XML Schema For Writing ISO 15189: 2007 - Compliant SOPs For Clinical Laboratory Examinations

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Abstracts: Standard Operating Procedures are generally hard copy text documents at clinical laboratories. Due to wider access to computer based technology, Standard Operating Procedures are increasingly kept in electronic form allowing easier and wider access to its users. Such electronic form of Standard Operating Procedures are generally in plain text form or some form of word-processor document. Such presentation-centric documents are difficult to append and revise and access online. Development of Standard Operating Procedures based on eXtended Markup Language(XML) can rectify these difficulties by separating data from its presentation. This study analyses requirements of IS/ISO:15189 and NABL, India for writing examination Standard Operating Procedures and develops appropriate schema for validation of Standard Operating Procedures for clinical laboratory examinations. [Patel S et al NJIRM 2012; 3(5) : 130-136]

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Introduction: Whenever a clinical laboratory plans for obtaining accreditation from National Accreditation Board for testing and calibration Laboratories (NABL), India, documents needs to be prepared by the laboratory as per guidelines issued by the NABL[1.]

For NABL accreditation clinical laboratory must prepare their documents using NABL-112[1] (Specific Criteria for Accreditation of Medical Laboratories) which, in turn uses IS/ISO 15189:2007[2] (Medical laboratories - Particular requirements for quality and competence). The laboratories are required to comply with all the requirements listed in the international standard IS/ISO 15189:2007. The Specific Criteria document must be used in conjunction with IS/ISO 15189. It provides an interpretation of the latter document and describes specific requirements for the clauses of IS/ISO 15189 which are general in nature[2.]

While preparing, amending and revising various NABL documents is a daunting task in general, SOPs are the most frequently used, amended and revised documents of all. This study is an effort to prepare SOPs in such a way that they can be prepared, used, revised and amended efficiently.

Clause 5.5 [particularly sub-clause 5.5.3] of IS/ISO 15189:2007 mentions requirements for documentation of examination procedures. NABL-112 have no specific criteria , over and above those mentioned in IS/ISO 15189:2007. Clause 5.5 of IS/ISO 15189:2007 also mentions that such documents can be kept in electronic form.

XML have been used as a preferred language for keeping medical documents and records in electronic form. Various international organizations have developed XML DTDs for healthcare information, e.g. ASTM XML Healthcare[3] from American Society for Testing and Materials and HL7 (Health Level Seven)[4] from Health Level Seven International.

Earlier efforts for using XML for writing medical laboratory SOPs using XML have ignored requirements of IS/ISO 15189:2007[5.] This study is an effort to use XML for documenting clinical laboratory examination SOPs in electronic form complaint with requirements of accreditation body in India i.e NABL, New Delhi and IS/ISO 15189:2007.

For finding requirements for documenting SOPs, ISO/IS 15189:2007 and NABL-112 was referred. XML Schema was developed to satisfy these requirements. Ubuntu 9.10 gEdit was used for writing the XML Schema, SOPs in XML format and XSLT. Ubuntu 9.10 command-line utility 'xmllint' was used to validate SOPs written in XML and Firefox was used to test XSLT. Relationship among XML Schema[6], XML, and XSLT[7] are shown in Table-1.

Table-1 Relationship among XML Schema, XML, and XSLT

File Type	Explanation for file type	Relationship in context of SOPs
XML Schema (.xsd)	Text document defining structure of XML document	Defines structure of SOPs as required by ISO/IS 15189:2007
XML (.xml)	Text document containing data	Actual SOPs written as per structure defined by XML Schema
XSLT (.xsl)	Text document used for retrieving and presenting XML data in web-browser.	This document define which data of SOPs should be displayed and what should be the format of its display in web-browsers like Firefox and Internet Explorer.

Table 2 lists various requirements by IS/ISO 15189:2007 sub-clause 5.5.3 for documenting SOPs.

Table-2 requirements by IS/ISO 15189:2007 sub-clause 5.5.3 for documenting SOPs
Document control identifiers
purpose of the examination
principle of the procedure used for examinations
performance specifications
primary sample system
type of container and additives
required equipment and reagents
calibration procedures
procedural steps
quality control procedures
Interferences
principle of procedure for calculating results, including measurement uncertainty
biological reference intervals
reportable interval of examination results
alert/critical values
laboratory interpretation
safety precautions
potential sources of variability

General structure of XML Schema for clinical laboratory SOPs: Complete XML Schema for clinical laboratory SOPs, example XML for Serum Creatinine and example XSL file are available as online supplement to this article. The highest level of XML element is named SOP(XML Schema code is in bold italics). It contain sequence of elements, each representing IS/ISO 15189:2007 requirements presented in Table-2.

```
<xs:element name="SOP">
  <xs:complexType>
   <xs:sequence>
    <xs:element ref="sop:Document_Control"/>
    <xs:element ref="sop:Purpose_of_Examination"/>
    <xs:element ref="sop:Principle_of_Examination"/>
    <xs:element ref="sop:Performance_Specifications"/>
    <xs:element ref="sop:Primary_Sample_Systems"/>
    <xs:element ref="sop:Required_Equipments_and_Reagents"/>
    <xs:element ref="sop:Procedural_Steps"/>
    <xs:element ref="sop:Interferences_and_Cross_Reactions"/>
    <xs:element ref="sop:Biological_Reference_Intervals"/>
```

```
    <xs:element ref="sop:Reportable_Interval_of_Examination_Results"/>
    <xs:element minOccurs="0" ref="sop:Critical_Values"/>
    <xs:element ref="sop:Laboratory_Interpretation"/>
    <xs:element ref="sop:Safety_Precaution"/>
    <xs:element ref="sop:Potential_Sources_of_Variability"/>
   </xs:sequence>
  </xs:complexType>
 </xs:element>
```

As some examinations need not have Critical Values (e.g Serum Cholesterol) it need not be present in all SOPs, hence their minOccurs=”0”. “type of container and additives” is absent as sequence of SOP element, because it is logical to add it as sequence of “primary sample systems”. Following is description of some very important elements contained in SOP.

Document control identifiers: To conform with clause 4.3 of IS/ISO 15189:2007, element “Document_Control” have sequence of Name, Doc_ID, Revision, Amendment, Laboratory_Name, Preparing_Authority, Approving_Authority.

```
<xs:element name="Document_Control">
 <xs:complexType>
 <xs:sequence>
 <xs:element ref="sop:Name"/>
 <xs:element ref="sop:Doc_ID"/>
 <xs:element ref="sop:Revision"/>
 <xs:element minOccurs="0" maxOccurs="unbounded" ref="sop:Amendment"/>
 <xs:element ref="sop:Laboraory_Name"/>
 <xs:element ref="sop:Preparing_Authority"/>
 <xs:element ref="sop:Approving_Authority"/>
 </xs:sequence>
 </xs:complexType>
 </xs:element>
```

Of special importance is “Amendment” element.

```
<xs:element name="Amendment">
 <xs:complexType>
 <xs:sequence>
 <xs:element ref="sop:Date"/>
 <xs:element ref="sop:Tag"/>
 <xs:element ref="sop:Before_Amendment"/>
 <xs:element ref="sop:After_Amendment"/>
 <xs:element ref="sop:Reason"/>
 </xs:sequence>
 <xs:attributeGroup ref="sop:attlist.Amendment"/>
 </xs:complexType>
 </xs:element>
```

It has facility to include unlimited number of amendments with ability to store date of amendment, reason for amendment, element Tag-name which is amended, content before amendment and content after amendment.

performance specifications: Table-3 lists some of the performance specifications mentioned in IS/ISO 15189:2007.

Table-3 performance specifications mentioned in IS/ISO 15189:2007 sub-clause 5.5.3 for documenting SOPs

Linearity
Precision
accuracy expressed as uncertainty of measurement
detection limit
measuring interval
trueness of measurement
analytical sensitivity
analytical specificity

Each of the performance specifications mentioned in Table-3 is mentioned as attribute “name” of the element "Performance_Specification". Choice is given to express performance specification as interval (e.g measuring interval, linearity) or point values (e.g analytical sensitivity).

```
<xs:element name="Performance_Specification">
 <xs:complexType>
 <xs:sequence>
 <xs:element ref="sop:Description"/>
 <xs:element minOccurs="0" ref="sop:Document"/>
 <xs:choice minOccurs="0">
 <xs:element ref="sop:Intervals"/>
 <xs:element ref="sop:Point_Values"/>
 </xs:choice>
 <xs:element minOccurs="0" ref="sop:Record"/>
 </xs:sequence>
 <xs:attributeGroup ref="sop:attlist.Performance_Specification"/>
 </xs:complexType>
 </xs:element>
 <xs:attributeGroup name="attlist.Performance_Specification">
 <xs:attribute name="name" use="required" type="xs:NMTOKEN"/>
 </xs:attributeGroup>
```

For each specifications, relevant supporting document(Kit literature, CLIA criteria etc.) and records(IQC, EQAS etc.) can be hyperlinked using respective elements present in element “Performance_Specification”.

Required_Reagents:“Required_Reagents” element have attribute “type” to indicate source of reagent as ready-to-use reagent kits or in-house reagents for some examinations.

```
<xs:element name="Required_Reagents">
 <xs:complexType>
 <xs:sequence>
 <xs:element ref="sop:Summary"/>
 <xs:element minOccurs="0" maxOccurs="unbounded" ref="sop:Reagent"/>
 </xs:sequence>
 <xs:attributeGroup ref="sop:attlist.Required_Reagents"/>
 </xs:complexType>
 </xs:element>
```

"Summary" element present in "Required_Reagents" is useful to summarize final reaction conditions, while "Reagent" element present in "Required_Reagents" contain separate section for documenting instructions for making and storing reagents.

```
<xs:element name="Reagent">
 <xs:complexType>
 <xs:sequence>
 <xs:element ref="sop:Making_Reagent"/>
 <xs:element ref="sop:Storing_Reagent"/>
 </xs:sequence>
 <xs:attributeGroup ref="sop:attlist.Reagent"/>
 </xs:complexType>
  </xs:element>
  <xs:attributeGroup name="attlist.Reagent">
    <xs:attribute name="name" use="required" type="xs:NMTOKEN"/>
  </xs:attributeGroup>
```

Procedural Steps: Element Procedural_Steps includes Sample_Receipt, Sample_Preparations, Equipment_Operation, Analytical_Procedure_Reference, Analytical_Work_Desk_Instructions, Calibration_Procedures, Principle_of_Procedure_for_Calculating_Results_and_Measurement_Uncertainty and Quality_Control_Procedures. .Calibration and Quality Control are included as children of Procedural Steps.

```
<xs:element name="Procedural_Steps">
   <xs:complexType>
    <xs:sequence>
      <xs:element ref="sop:Sample_Receipt"/>
      <xs:element ref="sop:Sample_Preparation"/>
      <xs:element ref="sop:Equipment_Operation"/>
      <xs:element ref="sop:Analytical_Procedure_Reference"/>
      <xs:element maxOccurs="unbounded" ref="sop:Analytical_Work_Desk_Instructions"/>
      <xs:element ref="sop:Calibration_Procedures"/>
      <xs:element

ref="sop:Principle_of_Procedure_for_Calculating_Results_and_Measurement_Uncertainty"/>
      <xs:element ref="sop:Quality_Control_Procedures"/>
    </xs:sequence>
   </xs:complexType>
  </xs:element>
```

Many of the above elements have Document as their child because they are common across SOPs e.g Sample_Receipt and Sample_Preparations.

```
<xs:element name="Document">
  <xs:complexType mixed="true">
   <xs:attributeGroup ref="sop:attlist.Document"/>
  </xs:complexType>
 </xs:element>
 <xs:attributeGroup name="attlist.Document">
  <xs:attribute name="reference" use="required"/>
 </xs:attributeGroup>
```

Element "Document" have attributes to make it a hyperlink. Such documents could be another XML file or a PDF User manual from equipment manufacturer even a hyperlink to login to LIS for reviewing IQC data for an examination.

Various Intervals and Values in SOPs:
Biological_Reference_Intervals, Reportable_Interval_of_Examination_Results, Critical_Values have "Interval" or "Point_Value" as their children to include "from-to" type of documentation or "greater than/less than" type of documentation.

Interval: Element "Interval" have three children, "From", "To" and "Unit".

```
<xs:element name="Interval">
  <xs:complexType>
   <xs:sequence>
    <xs:element ref="sop:Unit"/>
    <xs:element ref="sop:From"/>
    <xs:element ref="sop:To"/>
   </xs:sequence>
  </xs:complexType>
 </xs:element>
```

Point Value: Point Values have Value and Unit as its children and operator as its attribute.

```
<xs:element name="Point_Value">
  <xs:complexType>
   <xs:sequence>
    <xs:element ref="sop:Unit"/>
    <xs:element ref="sop:Value"/>
   </xs:sequence>
   <xs:attributeGroup ref="sop:attlist.Point_Value"/>
  </xs:complexType>
 </xs:element>
 <xs:attributeGroup name="attlist.Point_Value">
  <xs:attribute name="operator" use="required"/>
 </xs:attributeGroup>
```

The XSL schema is prepared in such a way that if it is used to validate the SOP written in XML, a successfully validated SOP will have all essential features required by ISO/IS 15189:2007. Moreover, online formatting of such SOPs in a web browser will require a common XSL file, their by unifying display of all SOPs. By selecting appropriate XSL, same XML code can be used for displaying SOPs in different context e.g SOP for technicians (which do not include reagent preparations), SOPs for chief Biochemist(Which include reagent preparations but need not show interpretations) or SOP for Authorized signatories which will emphasize interferences and interpretations and various ranges(e.g reference, critical and Reportable ranges).

Note for using Online supplement files for demonstrating XML SOPs: Store SOP.xml, SOP.xsd and Creatinine.xml in one folder. Open Creatinine.xml in any web browser like Firefox. All source code in these files is released under GNU license[8.]

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