Generation and publishing of statistical output for eCTD's at Novo Nordisk

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Mikkel Traun,
CDW Operations
Novo Nordisk A/S

mt@novonordisk.com

Generation and publishing of statistical output for eCTD's at Novo Nordisk

- At NN we have a process for **specification**, **planning**, **implementing** and **publishing** of statistical output for section 14 of the ICTR in the eCTD format
- This process and tools have been evolved over the years and we see it as part of our best practices
- A key element is a XML tagging of metadata for each output file
- And we continuously have ideas and visions for improvements

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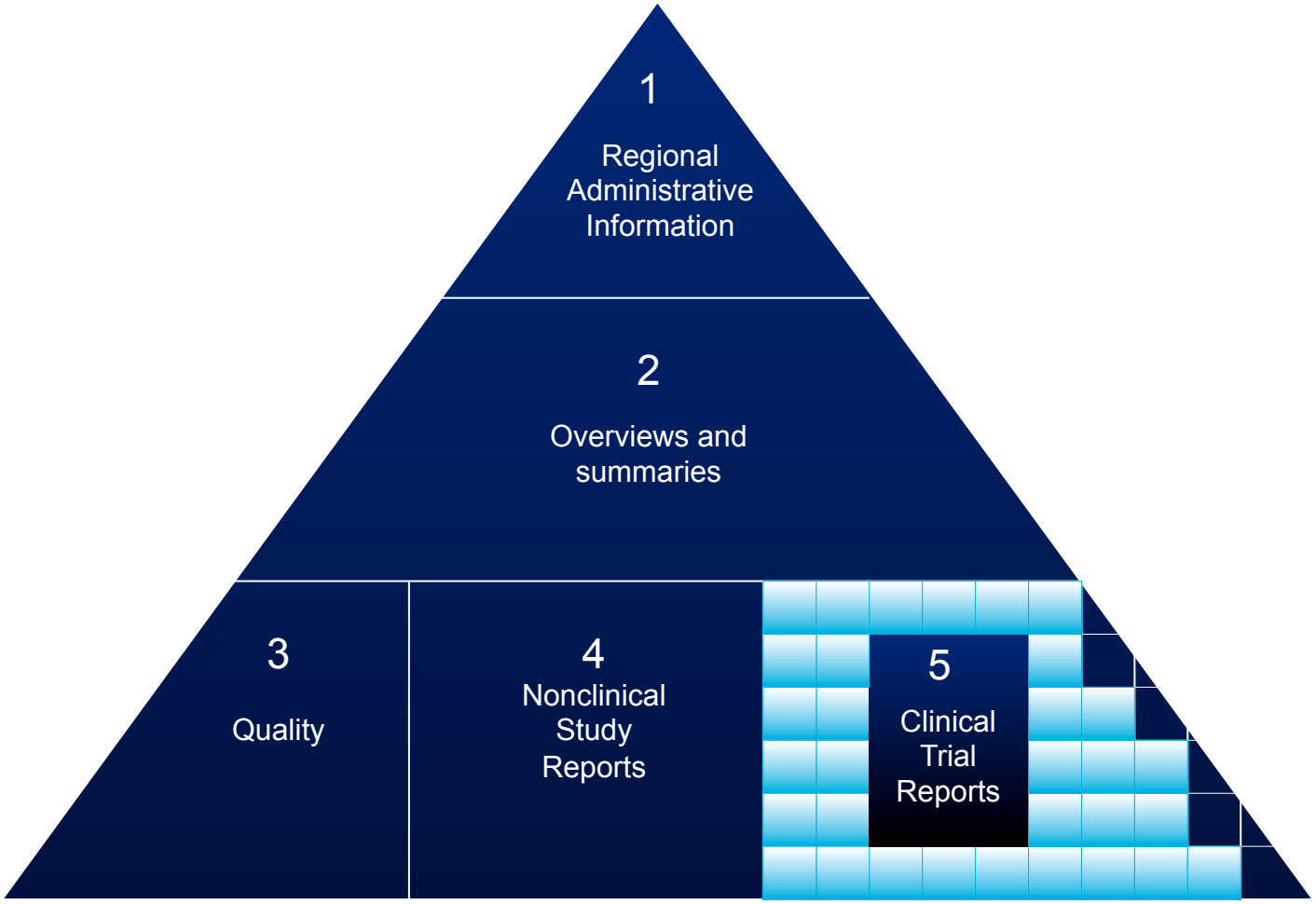
Electronic Common Technical Document (eCTD)



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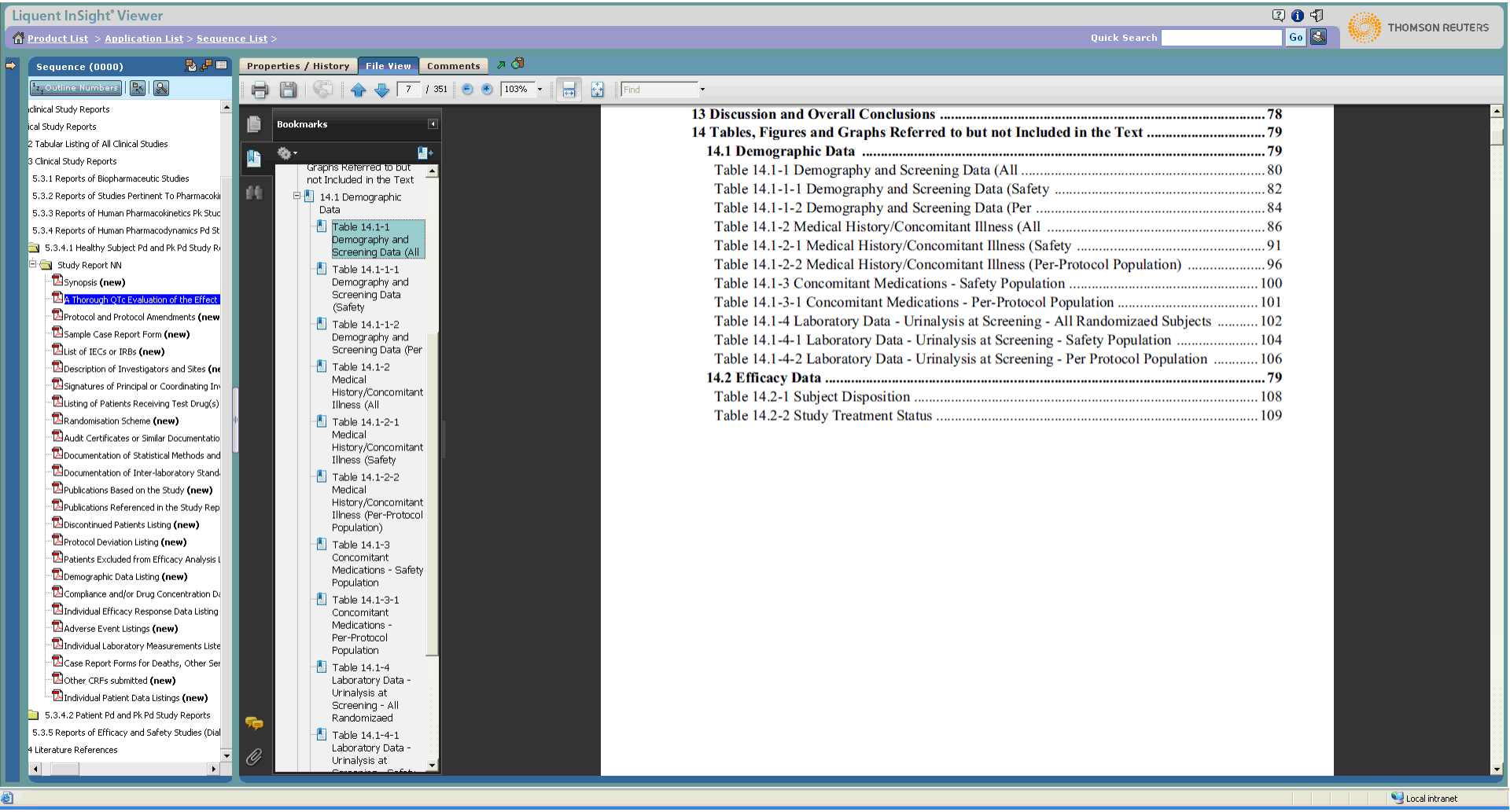
Sample eCTD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Product List > Application List > Sequence List >
Quick Search
Go
THOMSON REUTERS
Sequence (0000)
Outline Numbers
Study Report NN
Synopsis (new)
A Thorough QTc Evaluation of the Effect
Protocol and Protocol Amendments (new
Sample Case Report Form (new)
List of IECs or IRBs (new)
Description of Investigators and Sites (ne
Signatures of Principal or Coordinating Inv
Listing of Patients Receiving Test Drug(s)
Randomisation Scheme (new)
Audit Certificates or Similar Documentatio
Documentation of Statistical Methods and
Documentation of Inter-laboratory Stand
Publications Based on the Study (new)
Publications Referenced in the Study Rep
Discontinued Patients Listing (new)
Protocol Deviation Listing (new)
Patients Excluded from Efficacy Analysis
Demographic Data Listing (new)
Compliance and/or Drug Concentration D
Individual Efficacy Response Data Listing
Adverse Event Listings (new)
Individual Laboratory Measurements Liste
Case Report Forms for Deaths, Other Ser
Other CRFs submitted (new)
Individual Patient Data Listings (new)
5.3.4.2 Patient Pd and Pk Pd Study Reports
5.3.5 Reports of Efficacy and Safety Studies (Dial
4 Literature References
Properties / History
File View
Comments
7 / 351
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Find
Bookmarks
Graphs Referred to but not Included in the Text
14.1 Demographic Data
Table 14.1-1 Demography and Screening Data (All
Table 14.1-1-1 Demography and Screening Data (Safety
Table 14.1-1-2 Demography and Screening Data (Per
Table 14.1-2 Medical History/Concomitant Illness (All
Table 14.1-2-1 Medical History/Concomitant Illness (Safety
Table 14.1-2-2 Medical History/Concomitant Illness (Per-Protocol Population)
Table 14.1-3 Concomitant Medications - Safety Population
Table 14.1-3-1 Concomitant Medications - Per-Protocol Population
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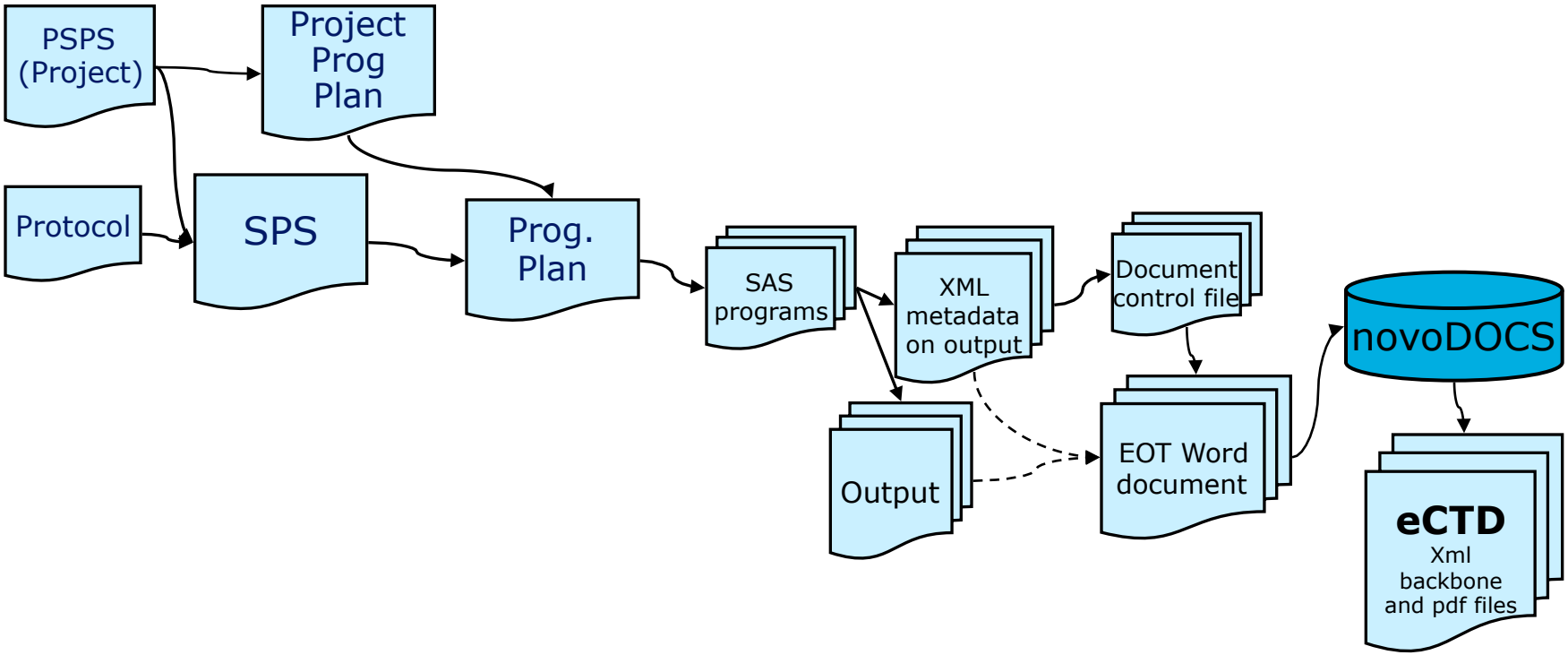
Local intranet

Process from specification to eCTD output

Specification → **Planning** → **Implementation** → **Publishing**



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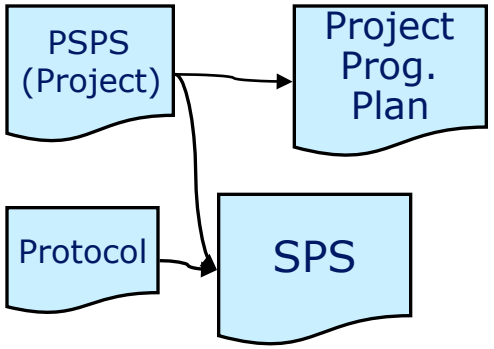
Specification | Planning | Implemen-tation | Publishing



- The Project Statistical Programming Specification (**PSPS**) holds the **standard Template Specification**
- The **Protocol** holds the SAP section and Trial Metadata specification
- The **Project Programming Plan** holds linkage between **standard templates** and use of **standard programs** and ID's
- The **SPS** holds detailed **specification** of all **output** that are to be part of the ICTR in a **SPS Template Section**

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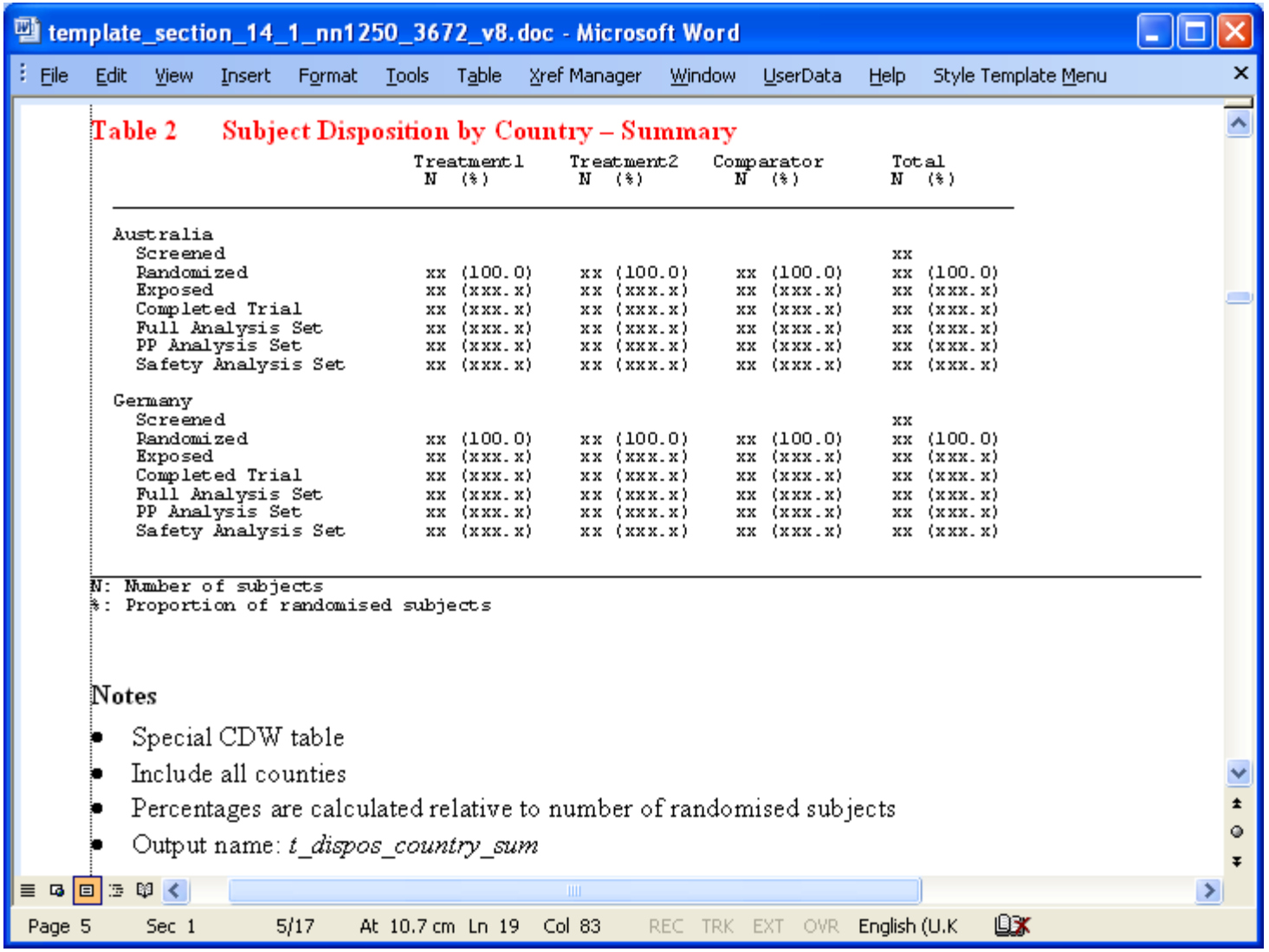
Sample SPS Template Specification



template_section_14_1_nn1250_3672_v8.doc - Microsoft Word

File Edit View Insert Format Tools Table Xref Manager Window UserData Help Style Template Menu

Table 2 Subject Disposition by Country – Summary

	Treatment1 N (%)	Treatment2 N (%)	Comparator N (%)	Total N (%)
Australia				
Screened				xx
Randomized	xx (100.0)	xx (100.0)	xx (100.0)	xx (100.0)
Exposed	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
Completed Trial	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
Full Analysis Set	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
PP Analysis Set	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
Safety Analysis Set	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
Germany				
Screened				xx
Randomized	xx (100.0)	xx (100.0)	xx (100.0)	xx (100.0)
Exposed	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
Completed Trial	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
Full Analysis Set	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
PP Analysis Set	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)
Safety Analysis Set	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)	xx (xxx.x)

N: Number of subjects
%: Proportion of randomised subjects

Notes

- Special CDW table
- Include all counties
- Percentages are calculated relative to number of randomised subjects
- Output name: *t_dispos_country_sum*

Page 5 Sec 1 5/17 At 10.7 cm Ln 19 Col 83 REC TRK EXT OVR English (U.K

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Specification | **Planning** | Implementation | Publishing

- Specify each **output** and **program** or **standard program** producing the output
- Tracks validation status, who, when, etc.

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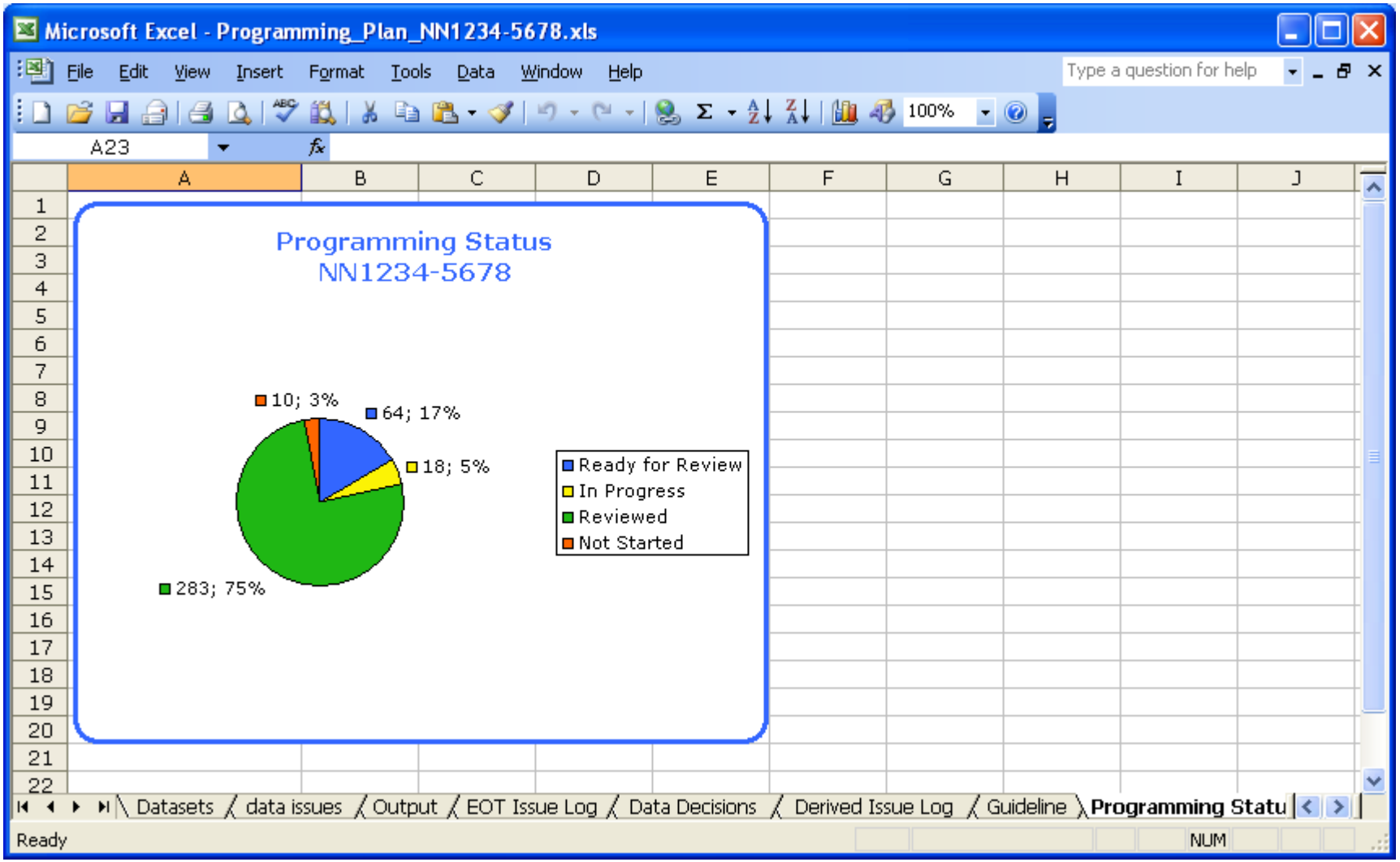
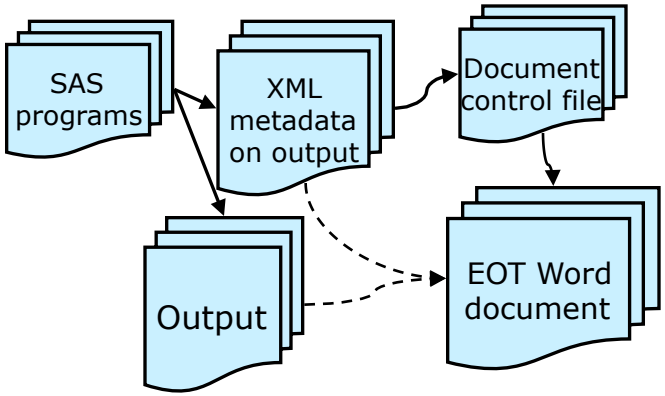
Status overview in ProgPlan



Specification | Planning | **Implementation** | Publishing

- SAS programs calls %init_start macro for generation of output
- SAS output directed to file in specified format
- XML file generated with metadata definition of output
  - Document section
  - Title
  - Sequence ID



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SAS program call %init_start

```
%init_start_v04(
    outtype              = Table
   ,level                = 2
   ,id                   = 1420100
   ,document             = 14_2
   ,exp_dataset          =
   ,pgmname              = t_subj_dis.sas
   ,paper_orientation    = land
   ,font_size            = 9
   ,output_format        =
   ,title_text           = Subject disposition by Treatment
   ,data                 =
   ,abbrev_cols          = row_lb
   ,usr_footnote         =
   ,usr_footnote_delim   = ~
   ,inc_auto_footnotes   = yes
   ,auto_filename        = yes
   ,pre_output_name      =
   ,post_output_name     = t_subj_dis_all
);
```

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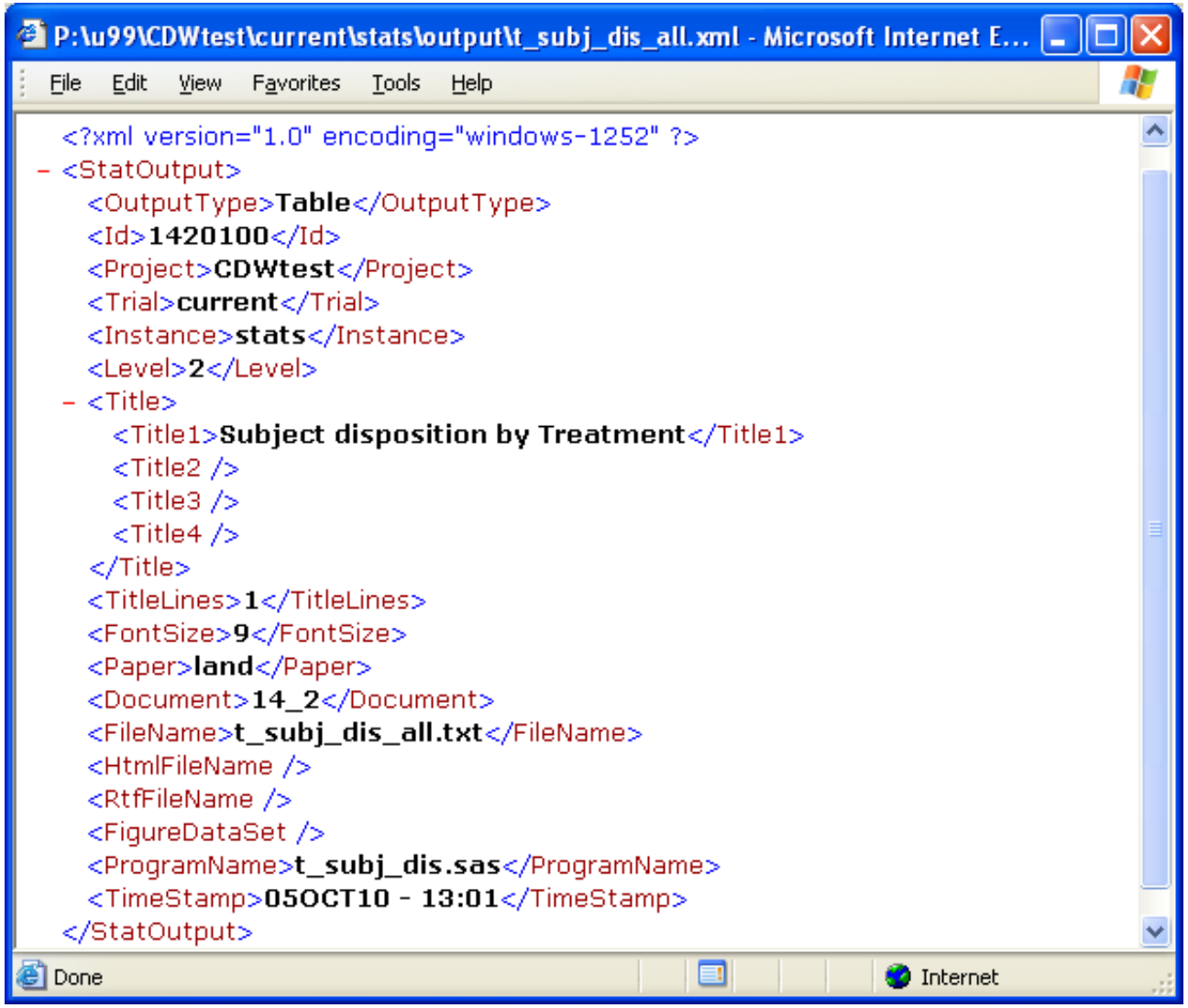
SAS Program makes output and XML



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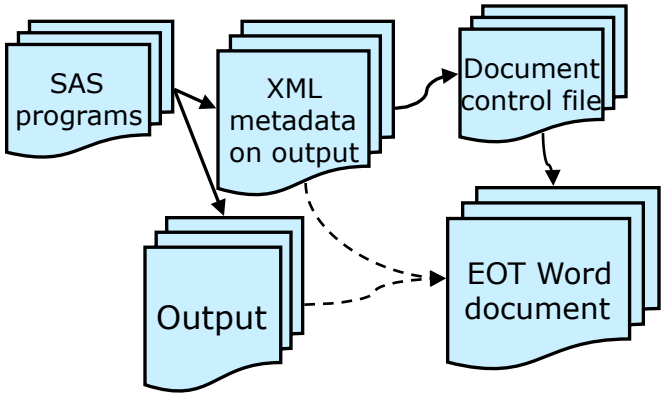
Specification | Planning | **Implementation** | Publishing

- SAS programs calls %init_start macro for generation of output
- SAS output directed to file in specified format
- XML file generated with metadata definition of output
  - Document section
  - Title
  - Sequence ID
- Automatic assembling of output files into section documents
- Automatic table numbering
- Automatic TOC and local bookmarks



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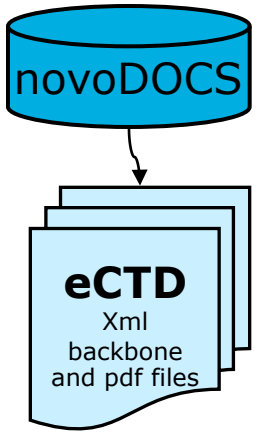
Specification | Planning | Implemen-tation | **Publishing**

- Integrate section documents into master documents
- Master TOC, bookmarks, etc.
- Volumes and page numbering



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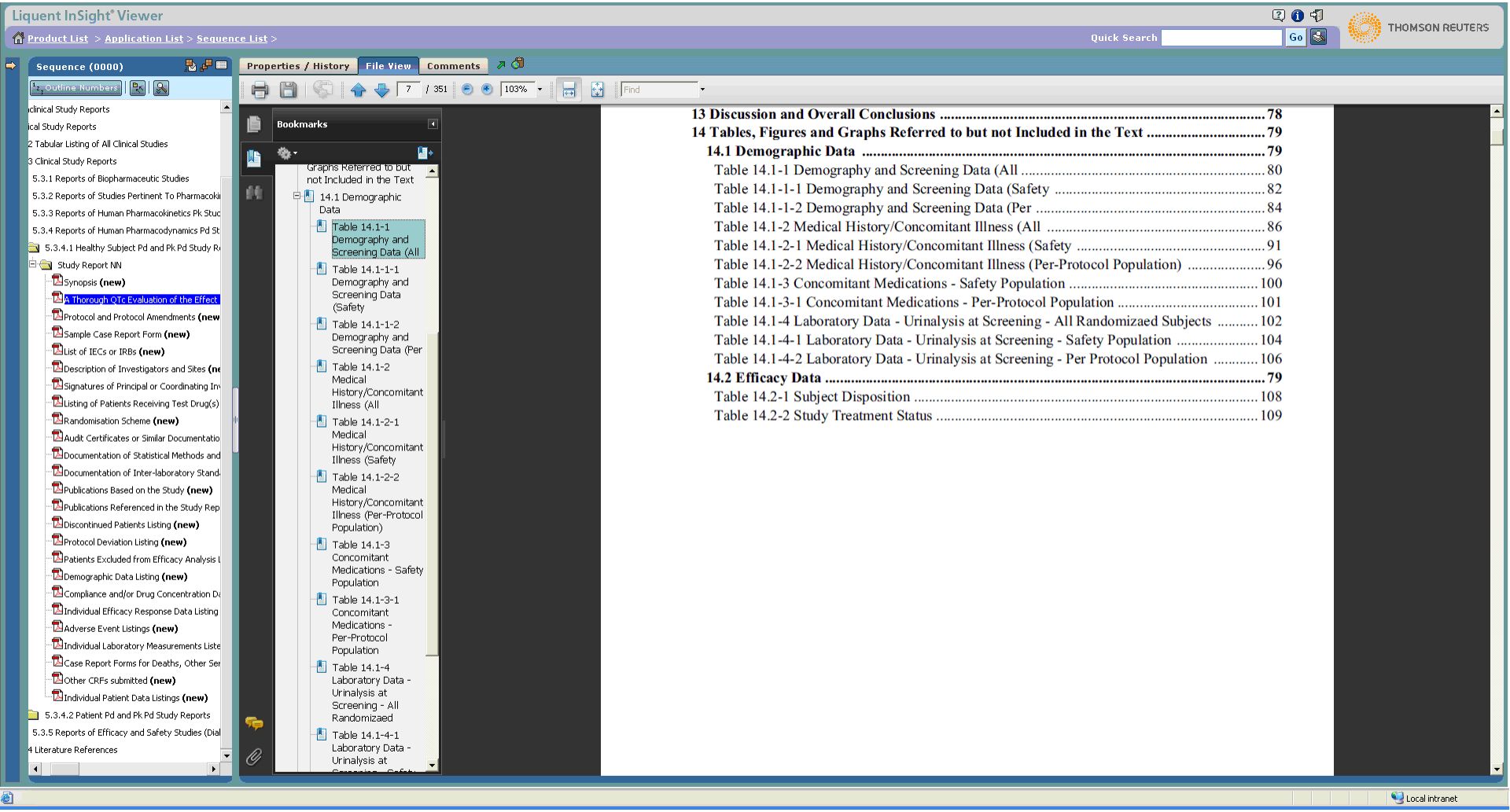
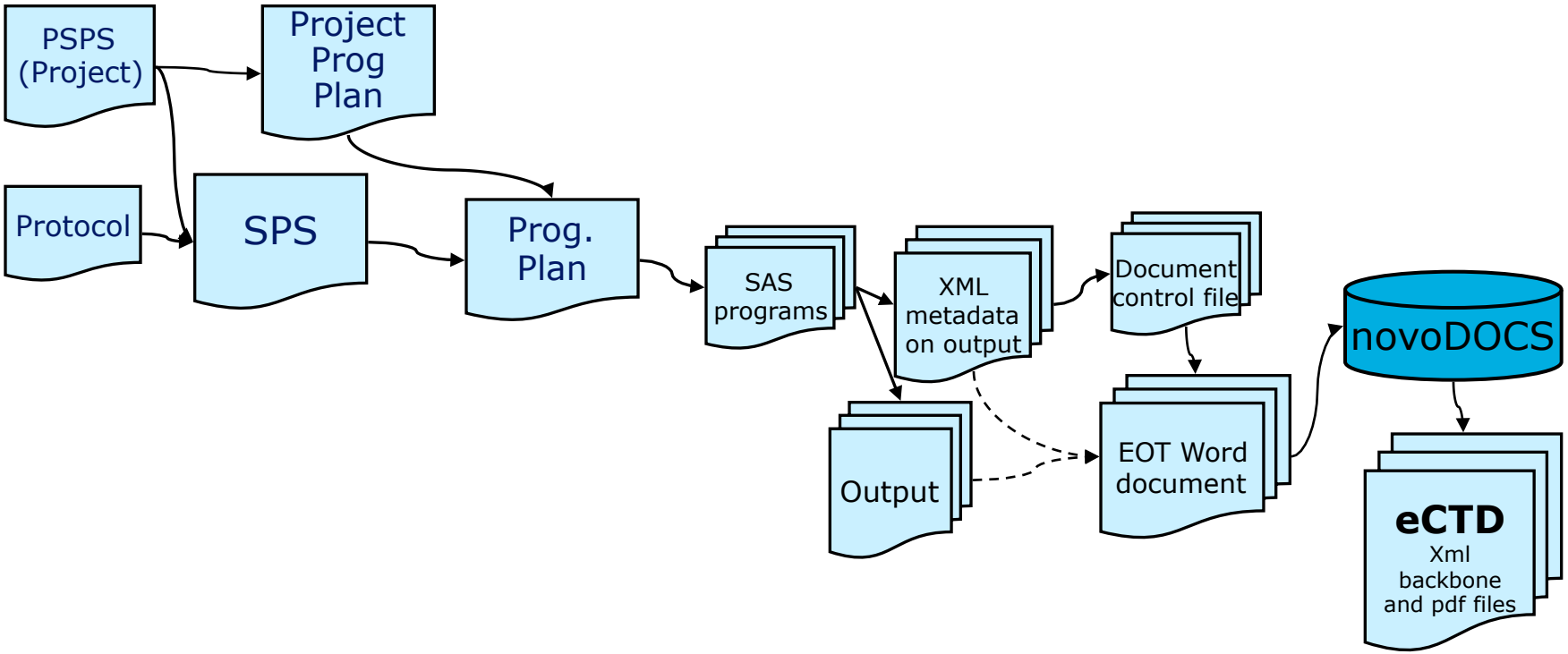
Sample NN eCTD



Process from specification to eCTD output

Specification → **Planning** → **Implementation** → **Publishing**



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Benefit and Issues in current process

- Benefits
  - Standard programs have been made generic and to a large extent metadata driven
  - Assembling of individual output files into document sections
- Issues
  - Too much flexibility in standard elements
  - Manual process of making trial SPS from 'P'SPS
  - Too much input is needed to call standard programs

- Improvements to the Trial SPS process is needed

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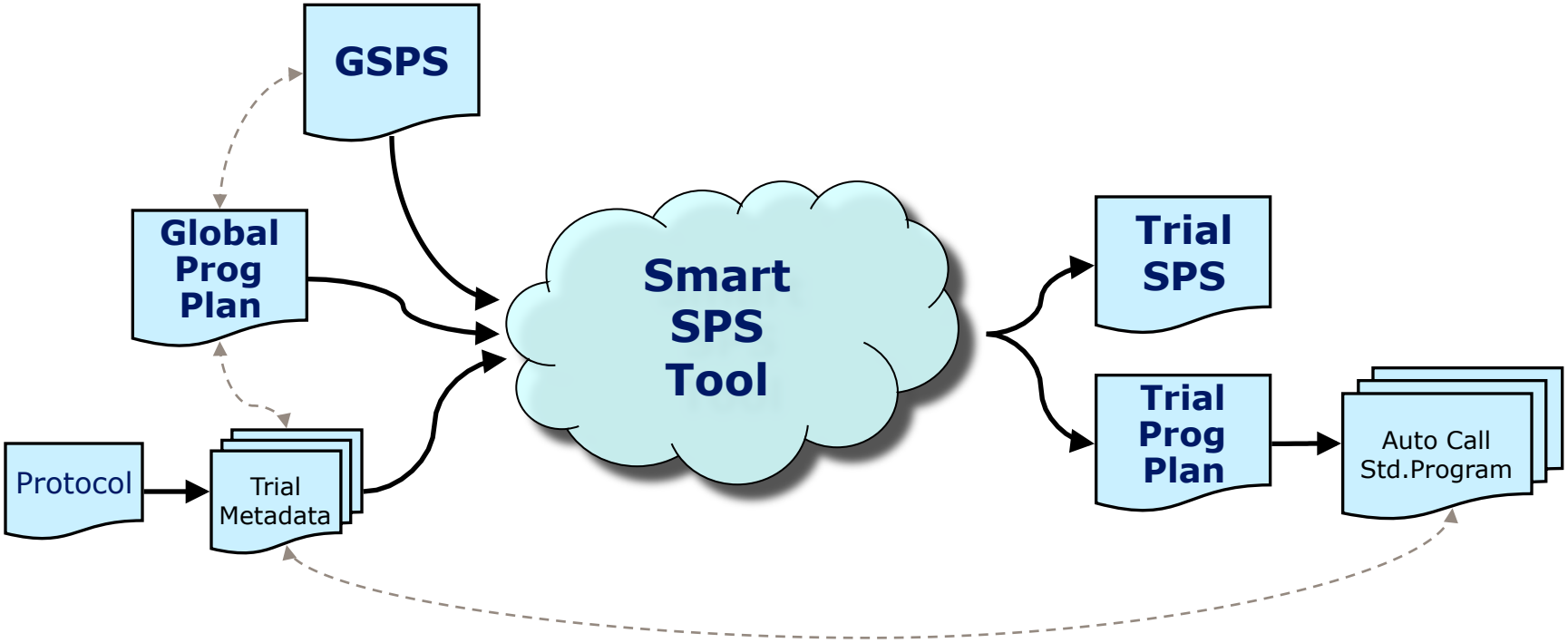
Visions and ideas for improvements



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