



***Dynamic document
creation framework
for
streamlining cSDRG***



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❑ **Umayal Annamalai** Assistant Manager, Statistical programming group at Algorics.

- Previous organizations : Umayal was associated with ICON clinical research, Fortrea (earlier Theorem Clinical Research), Alira Health (earlier CROS NT) across statistical programming roles and development of tools.
- Key skillset : SAS programming including Base SAS, SAS macros, SAS/STAT and with R programming including R Shiny, R Markdown, R Flex Dashboards and Python.

❑ **Madhu Annamalai** Technical lead at Algorics

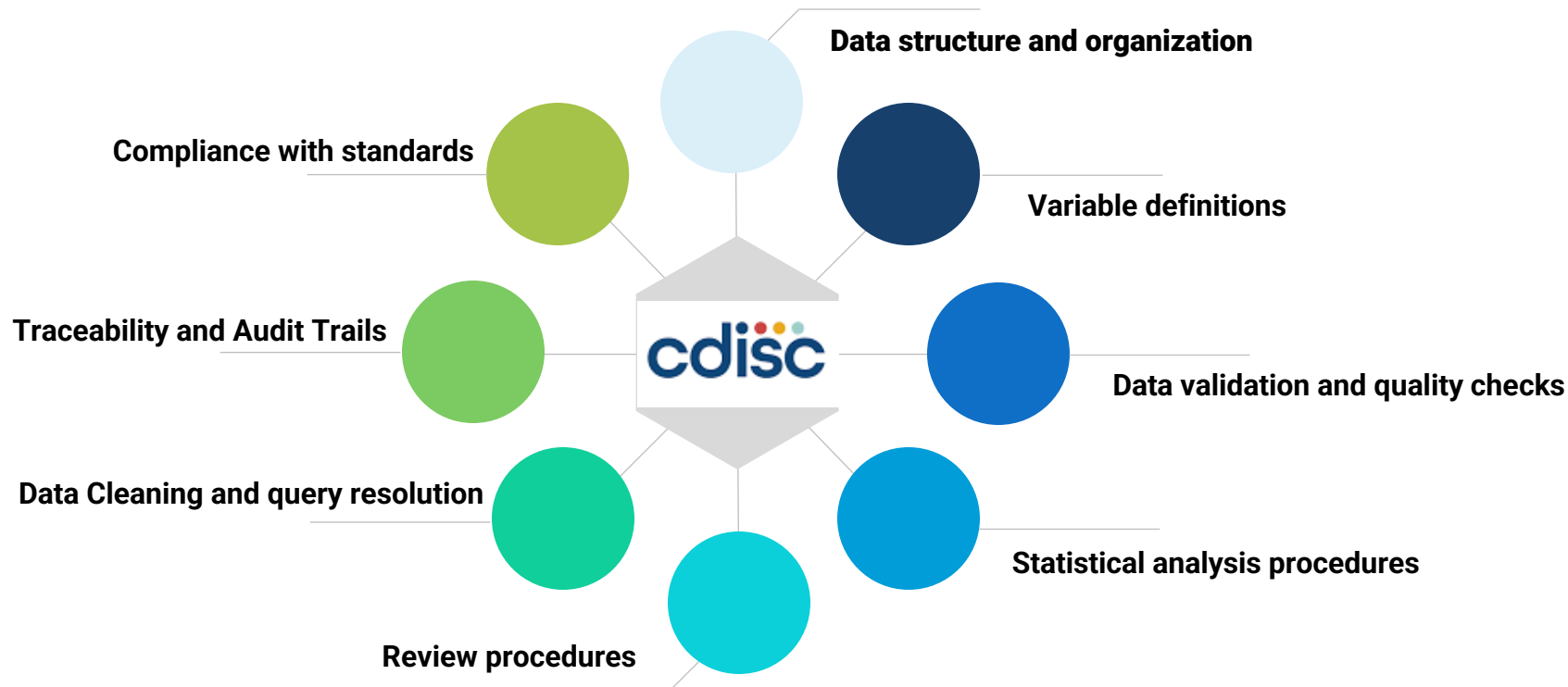
- Key Skillset : Base SAS, SAS macros, SAS/STAT, and R programming, complemented by her experience with various tools and testing processes.

Agenda

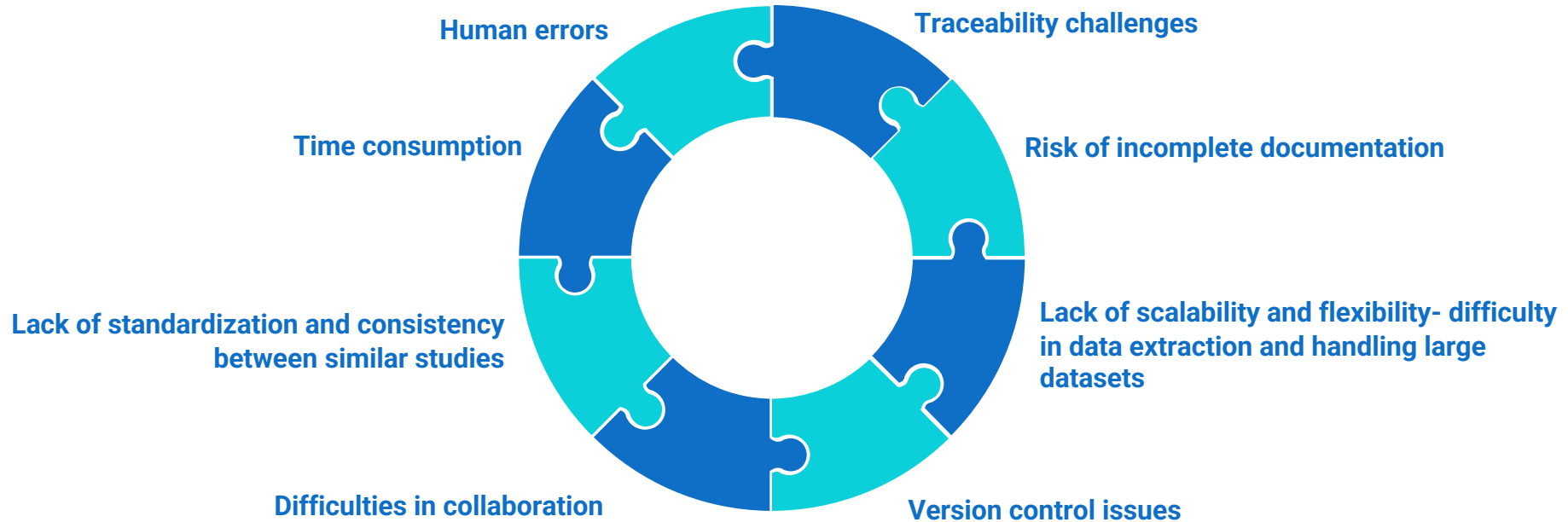


- cSDRG
- Challenges in cSDRG creation
- Need for dynamic approach
- Dynamic cSDRG creation - using R Markdown
 - Strategy
 - Prerequisites
 - Process flow
 - R markdown framework
 - Key examples
- Practical difficulties
- Key Takeaways

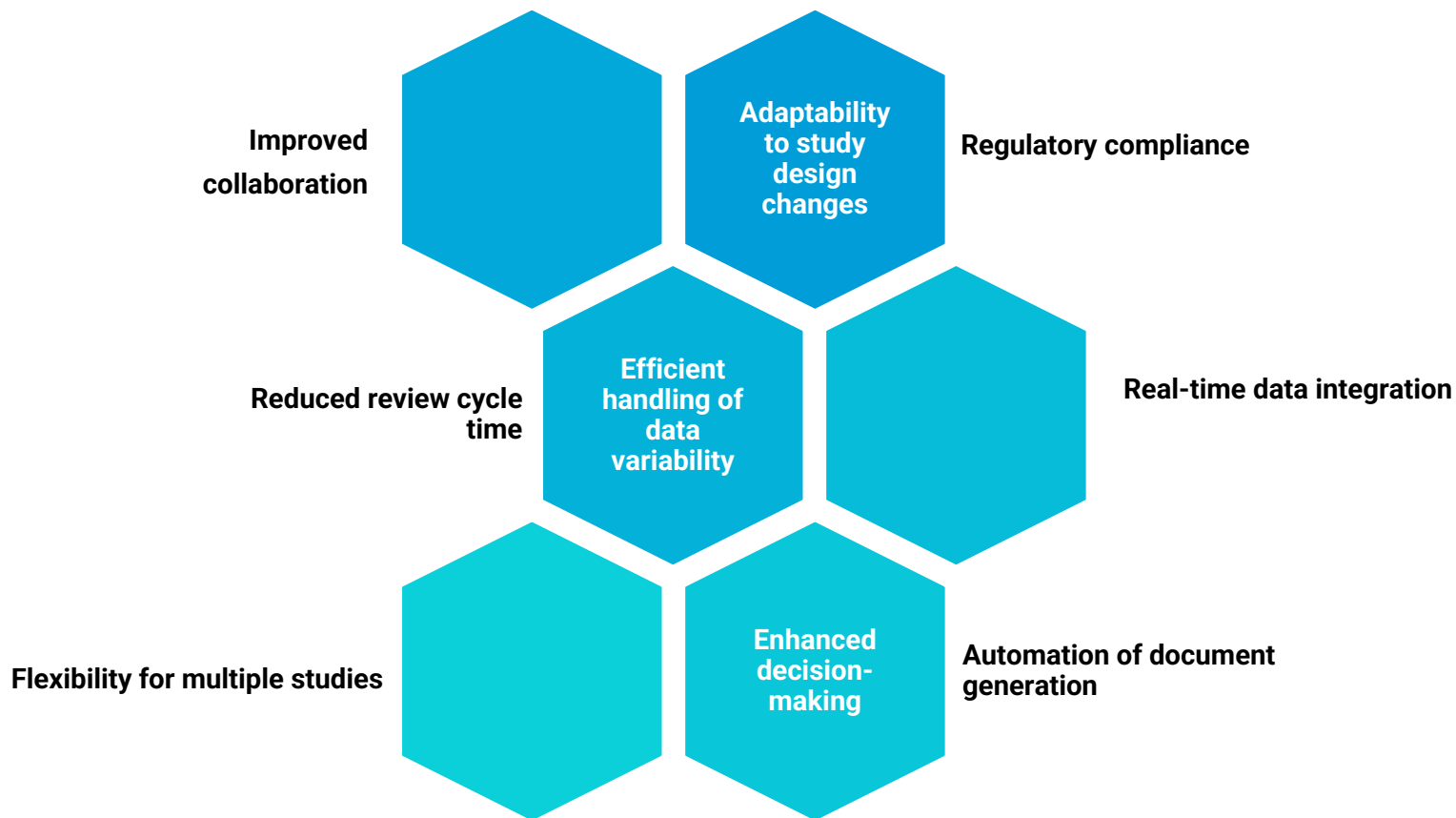
Clinical Study Data Reviewer Guide (cSDRG)



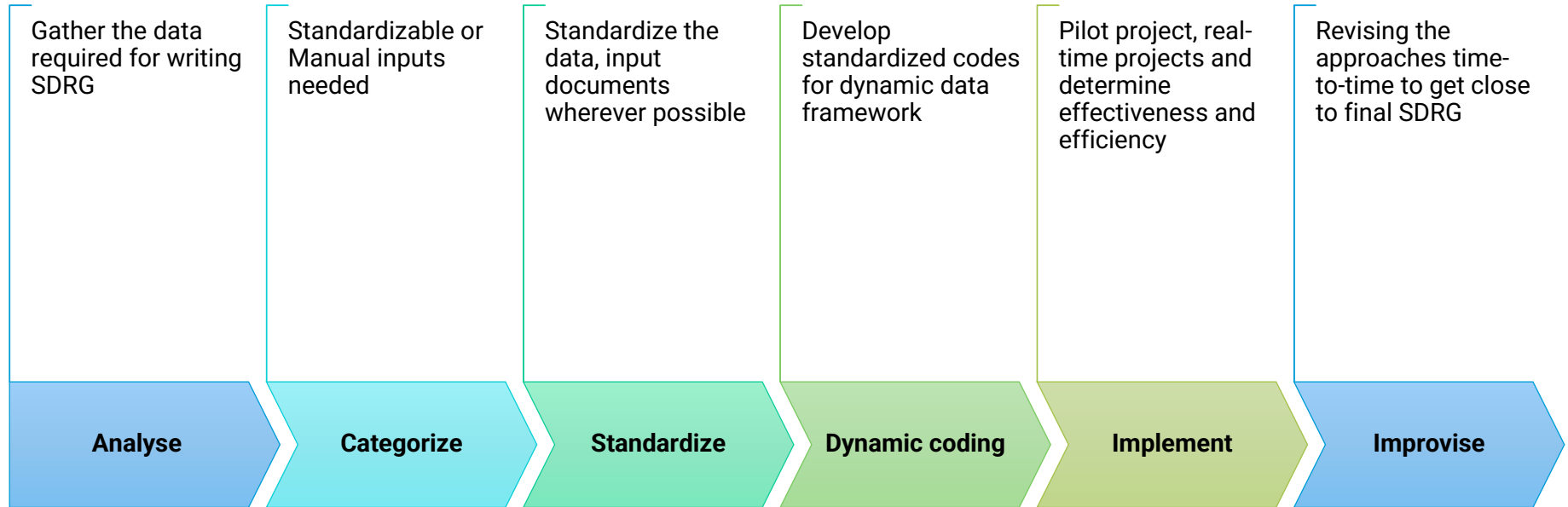
Challenges in manual cSDRG creation



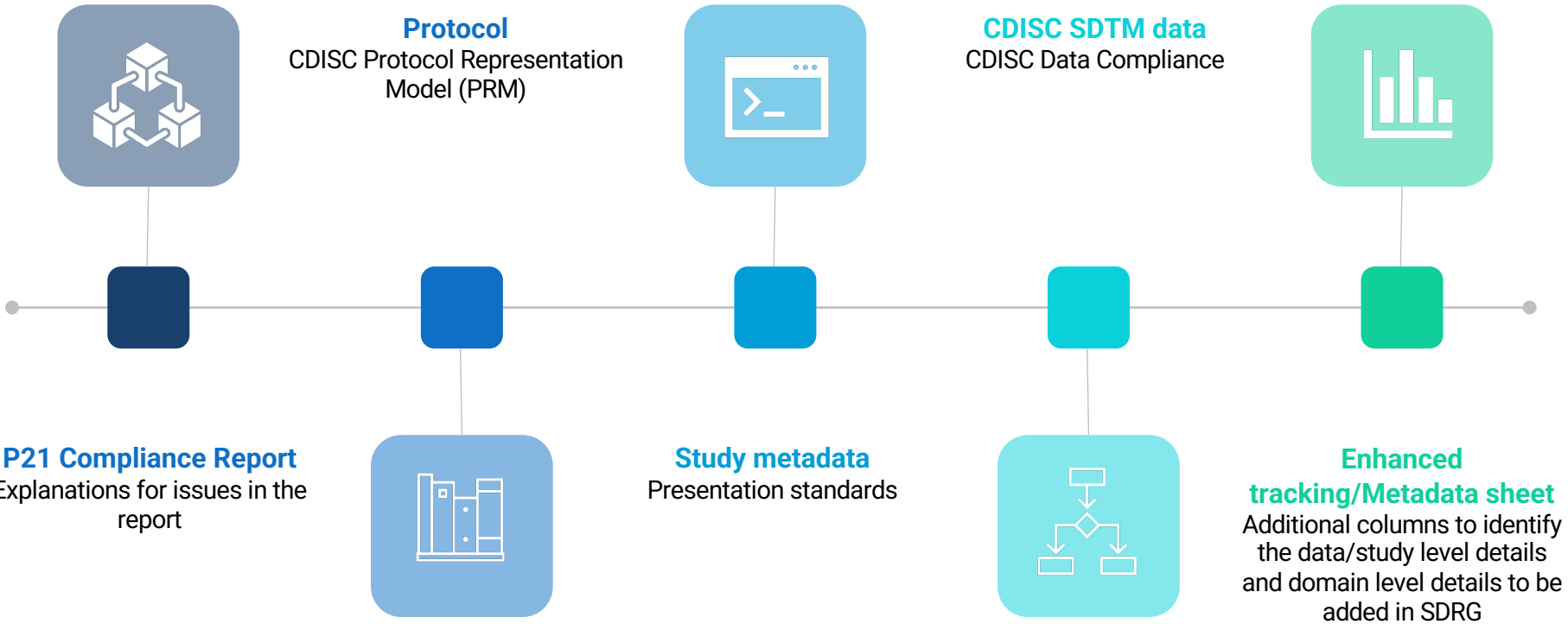
Need for dynamic cSDRG document creation



Dynamic cSDRG creation – Strategy



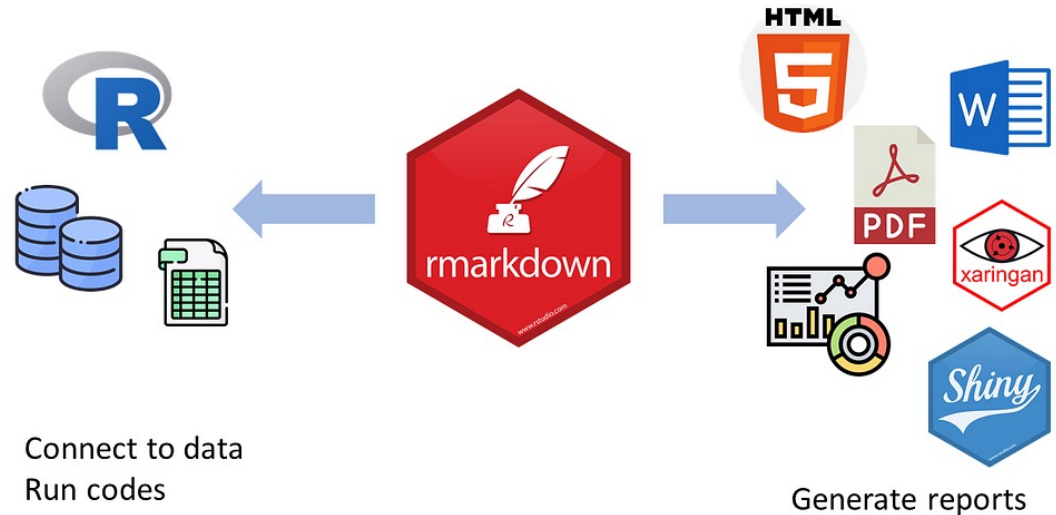
Prerequisite: Standardization of source documents



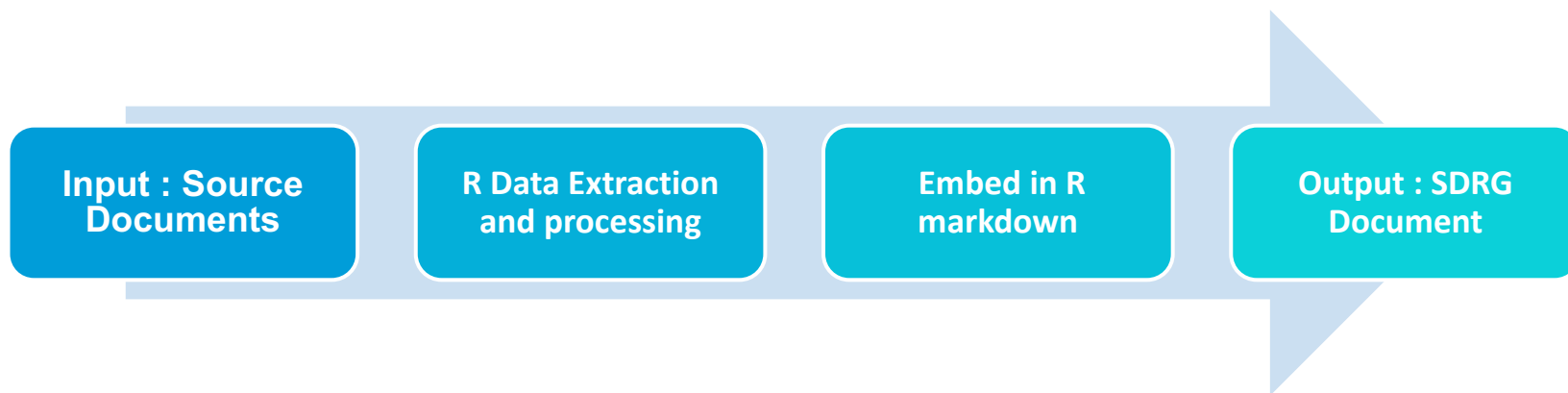
Why R-Markdown?

R Markdown allows to blending code, text, and results into a single document, making it an excellent choice for automating the creation of documents based on the data analysis.

- Dynamic Reporting
- Integration of code and narrative
- Reproducibility
- Flexibility and customization
- Wide adoption in data science
- Compatibility with R ecosystem



Dynamic cSDRG creation - Process flow



R Markdown framework



```
1 ---
2 title: "<span style='font-size:2em;font-weight:bold;'>Clinical Study Data Reviewer's Guide</span>"
3 subtitle: |
4   <span style='font-size:1.5em;font-weight:bold;'>SDRG, Inc</span> <br>
5   <span style='font-size:1.2em;font-weight:normal;'>Study SDRG001A </span> <br>
6   <span style='font-size:1.0em;font-weight:normal;'>cSDRG Template Version 2018 11 01 </span>
7
8 output:
9   officedown::rdocx_document
10  reference_docx: styles.docx
11 header-includes:
12 - \usepackage{fancyhdr}
13 - \usepackage{lastpage}
14 - \pagestyle{fancy}
15 - \fancyhf{}
16 - \fancyhead[L]{'SDRG001A'}
17 - \fancyhead[R]{'Clinical Study Data Reviewer's Guide'}
18 - \fancyfoot[L]{'This document is confidential'}
19 - \fancyfoot[C]{\thepage\ of \pageref{LastPage}}
20 ---
21
22 ```{r, results='asis', echo=FALSE}
23 cat("\nnewpage")
24
25
26 <span style='font-size:5em;font-weight:bold;'>Clinical Study Data Reviewer's Guide</span> <br>
27
28 Contents
29 <!--BLOCK_TOC-->
30
31 ```{r, include=FALSE}
32 ##R library preparation, functions reference & documents pre-processing codes here
33 cat("\nnewpage")
34
35
36 # *Introduction*
37
38 ## Purpose
39 ```{r eval=FALSE, include=FALSE}
40 ##Section 1.1 function calls here
41
42
43 ## Acronyms
44 ```{r eval=FALSE, include=FALSE}
45 ##Section 1.2 function calls here
46
47
48 ## Study Data Standards and Dictionary Inventory
49 ```{r eval=FALSE, include=FALSE}
50 ##Section 1.3 function calls here
51
52
53 # *Protocol Description*
54
55 ## Protocol Number and Title
56 ```{r}
57 ##Section 2.1 function calls here
58
59
60 ## Protocol Design
61 ```{r}
62 ##Section 2.2 function calls here
63
64
65 ## Trial Design Datasets
66 ```{r}
67 ##Section 2.3 function calls here
68
69
70 ### TI - Trial Inclusion/Exclusion Criteria
71 ```{r}
72 ##Section 2.3.1 function calls here
73
74
75 ### TS - Trial Summary
76 ```{r}
77 ##Section 2.3.2 function calls here
78
79
```

```
80 # *Subject data Description*
81
82 ## Overview
83 ```{r}
84 ##Section 3.1 function calls here
85
86
87 ## Traceability Flow Diagram
88 ```{r}
89 ##Section 3.2 function calls here
90
91
92 ## Annotated CRFs
93 ```{r}
94 ##Section 3.3 function calls here
95
96
97 ## SDTM Subject Domains
98 ```{r}
99 ##Section 3.4 function calls here
100
101
102 ### CV - Concomitant Medications
103 ```{r results='asis', echo=FALSE}
104 ##Section 3.4.1 function calls here
105
106
107 ## DS - Disposition
108 ```{r}
109 ##Section 3.4.2 function calls here
110
111
112 # *Data conformance summary*
113
114 ## Conformance Inputs
115
116 ```{r results='asis', echo=FALSE}
117 ##Section 4.1 function calls here
118
119
120
121 ## Issues Summary
122 ```{r results='asis', echo=FALSE}
123 ##Section 4.2 function calls here
124
125
126
127 ## Additional Conformance Details
128 ```{r echo=FALSE, results='asis'}
129 ##Section 4.3 function calls here
130
131
132 # *Appendix*
133
134 ## Appendix I
135 ```{r}
136 ##Section 5.1 function calls here
137
138
```

R Markdown framework - Cont.



SDRG001A	Study Data Reviewer's Guide
Study Data Reviewer's Guide	
SDRG, Inc	
Study SDRG001A	
Contents	
1. Introduction.....	3
1.1. Purpose.....	3
1.2. Acronyms.....	3
1.3. Study Data Standards and Dictionary Inventory.....	3
2. Protocol Description.....	3
2.1. Protocol Number and Title.....	3
2.2. Protocol Design.....	3
2.3. Trial Design Datasets.....	3
2.3.1. TI – Trial Inclusion/Exclusion Criteria.....	3
2.3.2. TS – Trial Summary.....	3
3. Subject data Description.....	3
3.1. Overview.....	3
3.2. Traceability Flow Diagram.....	3
3.3. Annotated CRFs.....	3
3.4. SDTM Subject Domains.....	3
3.4.1. CM – Concomitant Medications.....	3
3.4.2. DS – Disposition.....	3
4. Data conformance summary.....	4
4.1. Conformance Inputs.....	4
4.2. Issues Summary.....	4
4.3. Additional Conformance Details.....	4
5. Appendix.....	4
5.1. Appendix 1.....	4

SDRG001A	Study Data Reviewer's Guide
1. Introduction	
1.1. Purpose	
1.2. Acronyms	
1.3. Study Data Standards and Dictionary Inventory	
2. Protocol Description	
2.1. Protocol Number and Title	
##Section 2.1 function calls here	
2.2. Protocol Design	
##Section 2.2 function calls here	
2.3. Trial Design Datasets	
##Section 2.3 function calls here	
2.3.1. TI – Trial Inclusion/Exclusion Criteria	
##Section 2.3.1 function calls here	
2.3.2. TS – Trial Summary	
##Section 2.3.2 function calls here	
3. Subject data Description	
3.1. Overview	
##Section 3.1 function calls here	
3.2. Traceability Flow Diagram	
##Section 3.2 function calls here	
3.3. Annotated CRFs	
##Section 3.3 function calls here	
3.4. SDTM Subject Domains	
##Section 3.4 function calls here	
3.4.1. CM – Concomitant Medications	
3.4.2. DS – Disposition	
##Section 3.4.2 function calls here	
4. Data conformance summary	
4.1. Conformance Inputs	
4.2. Issues Summary	
4.3. Additional Conformance Details	
5. Appendix	
5.1. Appendix 1	
##Section 5.1 function calls here	

Section 1 & 2 examples



Code snapshot

```
- # *Introduction*
- ## Purpose
- ```{r echo=FALSE, results='asis'}
- #default standard text for purpose to be loaded into section1_1 function, if there is any special study needs to be mentioned,
- this has to be defined inside the function with key word
- section1_1 (type1)
- ##section1_1(type2)
- ...
- ## Acronyms
- ```{r echo=FALSE}
- ##Section 1.2 function calls here
- ...
- ## Study Data Standards and Dictionary Inventory
- ```{r echo=FALSE}
- #alignment of the table p21_tab1 which contains details on data standards and dictionary details brought up from the P21 report &
- metadata
- ft <- flextable(p21_tab1) %>%
-   align(align = "left", part = "all")%>%
-   set_table_properties(width = .8, layout = "autofit") %>%
-   set_table_font_size(size = 10) %>%
-   bold(part = "header")
- ft
- ...
- # *Protocol Description*
- ## Protocol Number and Title
- ```{r, results='asis', echo=FALSE}
- #Protocol number and title read from protocol based on pdfutils and data extraction techniques
- PROTPDF (protnum)
- PROTPDF (prottitle)
- ...
- ## Protocol Design
- ```{r, results='asis', echo=FALSE}
- #Protocol design read from protocol based on pdfutils and data extraction techniques
- PROTPDF (protdesign)
- ...
```

SDRG snapshot

1. Introduction

1.1. Purpose

This document provides context for tabulation datasets and terminology that benefit additional explanation beyond the Data Definitions document(define.xml). In addition, this document provides a summary of SDTM conformance findings.

1.2. Acronyms

##Section 1.2 function calls here

1.3. Study Data Standards and Dictionary Inventory

Standard or Dictionary	Versions Used
SDTM	SDTM v1.7, SDTM-IG v3.3
Medical Events Dictionary	MedDRA v22.1
MED-RT	2021-11-01
UNII	2021-12-13

2. Protocol Description

2.1. Protocol Number and Title

Protocol Number: SDRG001A

Protocol Title: Phase I, Single Dose, Open-Label, Dose Escalation Pharmacokinetics Study of New drug in Healthy Subjects

2.2. Protocol Design

There are no additional details to be documented.

Section 3 example



Source Document: Enhanced Metadata/Tracking Sheet

Dataset	Description	Class	Structure	Purpose	Key Variables	Repeating	Reference Data	Comment	Notes
CM	Concomitant Medications	INTERVENTIONS	One record per recorded intervention occurrence or constant-dosing interval per subject	Tabulation	STUDYID, USUBJID, CMTRT, CMSTDTC	Yes	No		The CM domain that Concomitant medications (including ESA, IV iron, and blood transfusions) will be defined as all prescription and non-prescription medications taken from the Screening Visit to Follow-up.
SUPPCM	Supplemental Qualifiers for CM	RELATIONSHIP	One record per IDVAR, IDVARVAL, and QNAM value per subject	Tabulation	STUDYID, USUBJID, IDVARVAL, QNAM	Yes	No		

Code snapshot

```
## CM - Concomitant Medications
{r results='asis', echo=FALSE}
#Details from Typical Enhanced tracking sheet is displayed based on the domain level inputs to the R functions
section3_4_1(CM)
section3_4_1(SUPPCM)

{r prepOutput, echo=FALSE}
#alignment of the table section3_4_1_CM which contains details on supplemental qualifiers brought up from the data/metadata
ft <- flextable(section3_4_1_CM) %>%
  align(align = "left", part = "all")%>%
  set_table_properties(width = .8, layout = "autofit") %>%
  set_table_font_size(size = 10) %>%
  bold(part = "header")
ft
```

SDRG snapshot

3.4.1. CM – Concomitant Medications

The CM domain that Concomitant medications (including ESA, IV iron, and blood transfusions) will be defined as all prescription and non-prescription medications taken from the Screening Visit to Follow-up.

Supplemental details were represented in SUPPCM as follows:

QNAM	Description
ATC1	ATC Level 1 Text
ATC1CD	ATC Drug Class 1 Code
ATC2	ATC Level 2Text
ATC2CD	ATC Drug Class 2 Code
ATC3	ATC Level 3 Text
ATC3CD	ATC Drug Class 3 Code
ATC4	ATC Level 4 Text
ATC4CD	ATC Drug Class 4 Code

Section 4 example



Source Document: P21 compliance report

Source	Pinnacle 21 ID	Message	Severity	Found	Domain	Explanation
AE	SD1143	No Details info for AESMIE Adverse Event in SUPPAE domain		32	AE	Other Values are not collected in CRF
CM	CT2002	CMROUTE value not found in 'Route of Administration Response' extensible codelist		99	CM	Codelist is extensible. Added the codelist terms to Metadata.
	SD1031	Value for CMENRF is populated, when RFENDTC is NULL		5	CM	Ongoing Status is collected in CRF. But RFENDTC is blank because it is a 'NOT TREATED' Subject.
	SD1339	Missing EPOCH value, when a start or observation date is provided		28	CM	The few medications have started before screening. Hence EPOCH is missing.

Code snapshot

```
# *Data conformance summary*
## Conformance Inputs
```{r results='asis', echo=FALSE}
#individual questions are framed & ordered based on standard questions from guidelines and responses are written based on details
imported from p21 inside R function to create an output table p21_tab, which is displayed here.
kable(p21_tab1,"html",col.names = rep("", ncol(p21_tab1)))
```
## Issues Summary
```{r results='asis', echo=FALSE}
#reporting of the table
ft <- flextable(p21_Is1) %>% flextable::align(align = "left", part = "all")
ft <- flextable::set_table_properties(ft, layout = "autofit")
ft
#p21_Is1 is a data table created in the dedicated pre-processing R chunk based on functions created to import and process the
required details from P21 report
```
## Additional Conformance Details
```{r echo=FALSE, results='asis'}
#Function calls to include standard statements based on inputs
section4_3("no")
##if there is details to report, process same as previous sections
section4_3_yes(p21_Is2)
```
```

SDRG snapshot

4. Data conformance summary

4.1. Conformance Inputs

Was Pinnacle21 used to evaluate conformance? Yes

If yes, specify the versions of Pinnacle21 and the Pinnacle21 validation rules: Pinnacle 21 Community version 4.0.1

Were sponsor-defined validation rules used to evaluate conformance? No

Were the SDTM datasets evaluated in relation to define.xml? Yes

Was define.xml evaluated? No

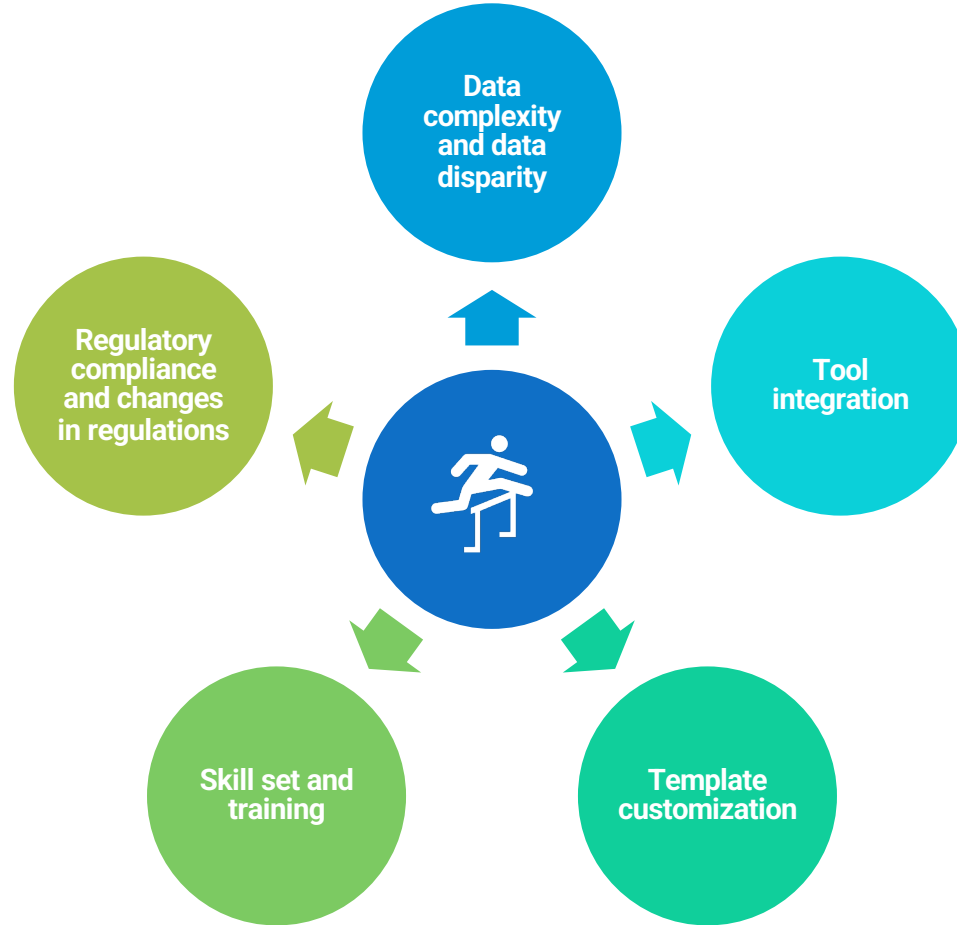
4.2. Issues Summary

| Dataset | Diagnostic Message | Severity | Count | Explanation |
|---------|---|----------|-------|---|
| AE | No Details info for AESMIE Adverse Event in SUPPAE domain | | 32 | Other Values are not collected in CRF |
| CM | CMROUTE value not found in 'Route of Administration Response' extensible codelist | | 99 | Codelist is extensible. Added the codelist terms to Metadata. |
| CM | Value for CMENRF is populated, when RFENDTC is NULL | | 5 | Ongoing Status is collected in CRF. But RFENDTC is blank because it is a 'NOT TREATED' Subject. |
| CM | Missing EPOCH value when a start or observation date is provided | | 28 | The few medications have started before screening. Hence EPOCH is missing. |

4.3. Additional Conformance Details

There are no additional details to be documented.

Practical difficulties



Key takeaways

- Streamlined clinical SDRG document creation process
- Paves the way for future enhancements and continuous improvements
- Optimization of resources which helps us save time and focus on more strategic and value-added activities
- Timeliness in quality assurance and regulatory submissions
- Clear audit trail



Thank you

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