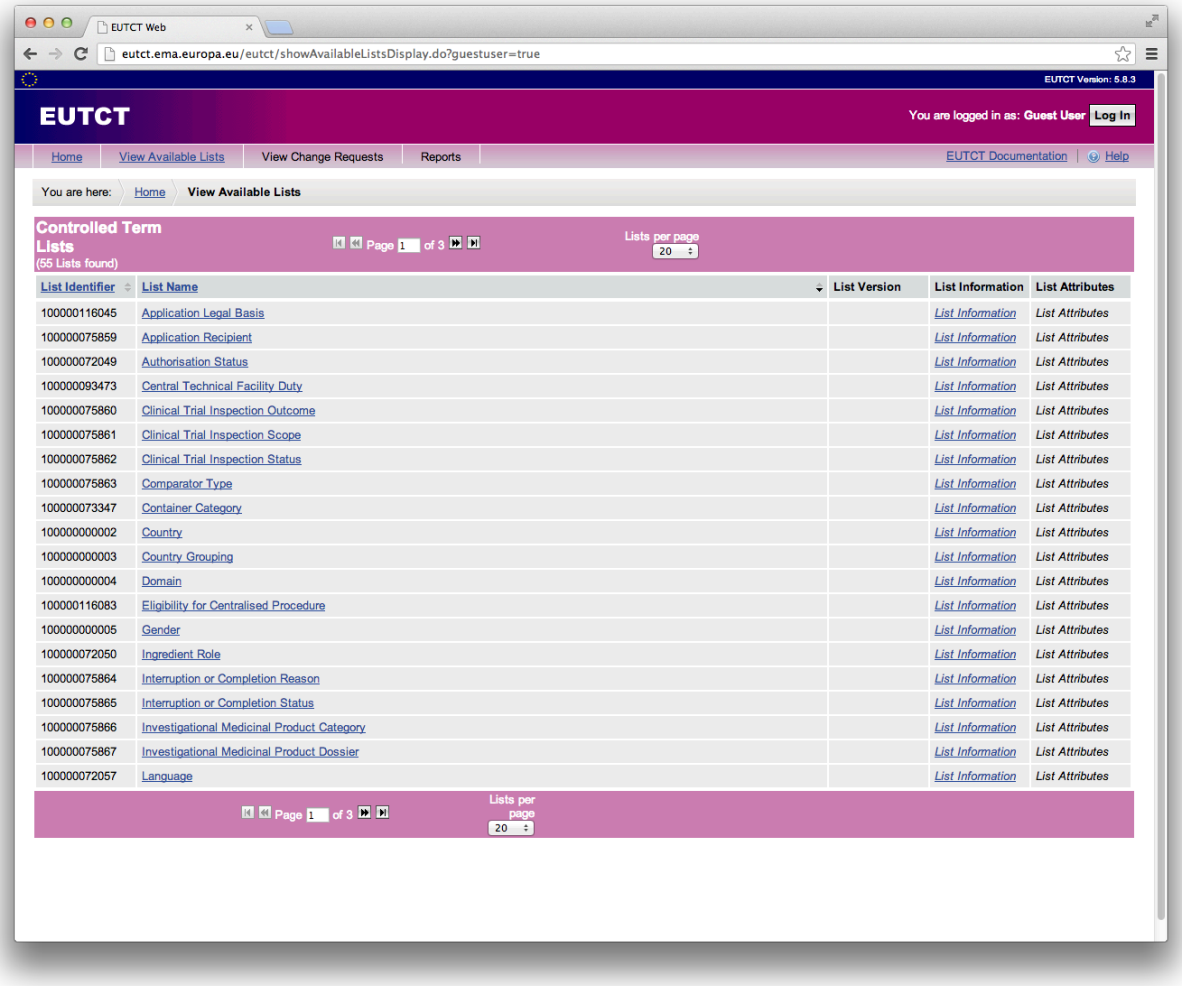

Figure 1: Lists of terms available on http://eutct.ema.europa.eu

Example:

The controlled term lists and their respective controlled terms can easily be browsed using a web browser.

The identifier for the controlled term list Country is 100000000002. In order to retrieve, from EUTCT, the list of countries in that list, the user must create a request with that list identifier: http://eutct.ema.europa.eu/eutct/viewListDisplay.do?listId=100000000002, this will show a page with 20 countries, out of a total or more than 200, sorted alphabetically:

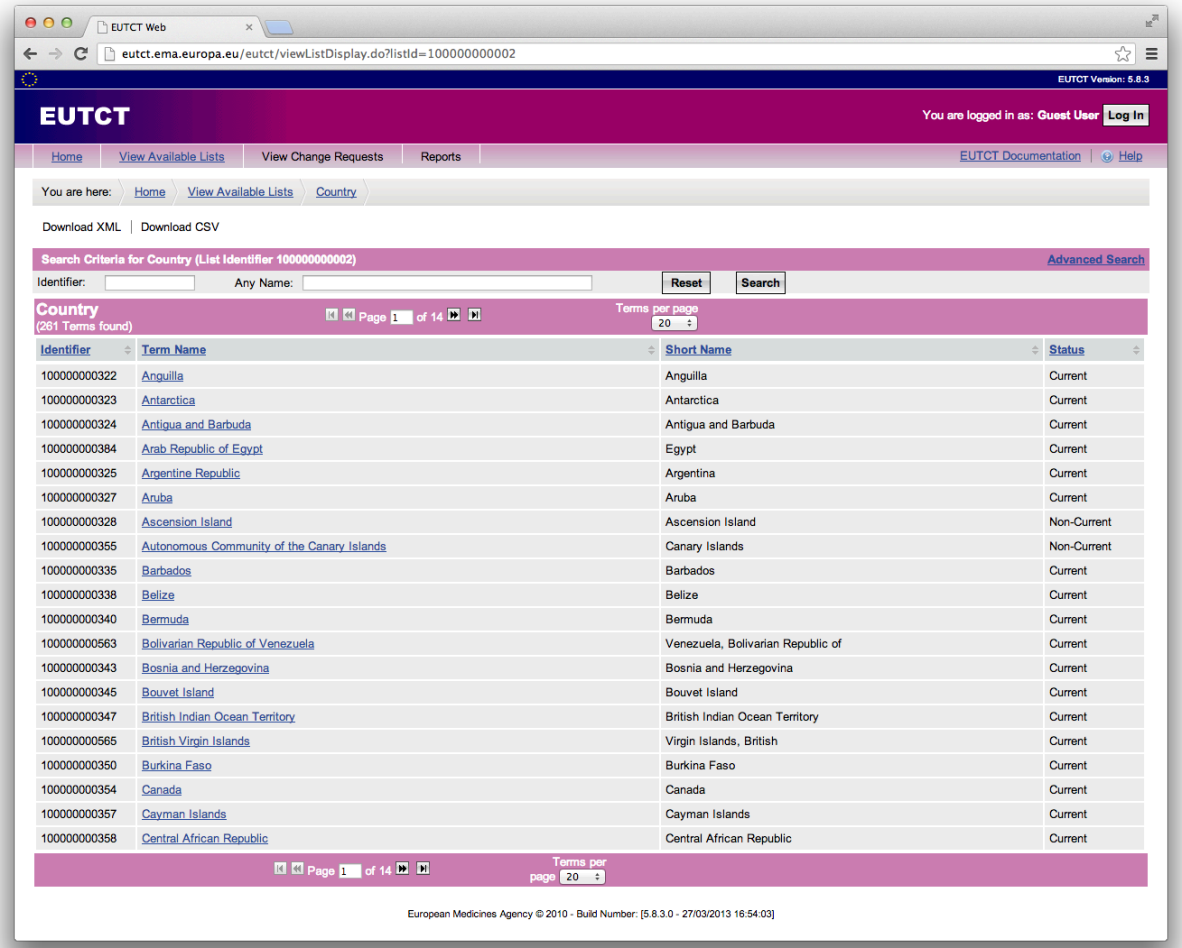

Figure 2: List of countries available under the list "Country".

By navigating to the page which contains the term with name ‘Kingdom of Belgium’ and clicking on the corresponding link ‘Kingdom of Belgium’, the browser will display all the information for that country term:

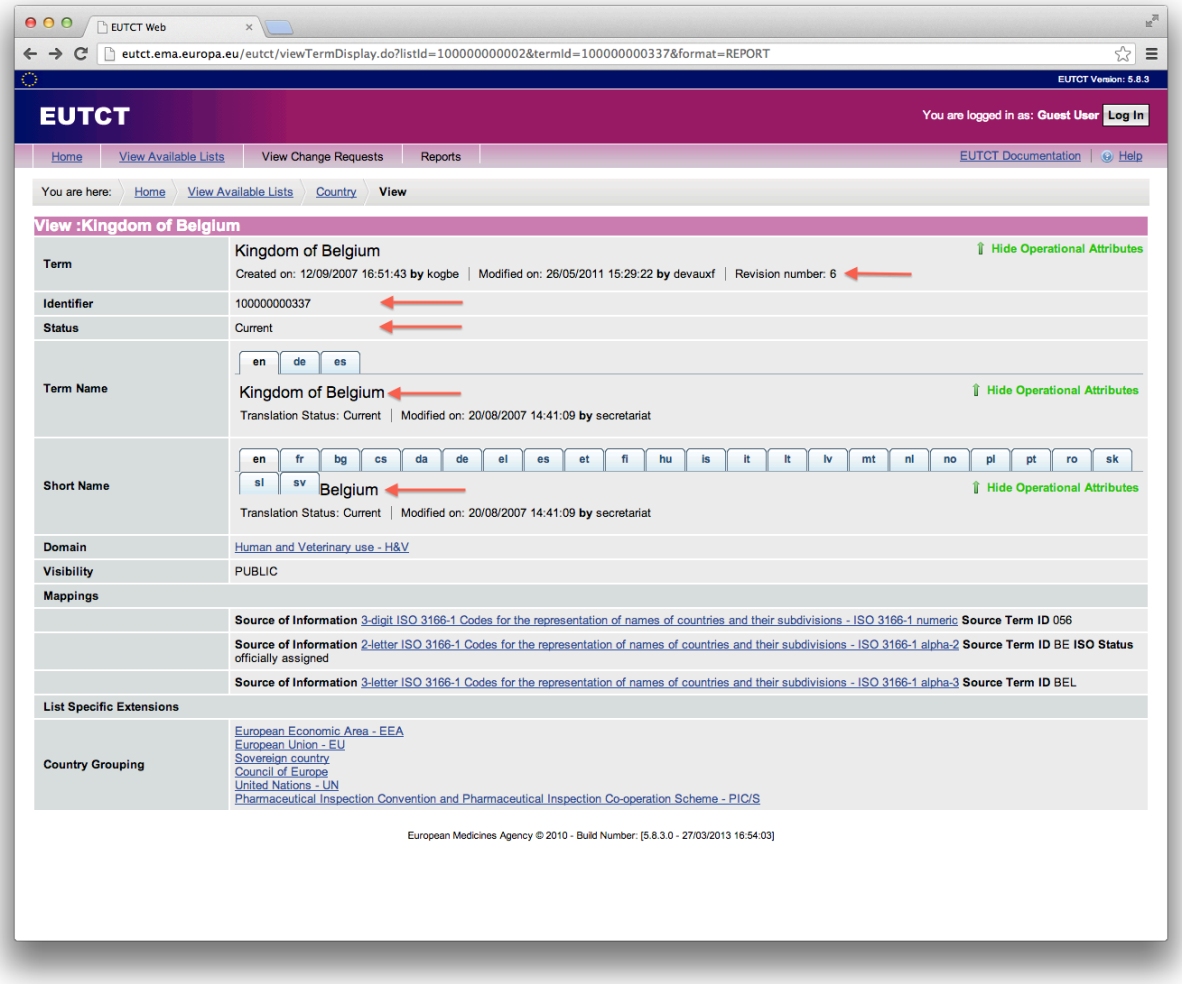

Figure 3: Detailed view of a particular term.

The most relevant attributes of the controlled term selected are indicated by horizontal arrows.

4.1.3. References

You can obtain more detailed information from the EUTCT website http://eutct.ema.europa.eu/eutct/showAvailableListsDisplay.do?guestuser=true:

1. EUTCT Documentation (http://eutct.ema.europa.eu/help/allusers/EUTCT_Documentation.html): information specific to the concepts modelled in EUTCT. This page refers to a set of documents such as:
    a. EUTCT Frequently Asked Questions (http://eutct.ema.europa.eu/help/supportdocs/EUTCT%20FAQs.pdf)
    b. EUTCT Glossary (http://eutct.ema.europa.eu/help/supportdocs/Glossary%20EUTCT.pdf)
2. Help (http://eutct.ema.europa.eu/help/guest/guest_login.html): Useful information to understand how to navigate and make the best use the EUTCT website.

4.2. EDQM lists

EDQM (see [REF-5]) is a source for the following lists of terms used in EudraCT Results:

1. Route of Administration
2. Dosage form

While their use is mandatory, EMA is however not allowed, under its current licensing agreements with EDQM, to make the content of those lists open to the public. Data providers should make sure they obtain the necessary license from EDQM in order to use those lists.

4.2.1. Concepts

The concepts of terms sourced form EDQM are the same as those sourced from EUTCT. The controlled terms have similar attributes to those managed by EUTCT; note that the format of the value for those attributes can be different than in EUTCT.

Example:

From the list Route of Administration and for the term *Nasal use*, the following attributes are retrieved:

Attribute	Value
Identifier:	20049000
Name:	Nasal use
Short name:	Nasal use
Status:	Current
Revision number:	5

4.2.2. Accessing EDQM terms

You can obtain detailed information on those terms directly from EDQM (http://www.edqm.eu).

4.3. EudraCT lists

EudraCT is a source for the following lists of terms used in EudraCT Results:

1. Adverse event assessment method: systematic, non-systematic
2. Allocation method: randomised controlled, non-randomised controlled, N/A
3. Analysis method: ANOVA, ANCOVA, Chi-squared …
4. Analysis specification: pre-specified, post-hoc
5. Arm type: experimental, placebo comparator, active comparator, no imp
6. Blinding method: single blind, double blind, N/A
7. Central tendency type: arithmetic mean, median, least squares mean …
8. Clinical trial role: subject, investigator, monitor, data analyst, carer, assessor
9. Comparison operator: <, >, =, ≤, ≥

10. Confidence interval sides: 1-sided, 2-sided
11. Dictionary: MedDRA, SNOMED
12. Effect estimate: Cox proportional hazard, Hazard ratio, Hazard ratio log, Mean difference …
13. End point type: Primary, Secondary, Other pre-specified, Post-hoc
14. Range type: Full range (min-max), Interquartile range (min-max)
15. Reason joined type: Transferred in from other arm/group, late recruitment
16. Reason not completed: Adverse event: not serious, Adverse event: serious fatal, Adverse event: serious non-fatal, Consent withdrawn by subject, Lack of efficacy, Physician decision, Pregnancy, Protocol violation, Transferred to other arm/group
17. Statistical analysis type: non-inferiority, equivalence, superiority, other
18. Study analysis stage: Interim, Final
19. Subject analysis set type: per protocol, intent to treat, full analysis set, safety population, sub-group analysis set

See Appendix 1: List of EudraCT terms for the full list of terms.

4.3.1. Concepts

The EudraCT controlled terms have a simpler structure than both EUTCT and EDQM controlled terms. They consist in just one attribute which is the name of the term; the format of that attribute is a string of characters.

Example:

BLINDING.double

HYPOTHESIS_METHOD.ancova

4.3.2. Accessing EudraCT terms

See Appendix 1: List of EudraCT terms for the full lists of terms.

5. Validation

EudraCT will only accept messages that meet a number of conditions. These conditions are, from the most general to the more specific:

1. The XML message must be well-formed: it must adhere to the syntax rules specified by the XML 1.0 specification in that it must satisfy both physical and logical structures. See [REF-1].
2. The XML message must be valid: it must conform to the EudraCT Result schema. See [REF-2] and [REF-3].
3. The XML message must be valid according to a well-defined set of validation rules. See Appendix 2: Validation rules.

6. Data types

6.1. Date and time

The lexical representation for the data type dateTime is:

'-'? yyyy '-' MM '-' dd 'T' hh ':' mm ':' ss ('.' s+)? (zzzzzz)?

- '-'?: optional leading negative sign.
- yyyy: 4 digit numeral that represents the year.
- MM: 2 digit numeral that represents the months, [01, 12].
- dd: 2 digit numeral that represents the day of the month, [01, 31].
- 'T': separator literal.
- hh: 2 digit numeral that represents the hour of the day, [00, 24]. Note that if hh is equal to 24 then mm must be equal to 00.
- mm: 2 digit numeral that represent the minute, [00, 59].
- ss: 2 digit numeral that represents the whole second, [00, 59].
- '.' s+: if present, represents the fractional seconds.
- zzzzzz: if present, represents the timezone. When a timezone is added to a UTC dateTime, the result is the date and time in that timezone.

6.1.1. Timezones

Timezones are expressed as durations with hour and minute properties.

The lexical representation for the timezone is: (('+' | '-') hh ':' mm) | 'Z'

- hh: a 2 digit numeral that represents the hours.
- mm: a 2 digit numeral that represents the minutes.
- '+': indicates a non-negative duration.
- '-': indicates a non-positive duration.
- 'Z': indicates that the timezone is UTC.

Examples:

1. **2013-02-25T00:00:00Z**: 25 February 2013, midnight (beginning of the calendar day) in UTC, it is equivalent to:
    a. **2013-02-24T22:00:00-02:00**
    b. **2013-02-25T07:00:00+07:00**
2. **2011-05-13T17:00:00Z**: 13 May 2011, 5pm in UTC, it is equivalent to:
    a. **2011-05-13T13:00:00-04:00**
    b. **2011-05-13T22:00:00+05:00**

6.2. Boolean

The lexical representation for the type boolean is: {true, false, 1, 0}

Examples:

1. **<dictionaryOverridden>true</dictionaryOverridden>** is equivalent to **<dictionaryOverridden>1</dictionaryOverridden>**
2. **<dictionaryOverridden>false</dictionaryOverridden>** is equivalent to **<dictionaryOverridden>0</dictionaryOverridden>**

6.3. Controlled terms

6.3.1. EUTCT

The XML representation of the country 'Kingdom of Belgium':

```
<country>
  <eutctId>100000000337</eutctId>
  <version>6</version>
</country>
```

The XML representation of the MedDRA System Organ Class 'Eye disorders':

```
<organSystem>
  <eutctId>100000004853</eutctId>
  <version>14</version>
</organSystem>
```

6.3.2. EDQM

The XML representation of the route of administration 'Nasal use':

```
<routeOfAdministration>
  <eutctId>100000073615</eutctId>
  <version>5</version>
</routeOfAdministration>
```

6.3.3. EudraCT

The XML representation of the clinical trial role 'assessor':

```
<clinicalTrialRole>
  <value>TRIAL_ROLE.assessor</value>
</clinicalTrialRole>
```

7. Creation of an XML file

With the information detailed in the previous sections it becomes possible to create an XML file for clinical trial results and for adverse events.

It is not the purpose of this section to go over the basics of XML but some examples are provided to help speed up the process of creating valid XML files.

It is important to note that the necessary pre-conditions for a successful uploads are first and foremost that the XML is well-formed and valid with regards to the XML schema definitions for CT results and adverse events. If the XML does not meet those 2 necessary requirements the system will report an error (see section 7.5. Examples of errors)

7.1. File name

The name of the XML file can be any valid file name. Note that when you download the XML file from EudraCT it will conveniently be named with the CTA number.

Example: Result-2008-002277-13.xml

7.2. Namespace

The root element of the XML file should contain the declaration of the namespaces as you best prefer to use them. The example below defines the namespaces **tns** for the CT results related elements and attributes and **xsi** for the XML related elements and attributes; those names are arbitrary and you may want to choose other names.

```
<?xml version="1.0" encoding="UTF-8"?>
<tns:result eudractNumber="2008-002277-13" sponsor=""
  xmlns:tns="http://eudract.ema.europa.eu/schema/clinical_trial_result"
  xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <trialInformation>
    <isrctnIdentifier>ISRCTN01234567</isrctnIdentifier>
    <usctnIdentifier xsi:nil="true" />
    <whoIdentifier xsi:nil="true" />
    <partOfPIP>false</partOfPIP>
    <art45Related>false</art45Related>
    <art46Related>false</art46Related>
    <isGlobalEndOfTrialReached>false</isGlobalEndOfTrialReached>
    <globalEndOfTrialPremature>false</globalEndOfTrialPremature>
    <longTermFollowUpPlanned>false</longTermFollowUpPlanned>
    <sponsors />
    <pipnumbers />
    <otherIdentifiers />
    <countrySubjectCounts />
    <populationAgeGroup>
      <inUtero xsi:nil="true" />
      <pretermNewbornInfants xsi:nil="true" />
      <newborns xsi:nil="true" />
      <infantsAndToddlers xsi:nil="true" />
      <children xsi:nil="true" />
      <adolescents xsi:nil="true" />
      <adults xsi:nil="true" />
      <elderly65To84 xsi:nil="true" />
      <elderlyOver85 xsi:nil="true" />
    </populationAgeGroup>
  </trialInformation>
</tns:result>
```

Note as well that the XML declaration must specify version **1.0** and **UTF-8** for encoding.

7.3. ID and IDREF

In order to guarantee the consistency of information, the XML must make use of the ID/IDREF as prescribed in the schema definition.

Indeed an element with an attribute of type **xs:ID** can then be referenced from one or more elements within the same XML. To achieve this, the value of that attribute must be unique in the whole XML file, not only within its containing element.

To use a data modelling analogy, ID is similar to the primary key, and IDREF is similar to the foreign key.

Example:

Schema (snippet of **results.xsd**):

```
...
<xs:complexType name="StartedMilestone">
  <xs:complexContent>
    <xs:extension base="tns:Milestone">
      <xs:sequence />
      <xs:attribute name="id" type="xs:ID" use="required" />
    </xs:extension>
  </xs:complexContent>
</xs:complexType>
...
<xs:complexType name="StartedMilestoneAchievement">
  <xs:complexContent>
    <xs:extension base="tns:MilestoneAchievement">
      <xs:sequence>
        <xs:element minOccurs="0" name="subjects">
          <xs:simpleType>
            <xs:restriction base="xs:long">
              <xs:minInclusive value="1" />
              <xs:maxInclusive value="99999999" />
            </xs:restriction>
          </xs:simpleType>
        </xs:element>
      </xs:sequence>
      <xs:attribute name="startedMilestoneId"
         type="xs:IDREF" use="required">
        <xs:annotation>
          <xs:documentation xml:lang="en">
            This IDREF attribute refers to the id of the startedMilestone in the same period.
          </xs:documentation>
        </xs:annotation>
      </xs:attribute>
    </xs:extension>
  </xs:complexContent>
</xs:complexType>
...
```

Sample XML (snippet):

```
...
<subjectDisposition>
  <postAssignmentPeriods>
    <postAssignmentPeriod id="PostAssignmentPeriod-3240">
      <completedMilestone id="CompletedMilestone-9333" />
      <startedMilestone id="StartedMilestone-9334">
        ...
      </startedMilestone>
      ...
      <arms>
        <arm id="Arm-18615">
          ...
          <startedMilestoneAchievement
             startedMilestoneId="StartedMilestone-9334" />
          <completedMilestoneAchievement
             completedMilestoneId="CompletedMilestone-9333">
             ...
          </completedMilestoneAchievement>
          <otherMilestoneAchievements />
          <notCompletedReasonDetails />
          <joinedReasonDetails />
        </arm>
      </arms>
    </postAssignmentPeriod>
  </postAssignmentPeriods>
  <reasonsNotCompleted />
  <reasonsJoined />
</subjectDisposition>
...
```

In the schema, the complex type **tns:Arm** contains exactly one element of type **tns:StartedMilestoneAchievement**, the attribute **startedMilestoneId**, of type **xs:IDREF** must refer to an element of type **tns:StartedMilestone** by its unique identifier.

Important notes:

1. The value of the attribute identifying the element must follow strictly the type xs:ID.
2. The value of the attribute must be unique in all elements with an attribute of the same type.
3. The values of the identifiers are logical and will not be retained by the system. You may therefor use any value which complies with **xs:ID**. For example you can create an XML with `<startedMilestone id="StartedMilestone-9334">` or `<startedMilestone id="SMS123">` as long as the above constraints are fulfilled. Another consequence is that when you download the XML from EudraCT, the identifiers will most likely be different from the identifiers in the XML file you created. This should not matter for your own system though.
4. The schema files contain documentation to indicate when there is a reference from the identifier of one element to another element (see example above).
5. It is the responsibility of the submitter to ensure that the references are logically correct. While it is perfectly valid, from a pure XML validation perspective, to have the value of the attribute **completedMilestoneId** referring to the id attribute of an element of type **tns:StartedMilestone**, it will be rejected by the system at the time of upload.
   Example:

```
...
<subjectDisposition>
  <postAssignmentPeriods>
    <postAssignmentPeriod id="PostAssignmentPeriod-3240">
      <completedMilestone id="CompletedMilestone-9333" />
      <startedMilestone id="StartedMilestone-9334">
        ...
      </startedMilestone>
      ...
      <arms>
        <arm id="Arm-18615">
          ...
          <startedMilestoneAchievement
             startedMilestoneId="CompletedMilestone-9333" />
          <completedMilestoneAchievement
             completedMilestoneId="StartedMilestone-9334">
             ...
          </completedMilestoneAchievement>
          <otherMilestoneAchievements />
          <notCompletedReasonDetails />
          <joinedReasonDetails />
        </arm>
      </arms>
    </postAssignmentPeriod>
  </postAssignmentPeriods>
  <reasonsNotCompleted />
  <reasonsJoined />
</subjectDisposition>
...
```

7.4. Adverse events

You can choose to upload the adverse events either as part of the full result set or separately, depending on your needs and business processes.

There is a separate XML schema definition, **adverseEvents.xsd**, which is imported by the schema definition of the full result set, **results.xsd**, but it can also be used on its own.

The schema **adverseEvents.xsd** defines all elements and types to describe the adverse events reported during the course of the clinical trial and the types defined in this schema do not depend on any type defined in the schema **results.xsd**.

7.4.1. Upload with the full result set

The adverse events are under the last element of the full result set:

```
<?xml version="1.0" encoding="UTF-8"?>
<xs:schema elementFormDefault="unqualified"
  targetNamespace="http://eudract.ema.europa.eu/schema/clinical_trial_result"
  version="1.0"
  xmlns:aev="http://eudract.ema.europa.eu/schema/clinical_trial_result/adverse_events"
  xmlns:tns="http://eudract.ema.europa.eu/schema/clinical_trial_result"
  xmlns:xs="http://www.w3.org/2001/XMLSchema">
  <xs:import

namespace="http://eudract.ema.europa.eu/schema/clinical_trial_result/adverse_events"
   schemaLocation="adverseEvents.xsd" />
  <xs:element name="result" type="tns:ResultSet" />
  <xs:complexType name="ResultSet">
    <xs:sequence>
      <xs:element minOccurs="0" name="trialInformation"
         type="tns:TrialInformation" />
      <xs:element minOccurs="0" name="subjectDisposition"
         type="tns:SubjectDisposition" />
      <xs:element minOccurs="0" name="baselineCharacteristics"
         type="tns:BaselineCharacteristics" />
      <xs:element minOccurs="0" name="endPoints" type="tns:EndPoints" />
      <xs:element minOccurs="0" name="trialChanges" type="tns:TrialChanges" />
      <xs:element minOccurs="0" name="subjectAnalysisSets">
        <xs:complexType>
          <xs:sequence>
            <xs:element maxOccurs="unbounded" minOccurs="0"
               name="subjectAnalysisSet" type="tns:SubjectAnalysisSet" />
          </xs:sequence>
        </xs:complexType>
      </xs:element>
      <xs:element minOccurs="0" name="adverseEvents" type="aev:AdverseEvents" />
    </xs:sequence>
    <xs:attribute name="eudractNumber" type="xs:string" />
    <xs:attribute name="sponsor" type="xs:string" />
  </xs:complexType>
  ...
</xs:schema>
```

7.4.2. Upload of adverse events only

The default upload mode is for the full result set, but the user may decide to upload the section for adverse events only.

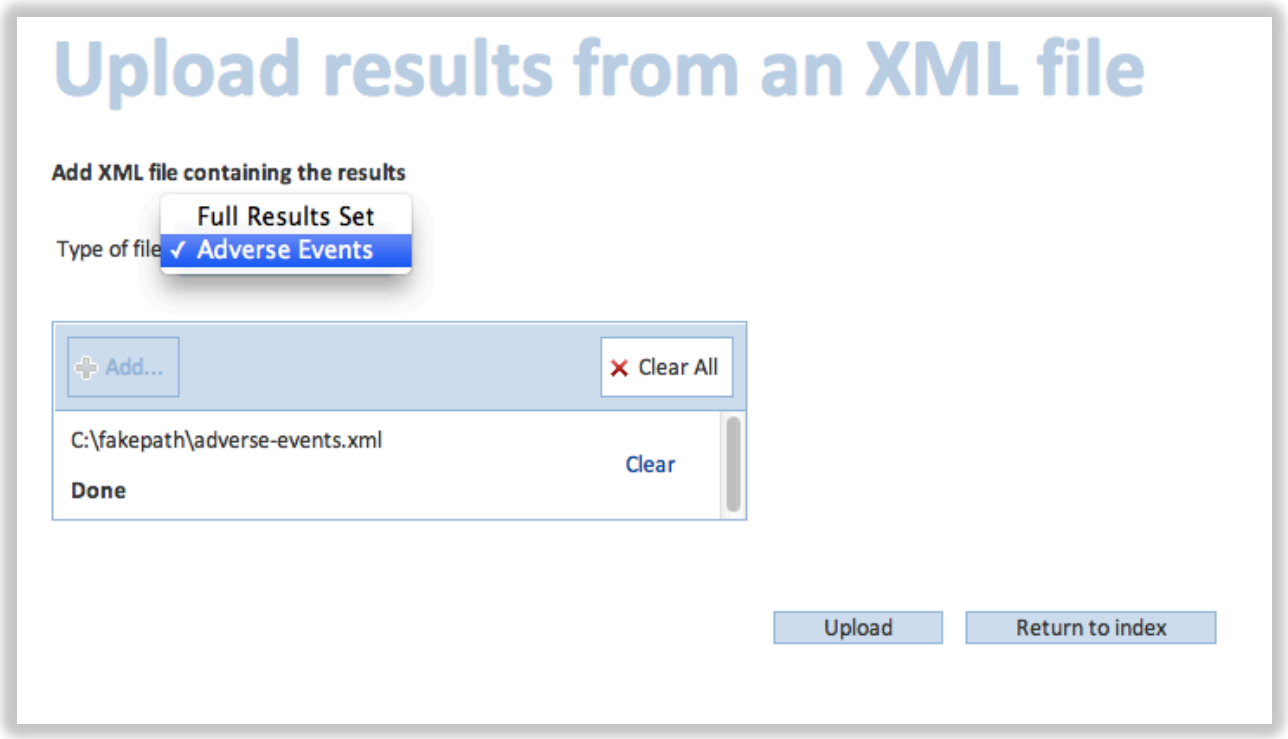

Figure 4: Detail of the XML upload page.

The adverse events in the XML file, here **`adverse-events.xml`**, will overwrite completely any adverse events definition previously in the system for that associated result set, the other sections will however be preserved.

Example:

A valid XML file for adverse events. The XML below is for 1 reporting group and 1 non-serious adverse event:

```
<?xml version="1.0" encoding="UTF-8"?>
<aev:adverseEvents
  xmlns:aev="http://eudract.ema.europa.eu/schema/clinical_trial_result/adverse_events"
  xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <description>AE additional description</description>
  <nonSeriousEventFrequencyThreshold>2</nonSeriousEventFrequencyThreshold>
  <timeFrame>Timeframe for AE</timeFrame>
  <assessmentMethod>
    <value>ADV_EVT_ASSESS_TYPE.systematic</value>
  </assessmentMethod>
  <dictionary>
    <otherName xsi:nil="true" />
    <version>14.0</version>
    <name>
      <value>ADV_EVT_DICTIONARY_NAME.meddra</value>
    </name>
  </dictionary>
  <reportingGroups>
    <reportingGroup id="ReportingGroup-0">
      <title>AE-group-1-0</title>
      <description xsi:nil="true" />
      <subjectsAffectedByNonSeriousAdverseEvents>
        2
      </subjectsAffectedByNonSeriousAdverseEvents>
      <subjectsAffectedBySeriousAdverseEvents>
        0
      </subjectsAffectedBySeriousAdverseEvents>
      <subjectsExposed>100</subjectsExposed>
      <deathsAllCauses>0</deathsAllCauses>
      <deathsResultingFromAdverseEvents>0</deathsResultingFromAdverseEvents>
```

```
      </reportingGroup>
    </reportingGroups>
    <nonSeriousAdverseEvents>
      <nonSeriousAdverseEvent>
        <term>Headache</term>
        <organSystem>
          <eutctId>100000004853</eutctId>
          <version>15</version>
        </organSystem>
        <assessmentMethod>
          <value>ADV_EVT_ASSESS_TYPE.systematic</value>
        </assessmentMethod>
        <dictionaryOverridden>false</dictionaryOverridden>
        <values>
          <value reportingGroupId="ReportingGroup-0">
            <occurrences>2</occurrences>
            <subjectsAffected>2</subjectsAffected>
            <subjectsExposed>100</subjectsExposed>
          </value>
        </values>
      </nonSeriousAdverseEvent>
    </nonSeriousAdverseEvents>
    <seriousAdverseEvents />
  </aev:adverseEvents>
```

Note also that the adverse events cannot be downloaded separately from the full result set.

7.5. Examples of errors

There are multiple reasons that can lead for the uploaded XML data to be rejected by the system. The sections below will show typical errors and how the system informs the submitter of the problem.

When the system reports an error it guarantees that the data already saved before the upload are preserved.

7.5.1. XML is not well-formed

The XML is not well formed as per the definition of XML 1.0 (see [REF-1]). In this example, the closing bracket of the element trialInformation was omitted.

```
<?xml version="1.0" encoding="UTF-8"?>
<tns:result eudractNumber="2008-002277-13" sponsor=""
  xmlns:tns="http://eudract.ema.europa.eu/schema/clinical_trial_result"
  xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <trialInformation
    <isrctnIdentifier>ISRCTN01234567</isrctnIdentifier>
```

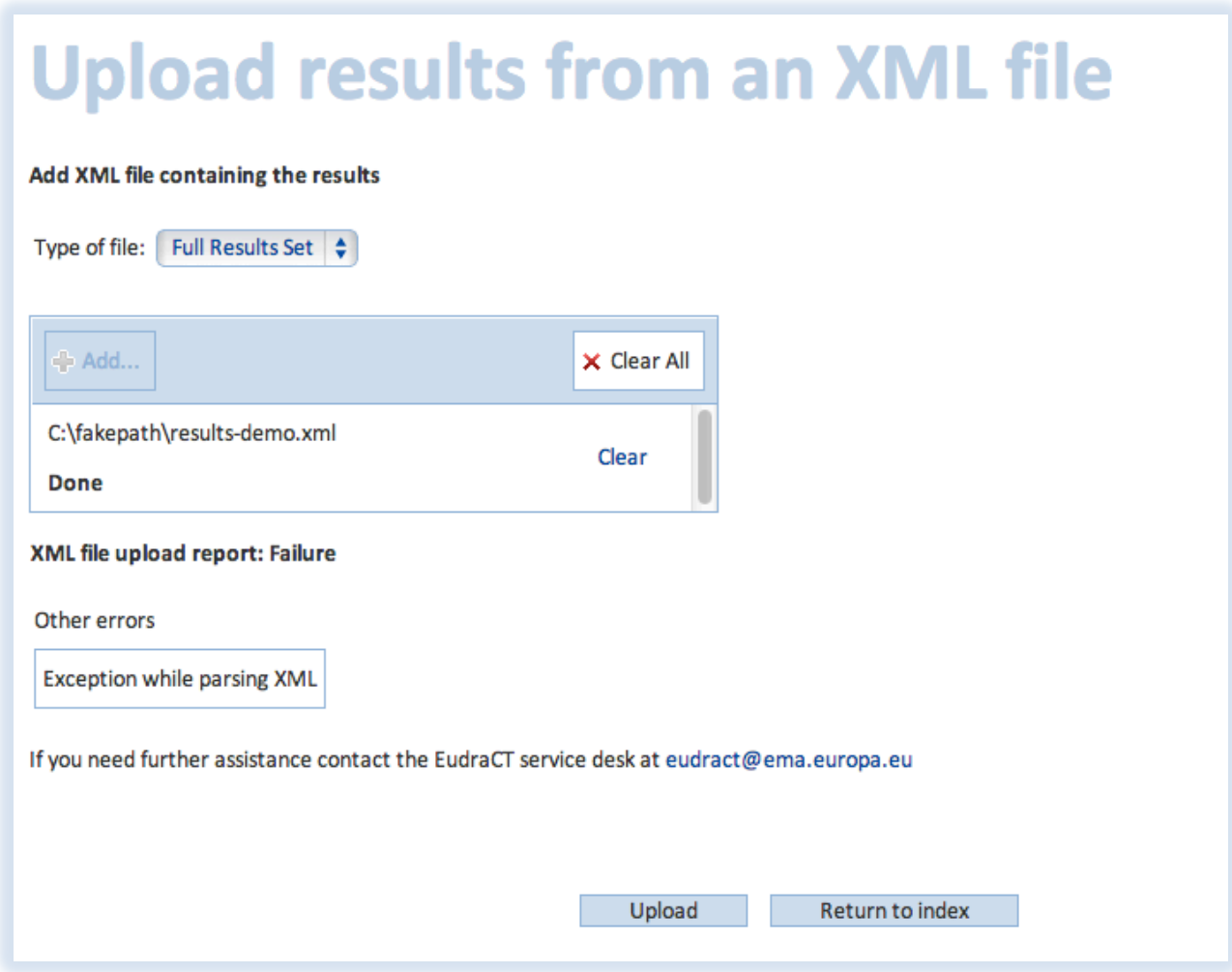

Figure 5: XML is not well formed.

7.5.2. Wrong type for element

The value of the mandatory element **`partOfPIP`** must be of the type boolean, but for the sake of the example it was changed to **`negative`**; the problem is fixed by changing the value to **`true`** or **`false`**.

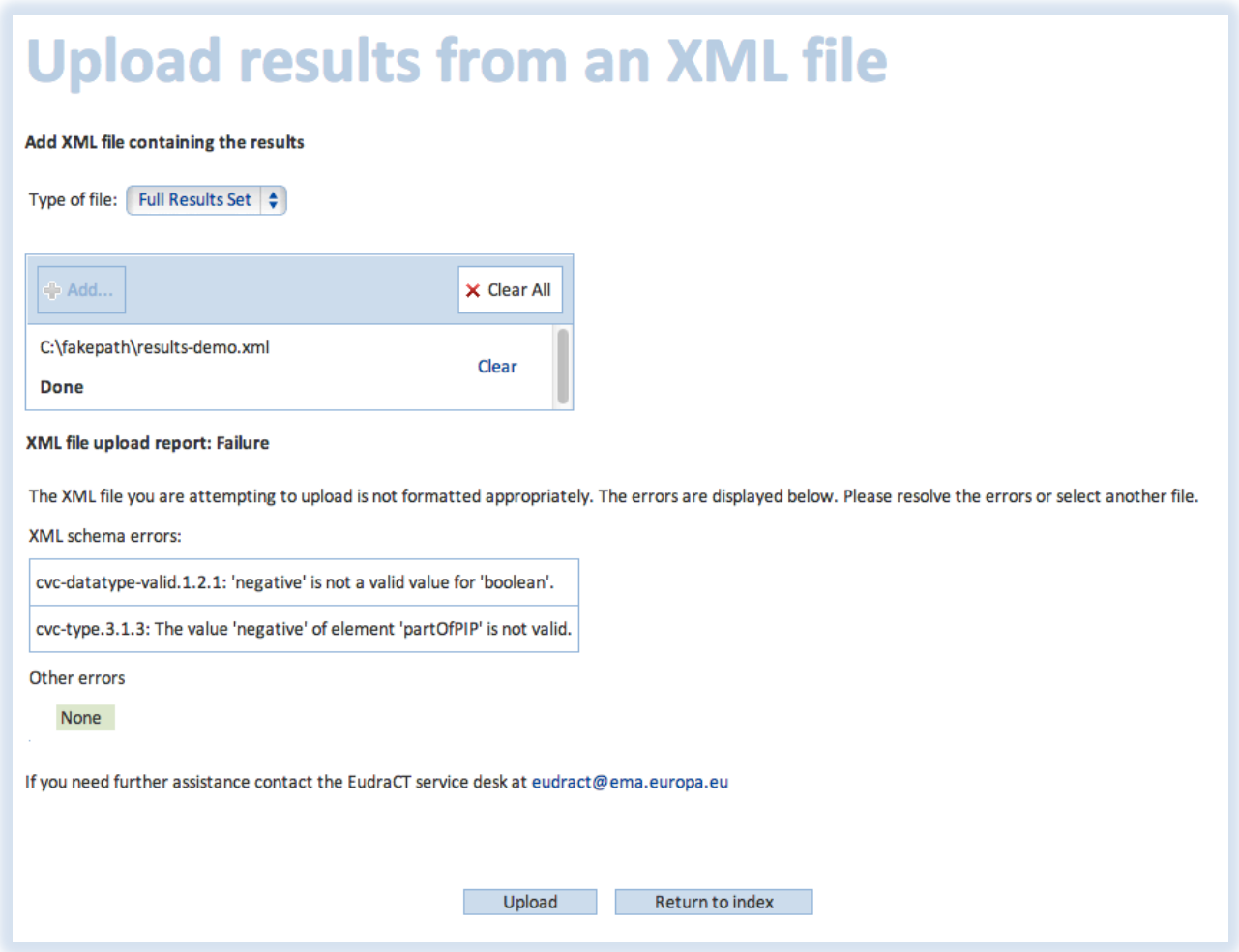

Figure 6: Wrong type for element.

7.5.3. Missing element

The mandatory element **`elederlyOver85`** is missing from its parent element **`populationAgeGroup`**; the problem is fixed by adding the mandatory element **`elederlyOver85`**.

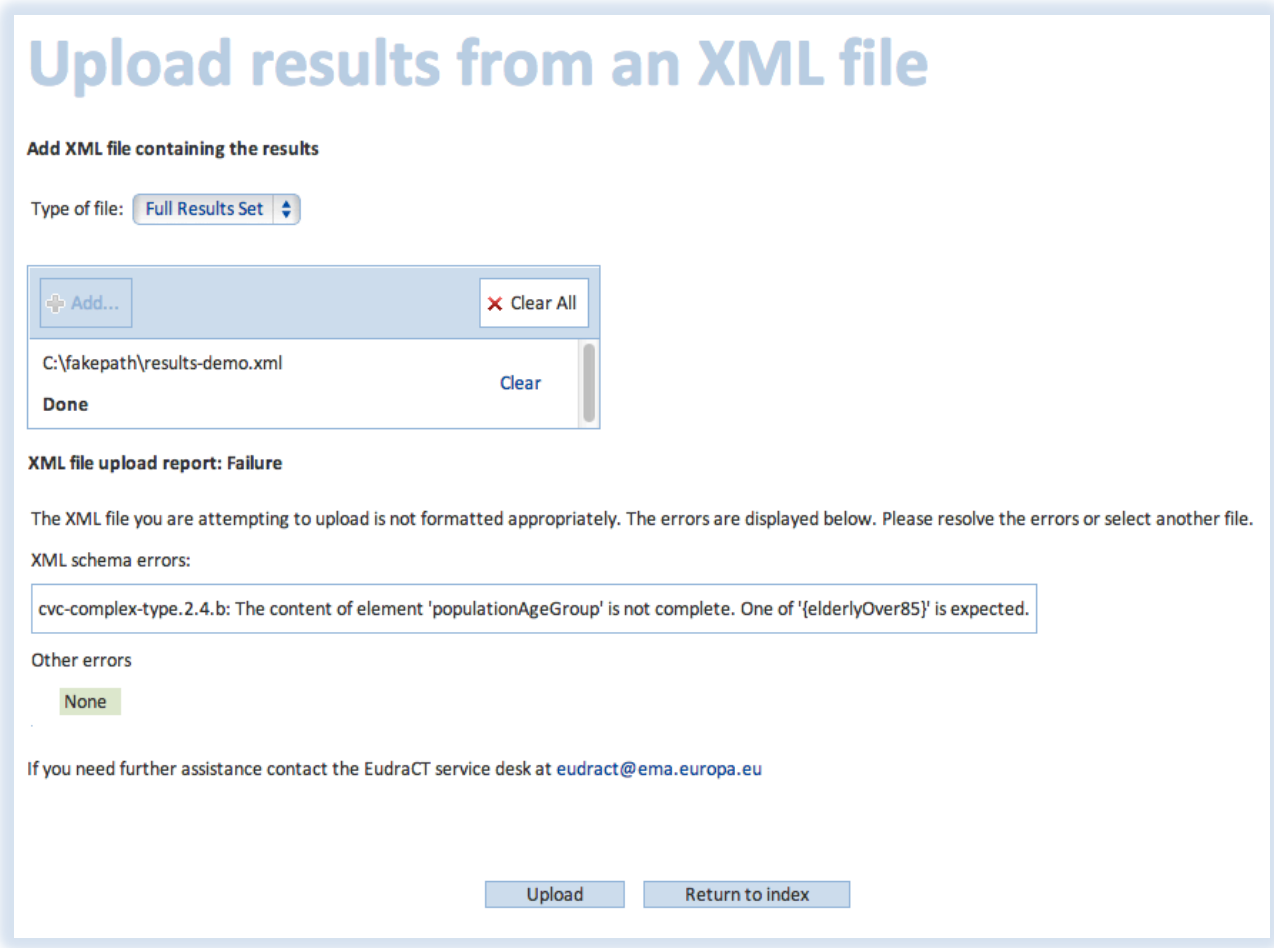

Figure 7: Missing element.

7.5.4. Incorrect reference id.

The XML violates the constraint of integrity that must be respected by id and idref. The section violating this constraint is:

```
<genderCategoricalCharacteristic>
  ...
  <totalBaselineGroup id="TotalBaselineGroup-4653">
    <title>Total title</title>
    <countableValues>
      <countableValue categoryId="Category-17625">
        <value xsi:nil="true" />
      </countableValue>
      <countableValue categoryId="Category-17624">
        <value xsi:nil="true" />
      </countableValue>
    </countableValues>
  </totalBaselineGroup>
  <categories>
    <category id="Category-17623">
      <name>Female</name>
    </category>
    <category id="Category-17624">
      <name>Male</name>
    </category>
  </categories>
  ...
</genderCategoricalCharacteristic>
```

In this section, the value of the attribute **categoryId** of the first element **countableValue** must have a value that is equal to **Category-17623**.

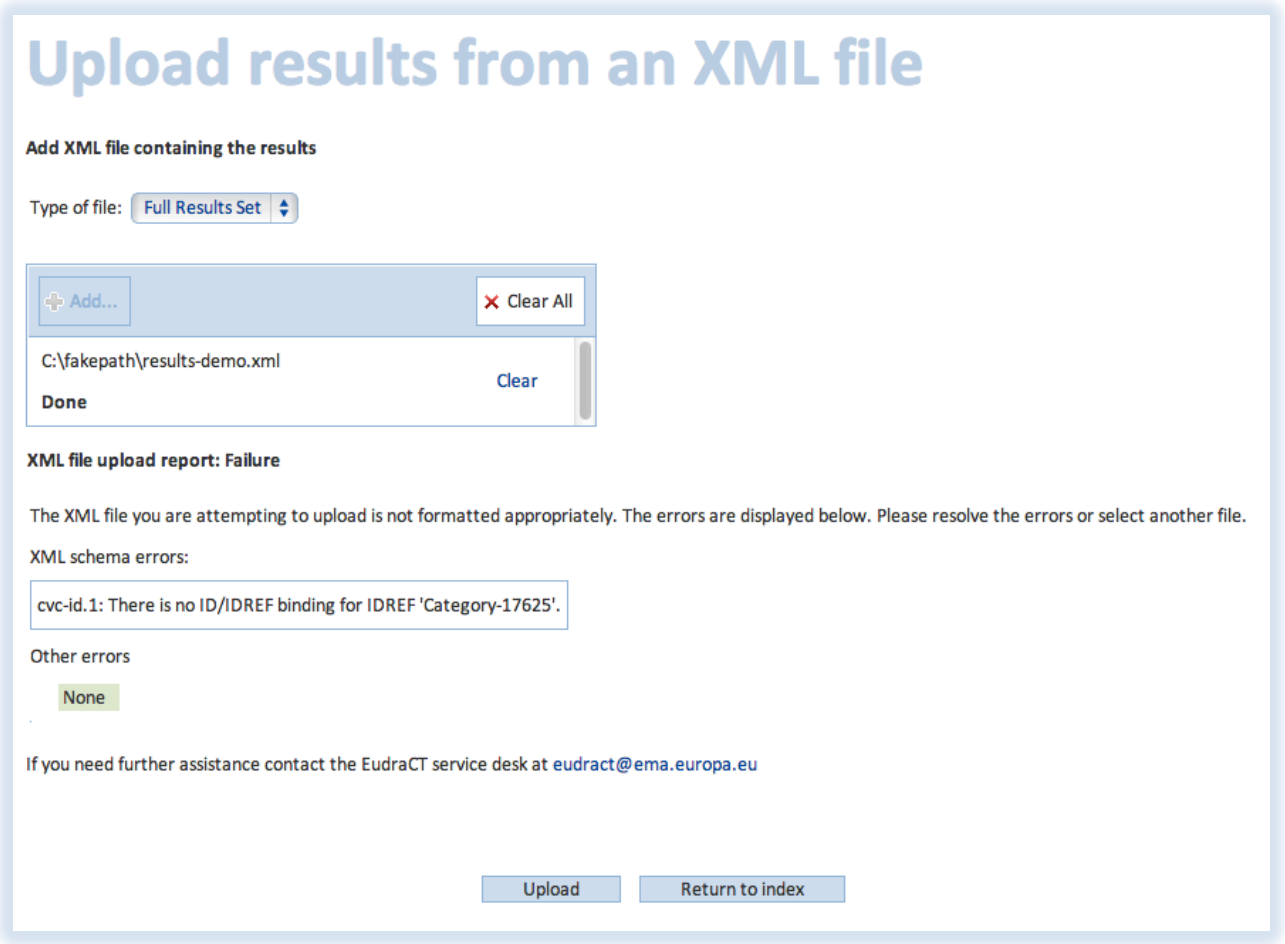

Figure 8: id and idref constraint violation.

7.5.5. Invalid term

The XML does not respect the list of controlled terms. The section violating the constraint is:

```
<subjectDisposition>
  <postAssignmentPeriods>
    <postAssignmentPeriod id="PostAssignmentPeriod-3240">
      ...
      <clinicalTrialRoles />
      <blindingType>
        <value>BLINDING.not</value>
      </blindingType>
      <allocation>
        <>rand-controlled</value>
      </allocation>
    </postAssignmentPeriod>
  </postAssignmentPeriods>
</subjectDisposition>
```

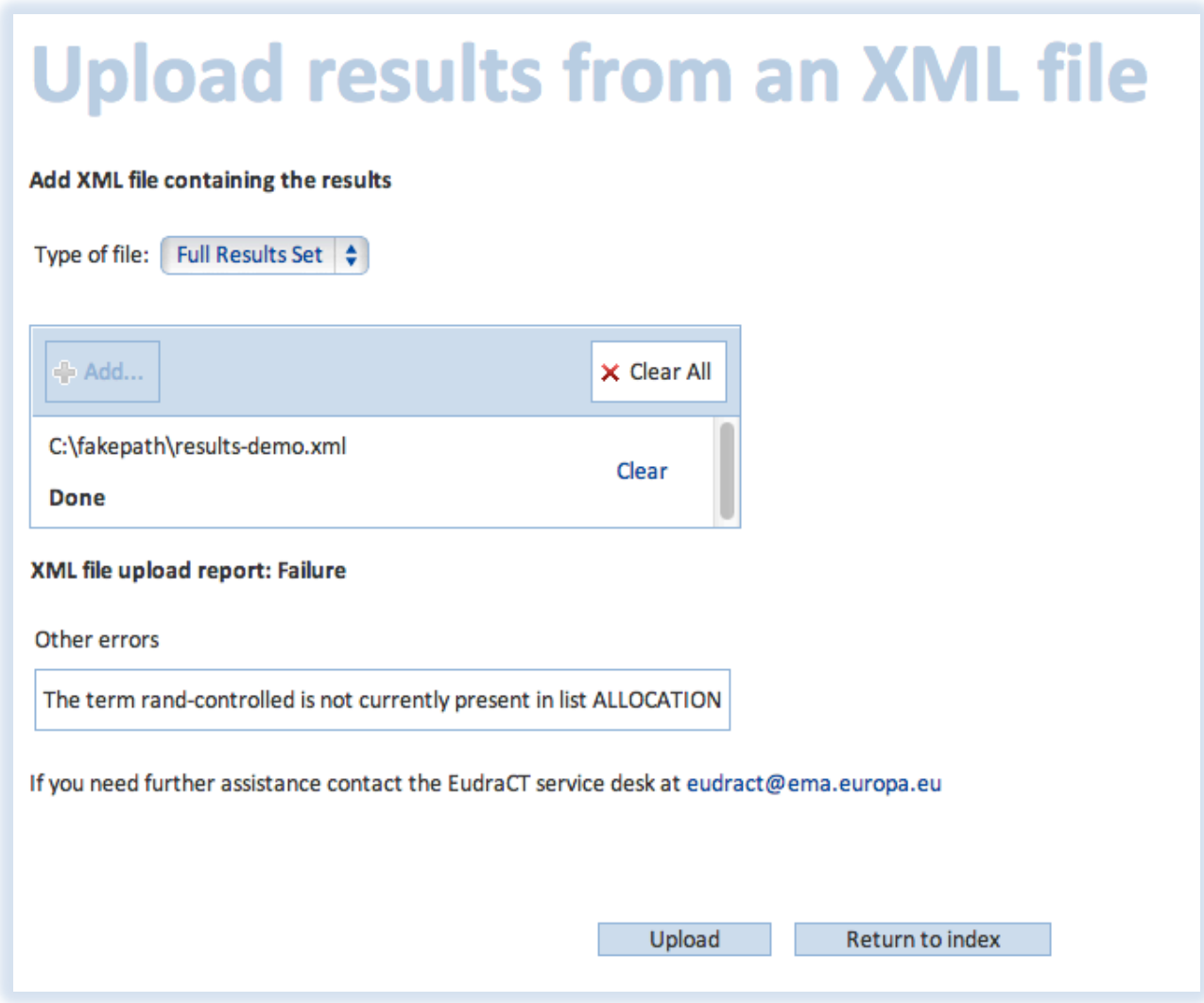

Figure 9: Invalid term.

The problem is fixed by using the appropriate term identifier, example: **`ALLOCATION.randControlled`**.

7.5.6. Multiple errors

If the XML has multiple errors, EudraCT will display them all in a table-like structure and not stop at the first error. The errors in the XML are highlighted:

```
<?xml version="1.0" encoding="UTF-8"?>
<tns:result eudractNumber="2008-002277-13"
xmlns:tns="http://eudract.ema.europa.eu/schema/clinical_trial_result"
  xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
  <trialInformation>
    <isrctnIdentifier>ISRCTN01234666</isrctnIdentifier>
    <usctnIdentifier xsi:nil="true" />
    <whoIdentifier xsi:nil="true" />
    <partOfPIP>toto</partOfPIP>
    <art45Related>false</art45Related>
    <art46Related>false</art46Related>
    <isGlobalEndOfTrialReached>false</isGlobalEndOfTrialReached>
    <globalEndOfTrialPremature>false</globalEndOfTrialPremature>
    <longTermFollowUpPlanned>false</longTermFollowUpPlanned>
    <sponsors />
    <pipnumbers />
    <otherIdentifiers />
    <countrySubjectCounts />
    <populationAgeGroup>
```

```
      <inUtero xsi:nil="true" />
      <pretermNewbornInfants xsi:nil="true" />
      <newborns xsi:nil="true" />
      <infantsAndToddlers xsi:nil="true" />
      <children xsi:nil="true" />
      <adolescents xsi:nil="true" />
      <adults xsi:nil="true" />
      <elderly65To84 xsi:nil="true" />
      <!–
        <elderlyOver85 xsi:nil="true" />
      -->
    </populationAgeGroup>
  </trialInformation>
</tns:result>
```

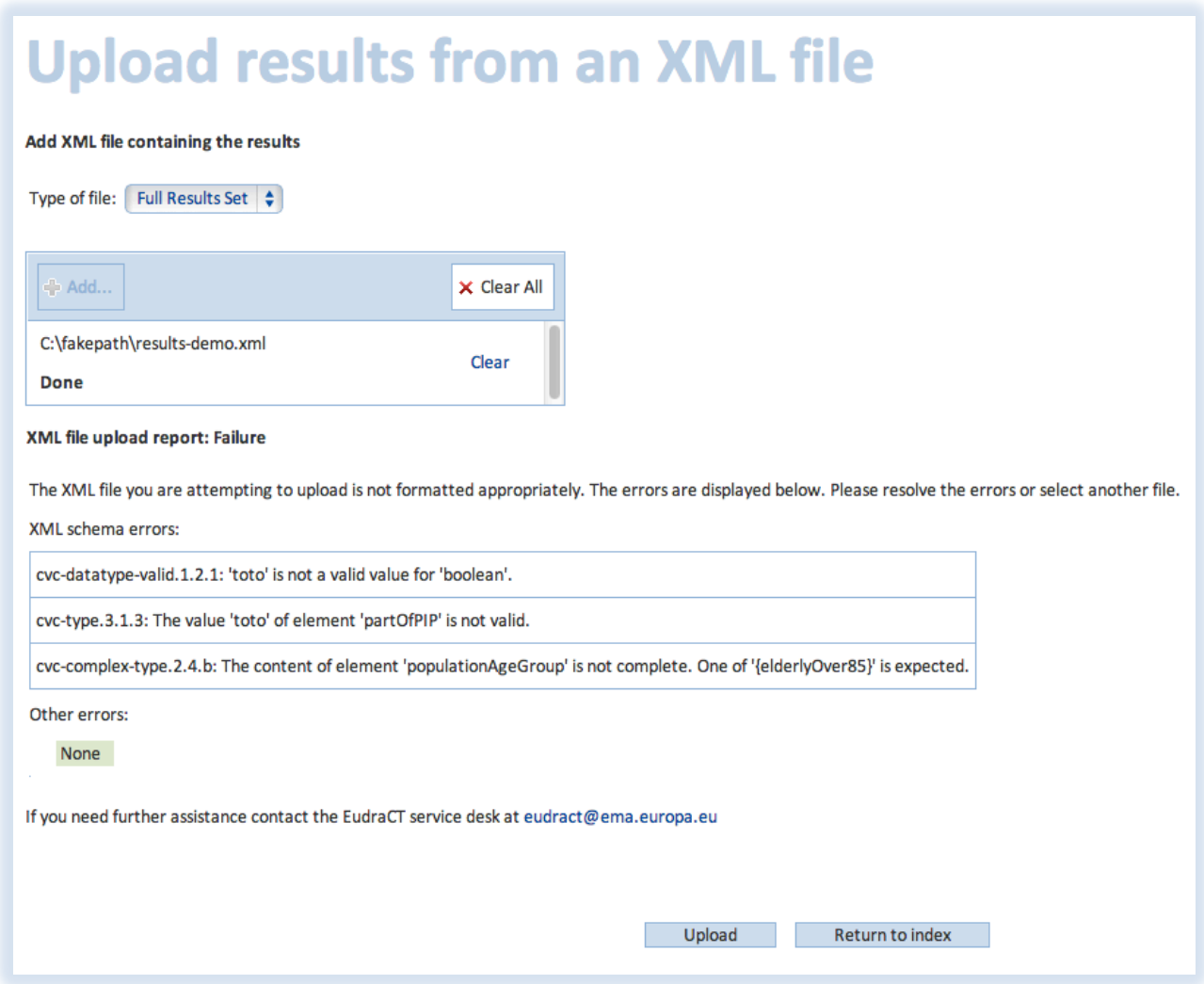

Figure 10: Multiple errors.

8. References and resources

[REF-1]	Extensible Markup Language (XML) 1.0	http://www.w3.org/TR/REC-xml
[REF-2]	XML Schema Part 1: Structures Second Edition	http://www.w3.org/TR/xmlschema-1
[REF-3]	XML Schema Part 2: Datatypes Second Edition	http://www.w3.org/TR/xmlschema-2
[REF-4]	European Union Telematics Controlled Terms	http://eutct.ema.europa.eu

	(EUTCT)	
[REF-5]	European Directorate for the Quality of Medicines & Healthcare (EDQM)	http://www.edqm.eu

9. Revisions

- 31/07/2013:
  - Addition of an example for organSystem in section 6.3.1.
  - Both the schemas results.xsd and adverseEvents.xsd have been modified to incorporate comments raised during the pilot.
- 10/10/2013:
  - Changes related to the draft status of the XML schemas.
- 09/12/2013:
  - Minor updates and addition of the section 7.
- 24/02/2014:
  - Updates to reflect minor changes to the XML schemas.
- 20/06/2014:
  - Note that the results schema (results.xsd) has been updated and the version incremented from 1.0 to 1.1. Please refer to the schema file (results.xsd) or the schema documentation file (results.pdf) for the details. Version 1.1 is effective from EudraCT version 10.1.2.

Appendix 1: List of EudraCT terms

List name		
Term name	**Term identifier**	
Adverse event assessment method		
systematic	**ADV_EVT_ASSESS_TYPE.**	**systematic**
non-systematic		**non_systematic**
Age unit		
day	**AGE_UNITS.**	**days**
hour		**hours**
minute		**minutes**
month		**months**
week		**weeks**
year		**years**
Allocation method		
randomised	**ALLOCATION.**	**randControlled**
non-randomised		**nonRandControlled**
n/a		**na**
Analysis method		
ANCOVA	**HYPOTHESIS_METHOD.**	**ancova**
ANOVA		**anova**
Chi-squared		**chisquared**
Chi-squared corrected		**chisquaredCorrected**
Cochran-Mantel-Haenszel		**cochranMantelHaenszel**
Fisher exact		**fisher**
Kruskal-wallis		**kruskalWallis**
Logrank		**logrank**
Mantel-Haenszel		**mantelHaenszel**
Mcnemar		**mcnemar**
Mixed models analysis		**mixedModel**
Regression, Cox		**regressionCox**
Regression, Linear		**regressionLinear**

Regression, Logistic		**regressionLogistic**
Wilcoxon (Mann-Whitney)		**wilcoxon**
Other		**other**
Analysis specification		
Pre-specified	**ANALYSIS_SPEC.**	**preSpecified**
Post-hoc		**postHoc**
Arm type		
Experimental	**ARM_TYPE.**	**experimental**
Active comparator		**activeComp**
Placebo		**placeboComp**
No IMP		**noImp**
Other		**other**
Baseline reporting model		
Arm	**BASELINE_REPORTING_MODEL.**	**arms**
Period		**period**
Blinding method		
Double blind	**BLINDING.**	**double**
Single blind		**single**
Not blinded		**not**
Central tendency		
arithmetic mean	**CENTRAL_TENDENCY.**	**arithmetic**
median		**median**
least squares mean		**leastSquares**
geometric mean		**geometric**
log mean		**log**
Comparison operator		
Confidence interval side		
1-sided	**CONF_INTERVAL_SIDE.**	**oneSided**
2-sided		**twoSided**
Dictionary		
MedDRA	**ADV_EVT_DICTIONARY_NAME.**	**Meddra**

SNOMED		**Snomed**
Other (specify)		**other**
Dispersion		
standard deviation	**DISPERSION.**	**standardDeviation**
inter-quartile range (min-max)		**interQuartile**
full range (min-max)		**fullRange**
Effect estimate		
Cox proportional hazard	**PARAMETER_TYPE.**	**coxProportionalHazard**
Hazard ratio (HR)		**hr**
Hazard ratio log		**hrl**
Mean difference (final values)		**meanDiffFinal**
Mean difference (net)		**meanDiffNet**
Median difference (final values)		**medianDiffFinal**
Median difference (net)		**medianDiffNet**
Odds ratio (OR)		**or**
Odds ratio log		**orl**
Risk difference (RD)		**rd**
Risk ratio (RR)		**rr**
Risk ratio log		**rrl**
Slope		**slope**
Other		**other**
Endpoint dispersion		
Not applicable	**ENDPOINT_DISPERSION.**	**na**
Standard deviation		**standardDeviation**
inter-quartile range (min-max)		**interQuartileRange**
full range (min-max)		**fullRange**
standard error		**standardError**
confidence interval		**confidenceInterval**
geometric coefficient of variation		**geometricCoefficientVariation**

Endpoint type		
Primary	**ENDPOINT_TYPE.**	**Primary**
Secondary		**Secondary**
Other pre-specified		**Other**
Post-hoc		**posthoc**
Long term rationale		
Safety	**LONG_TERM_RATIONALE.**	**safety**
Efficacy		**efficacy**
Ethical reason		**ethical**
Regulatory reason		**regulatory**
Scientific research		**scientific**
Measure Type		
number	**MEASURE_TYPE.**	**number**
arithmetic		**arithmetic**
median		**median**
least squares mean		**leastSquares**
geometric mean		**geometric**
log mean		**log**
Reason joined		
Late recruitment	**JOIN_REASON.**	**lateRecruitment**
Transferred in from other group/arm		**transferred**
Other		**other**
Reason not completed		
Adverse event, not serious	**NOT_COMPLETED_REASON.**	**adverseNotSerious**
Adverse event, serious fatal		**adverseSeriousFatal**
Adverse event, serious non-fatal		**adverseSeriousNonFatal**
Consent withdrawn by subject		**consentWithdrawn**
Lack of efficacy		**lackEfficacy**
Lost to follow-up		**lostFollowup**
Physician decision		**physicianDecision**
Pregnancy		**pregnancy**

Protocol deviation		**protocolViolation**
Transferred to other arm/group		**transferred**
Other		**other**
Statistical analysis type		
non-inferiority	**ANALYSIS_TYPE.**	**nonInferiority**
Equivalence		**equivalence**
Superiority		**superiority**
other		**other**
Study analysis stage		
interim	**ANALYSIS_STAGE.**	**Interim**
final		**final**
Subject analysis set type		
Intention-to-treat	**SBJ_ANALYSIS_SET_TYPE.**	**intentToTreat**
Per protocol		**perProtocol**
Full analysis		**fullAnalysisSet**
Safety analysis		**safetyPopulation**
Sub-group analysis		**subgroup**
Modified intention-to-treat		**modIntentToTreat**
Term duration unit		
month	**LONG_TERM_DURATION_UNITS.**	**months**
year		**years**
Trial role		
Subject	**TRIAL_ROLE.**	**subject**
Investigator		**investigator**
Monitor		**monitor**
Data analyst		**dataAnalyst**
Carer		**carer**
Assessor		**assessor**
Variability estimate type		
Standard deviation	**VAR_ESTIMATE_TYPE.**	**standardDev**
Standard error of the mean		**standardError**

Appendix 2: Validation rules

[DATA-VAL-1]

In the post-assignment period, if no blinding is used then the provider must not submit a list of roles blinded.

valid

```
<clinicalTrialRoles>
  <clinicalTrialRole>
    TRIAL_ROLE.subject
  </clinicalTrialRole>
  <clinicalTrialRole>
    TRIAL_ROLE.investigator
  </clinicalTrialRole>
  <clinicalTrialRole>
    TRIAL_ROLE.carer
  </clinicalTrialRole>
</clinicalTrialRoles>
<blindingType>
  BLINDING.double
</blindingType>

--

<clinicalTrialRoles></clinicalTrialRoles>
<blindingType>BLINDING.not</blindingType>
```

invalid

```
<clinicalTrialRoles>
  <clinicalTrialRole>
    TRIAL_ROLE.subject
  </clinicalTrialRole>
</clinicalTrialRoles>
<blindingType>BLINDING.not</blindingType>
```

[DATA-VAL-2]

For all lists that have ‘other’ as an option, the field containing the other term is used only in conjunction with the selection of the term ‘other’ from the list.

valid

```
<statisticalHypothesisTest>
  <comment>some comment</comment>
  <method>HYPOTHESIS_METHOD.anova</method>
  <value>1.12</value>
</statisticalHypothesisTest>

--

<statisticalHypothesisTest>
  <comment>some comment</comment>
  <method>HYPOTHESIS_METHOD.other</method>
  <otherMethod>G-test</otherMethod>
  <value>1.12</value>
</statisticalHypothesisTest>
```

invalid

```
<statisticalHypothesisTest>
  <comment>some comment</comment>
  <method>HYPOTHESIS_METHOD.anova</method>
  <otherMethod>G-test</otherMethod>
  <value>1.12</value>
</statisticalHypothesisTest>
```

[DATA-VAL-3]

If the question ‘Long term follow up planned?’ is answered ‘No’ then the rationales, duration and value fields must not be provided.

valid

invalid

<longTermFollowUpPlanned> false </longTermFollowUpPlanned> -- <longTermFollowUpPlanned> true </longTermFollowUpPlanned> <longTermDurationValue> 2 </longTermDurationValue> <longTermDurationUnits> LONG_TERM_DURATION_UNITS.years </longTermDurationUnits>	<longTermFollowUpPlanned> false </longTermFollowUpPlanned> <longTermDurationValue> 2 </longTermDurationValue> <longTermDurationUnits> LONG_TERM_DURATION_UNITS.years </longTermDurationUnits>

[DATA-VAL-4]
If the question 'Is trial part of an agreed Paediatric Investigation Plan (PIP)?' is answered 'No' then the EMA Paediatric Investigation Plan(s) field must be empty.

valid	*invalid*
<partOfPIP>**false**</partOfPIP> ... **<pipnumbers></pipnumbers>**	<partOfPIP>**false**</partOfPIP> ... <pipnumbers> **<pipNumber>EMEA-123456-PIP12-34</pipNumber>** **<pipNumber>EMEA-654321-PIP21-43</pipNumber>** </pipnumbers>

[DATA-VAL-5]
If the question 'Is this the analysis of the primary completion data?' is answered 'No' then the Primary completion date must not be provided.

valid	*invalid*
<analysisForPrimaryCompletion> **false** </analysisForPrimaryCompletion>	<analysisForPrimaryCompletion> **false** </analysisForPrimaryCompletion> **<primaryCompletionDate>** **2013-02-13T15:06:24Z** **</primaryCompletionDate>**

[DATA-VAL-6]
If the question 'Global end of trial date reached?' is answered 'No' then the Global end of trial date must not be provided.

valid	*invalid*
<isGlobalEndOfTrialReached> false	<isGlobalEndOfTrialReached> false

</isGlobalEndOfTrialReached>	</isGlobalEndOfTrialReached> <globalEndOfTrialDate> 2013-02-13T15:06:24Z </globalEndOfTrialDate>

[DATA-VAL-7]

The date of recruitment, the date of global end of trial and the date of primary completion are required to be in the past.

No example provided.

[DATA-VAL-8]

A maximum of one period will be considered the baseline period;

valid	*invalid*
<subectDispositions> <subectDisposition> <postAssignmentPeriods> <postAssignmentPeriod> ... **<baselinePeriod>** **true** **</baselinePeriod>** ... </postAssignmentPeriod> <postAssignmentPeriod> ... **<baselinePeriod>** **true** **</baselinePeriod>** ... </postAssignmentPeriod> </postAssignmentPeriods> </subjectDisposition> </subjectDispositions>	<subectDispositions> <subectDisposition> <postAssignmentPeriods> <postAssignmentPeriod> ... **<baselinePeriod>** **true** **</baselinePeriod>** ... </postAssignmentPeriod> <postAssignmentPeriod> ... **<baselinePeriod>** **true** **</baselinePeriod>** ... </postAssignmentPeriod> </postAssignmentPeriods> </subjectDisposition> </subjectDispositions>

[DATA-VAL-9]

If the status of an end point is ‘ready for collecting values’ at least one of the reporting groups or subject analysis sets must have been selected;

No example provided.

[DATA-VAL-10]

If the question ‘Do you want to use a different dictionary name and version or reporting this adverse event?’ is answered ‘No’, then the alternative dictionary name, alternative dictionary version and other dictionary name must not be provided.

valid	*invalid*
<dictionaryOverridden> **false** </dictionaryOverridden>	<dictionaryOverridden> **false** </dictionaryOverridden> **<dictionary>**

	<version>3</version> **<name>SNOMED</name>** **</dictionary>**

[DATA-VAL-11]

For any interruption, the restart date must not be before the interruption date.

valid	*invalid*

<globalInterruptions>
  <globalInterruption>
  <date>**2011-02-13T15:06:24Z**</date>
  <restartDate>
  2013-03-15T12:45:24Z
  </restartDate>
  </globalInterruption>
</globalInterruptions>
	<globalInterruptions>
	  <globalInterruption>
	  <date>**2011-02-13T15:06:24Z**</date>
	  <restartDate>
	  2010-04-08T12:45:24Z
	  </restartDate>
	  </globalInterruption>
	</globalInterruptions>

[DATA-VAL-12]

If the question ‘Were there any global substantial amendments to the protocol?’ is answered with the response ‘No’, then global amendments must not be provided.

valid	*invalid*

<hasGlobalAmendments>
  false
</hasGlobalAmendments>
<globalAmendments></globalAmendments>
	<hasGlobalAmendments>
	  false
	</hasGlobalAmendments>
	<globalAmendments>
	  <globalAmendment>
	  …
	  </globalAmendment>
	  <globalAmendment>
	  …
	  </globalAmendment>
	</globalAmendments>

[DATA-VAL-13]

If the question ‘Were there any global interruptions to the trial?’ is answered with the response ‘No’, then global interruptions must not be provided.

valid	*invalid*

<hasGlobalInterruptions>
  false
</hasGlobalInterruptions >
<globalInterruptions></globalInterruptions>
	<hasGlobalInterruptions>
	  false
	</hasGlobalInterruptions>
	<globalInterruptions>
	  <globalInterruption>
	  …
	  </globalInterruption>
	  <globalInterruption>
	  …
	  </globalInterruption>

	`</globalInterruptions>`

[DATA-VAL-14]

Terms referenced from EUTCT or EDQM must have their status to CURRENT.

No example provided.