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Single Day Event

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Automatic Generation of Multilingual Data Reviewer's Guide (DRG) in NDA Submission

Disclaimer

The views and opinions expressed in this presentation are those of the authors and do not necessarily reflect the official policy or position of Hengrui Pharmaceuticals (恒瑞) .

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- Structure

Clinical Study Data Reviewer's Guide

cSDRG

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Analysis Data Reviewer's Guide

ADRG

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② Protocol Description

③ Analysis Considerations Related to Multiple Analysis Datasets

④ Analysis Data Creation and Processing Issues

⑤ Analysis Dataset Descriptions

⑥ Data Conformance Summary

⑦ Submission of Programs

⑧ Appendix; Legacy Data

Why

- To tell th
- To discu

KEY: Y = yes (included), N = no (not included), O = optionally included

Topic	Description	define.xml*	cSDRG	ADRG
Protocol Information	Summary of protocol number, title, and design.	Y	Y	Y
Trial Design Data	Information pertaining to trial design datasets.	Y	Y	O
Acronyms	List of sponsor-specific acronyms.	N	Y	Y
Standards Versions	Summary of standards used for data and metadata.	Y	Y	
Dictionary Versions	Summary of external dictionaries used			
Annotated CRFs	Summary of annotati			
Study Data Overview	A high level sum data.			
	rmation source ed.			
Dataset Metada	ription			
Variable Metadata	D			
Value-Level Metadata				
Codelists/Controlled Terminology				
Computational Algorithms	D			
Comments	Not			
Analysis Results Metadata	In p			
Analysis Considerations	S de			
Conformance / Compliance Findings	Sumn checks an			
Legacy data conversion	Describes convers standard format.			

* Note that there are separate define.xml files provided to desc t packag aM). Information pertaining to data collection and the tabulation data should reside in the SDTM taining to analyses or study results should reside in the ADaM define file.

** Note that the tabulation define.xml contains links to the annotated CRFs.

- *It's hard to keep consistency in both template structure and contents during translation.*
- *DRG preparation process is time-consuming, laborious, and error-prone.*

Automatic Generation of SDRG – SDRG Dissection

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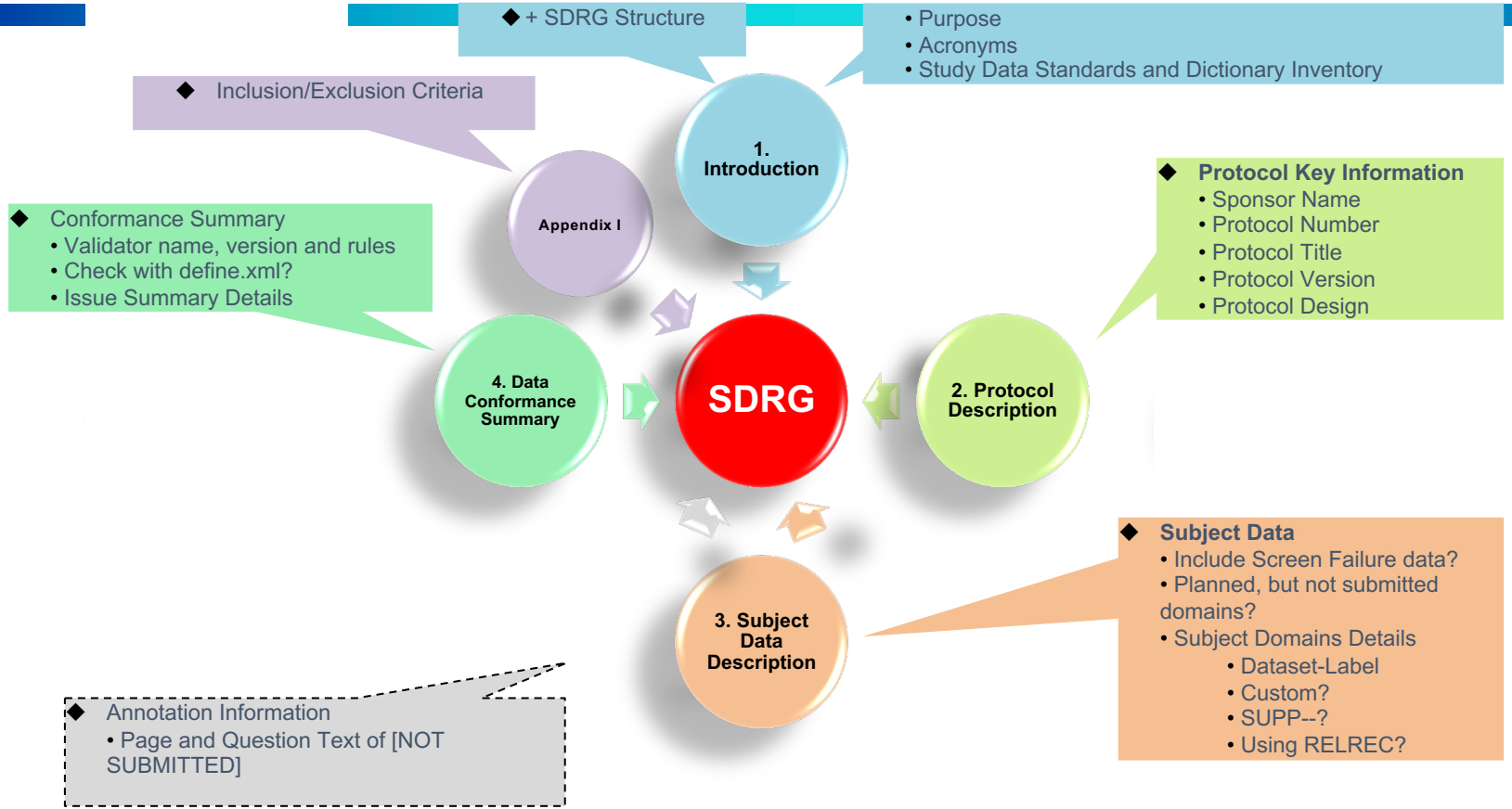
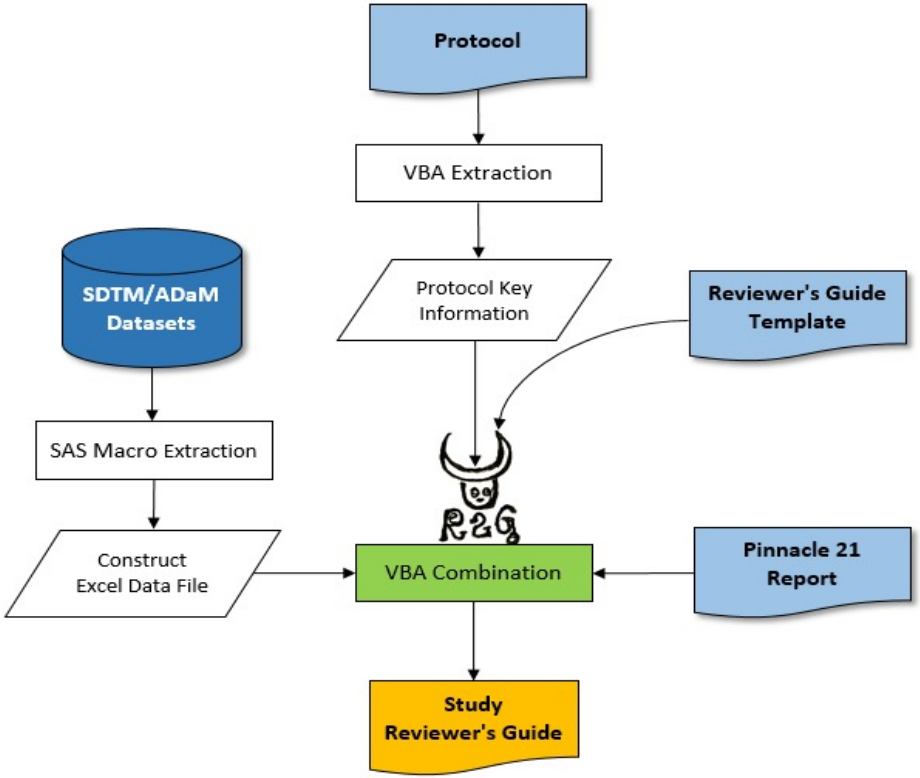
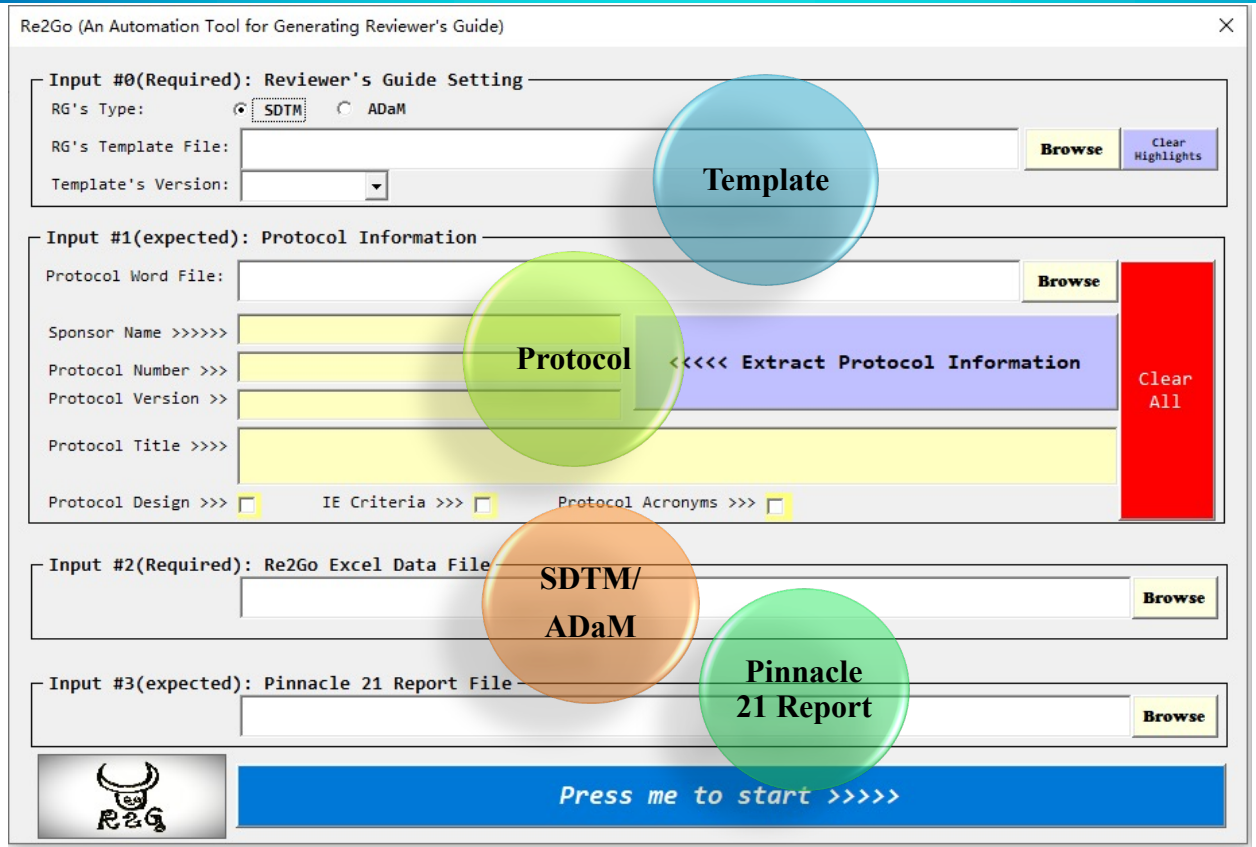


Automatic Generation of SDRG – Re2Go Flowchart

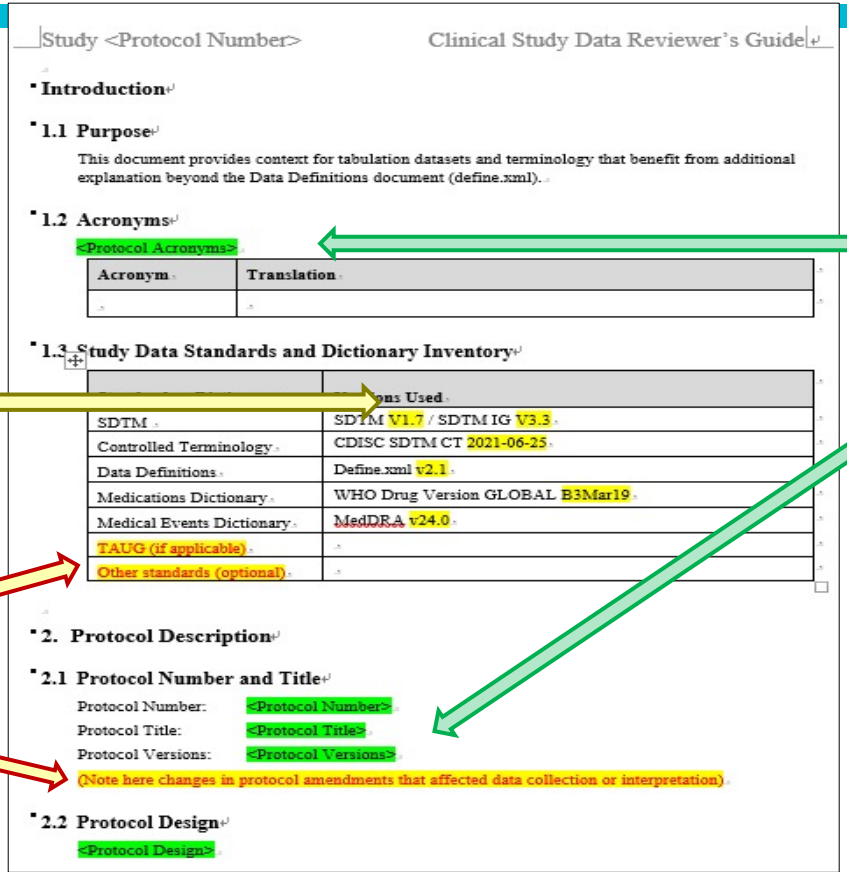


Automatic Generation of SDRG – Re2Go User-Interface



aCRF (pdf)

SDRG EN Template



Study <Protocol Number> Clinical Study Data Reviewer's Guide

Introduction

1.1 Purpose

This document provides context for tabulation datasets and terminology that benefit from additional explanation beyond the Data Definitions document (define.xml).

1.2 Acronyms

<Protocol Acronyms>

Acronym	Translation

1.3 Study Data Standards and Dictionary Inventory

	ns Used
SDTM	SDTM V1.7 / SDTM IG V3.3
Controlled Terminology	CDISC SDTM CT 2021-06-25
Data Definitions	Define.xml v2.1
Medications Dictionary	WHO Drug Version GLOBAL B3Mar19
Medical Events Dictionary	MedDRA v24.0
TAUG (if applicable)	
Other standards (optional)	

2. Protocol Description

2.1 Protocol Number and Title

Protocol Number: <Protocol Number>
Protocol Title: <Protocol Title>
Protocol Versions: <Protocol Versions>
(Note here changes in protocol amendments that affected data collection or interpretation)

2.2 Protocol Design

<Protocol Design>

This is where you perform manual modification.

You may delete this note.

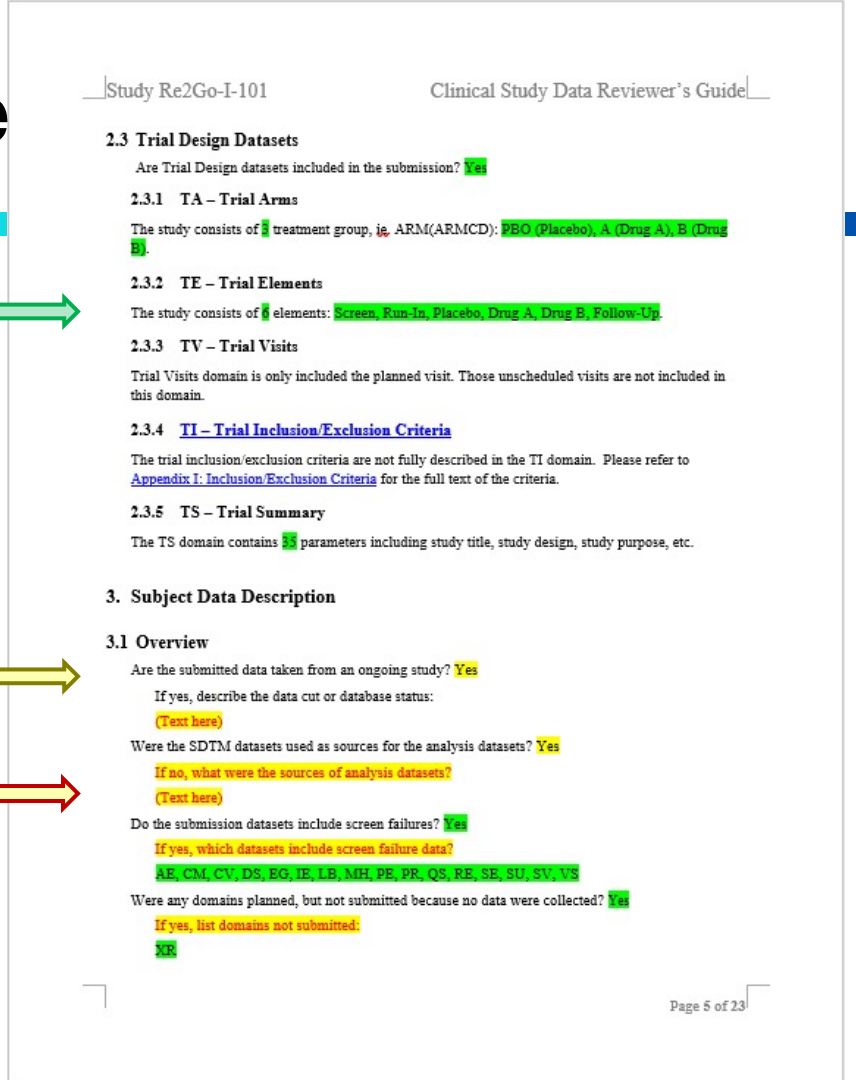
This is where the automation process occurs.

SDRG EN Template

This is where the automation process occurs.

This is where you perform manual modification.

You may delete this note.



2.3 Trial Design Datasets

Are Trial Design datasets included in the submission? Yes

2.3.1 TA – Trial Arms

The study consists of 3 treatment group, ie. ARM(ARMCD): PBO (Placebo), A (Drug A), B (Drug B).

2.3.2 TE – Trial Elements

The study consists of 6 elements: Screen, Run-In, Placebo, Drug A, Drug B, Follow-Up.

2.3.3 TV – Trial Visits

Trial Visits domain is only included the planned visit. Those unscheduled visits are not included in this domain.

2.3.4 TI – Trial Inclusion/Exclusion Criteria

The trial inclusion/exclusion criteria are not fully described in the TI domain. Please refer to Appendix I: Inclusion/Exclusion Criteria for the full text of the criteria.

2.3.5 TS – Trial Summary

The TS domain contains 35 parameters including study title, study design, study purpose, etc.

3. Subject Data Description

3.1 Overview

Are the submitted data taken from an ongoing study? Yes

If yes, describe the data cut or database status:

(Text here)

Were the SDTM datasets used as sources for the analysis datasets? Yes

If no, what were the sources of analysis datasets?

(Text here)

Do the submission datasets include screen failures? Yes

If yes, which datasets include screen failure data?

AE, CM, CV, DS, EG, IE, LB, MH, PE, PR, QS, RE, SE, SU, SV, VS

Were any domains planned, but not submitted because no data were collected? Yes

If yes, list domains not submitted:

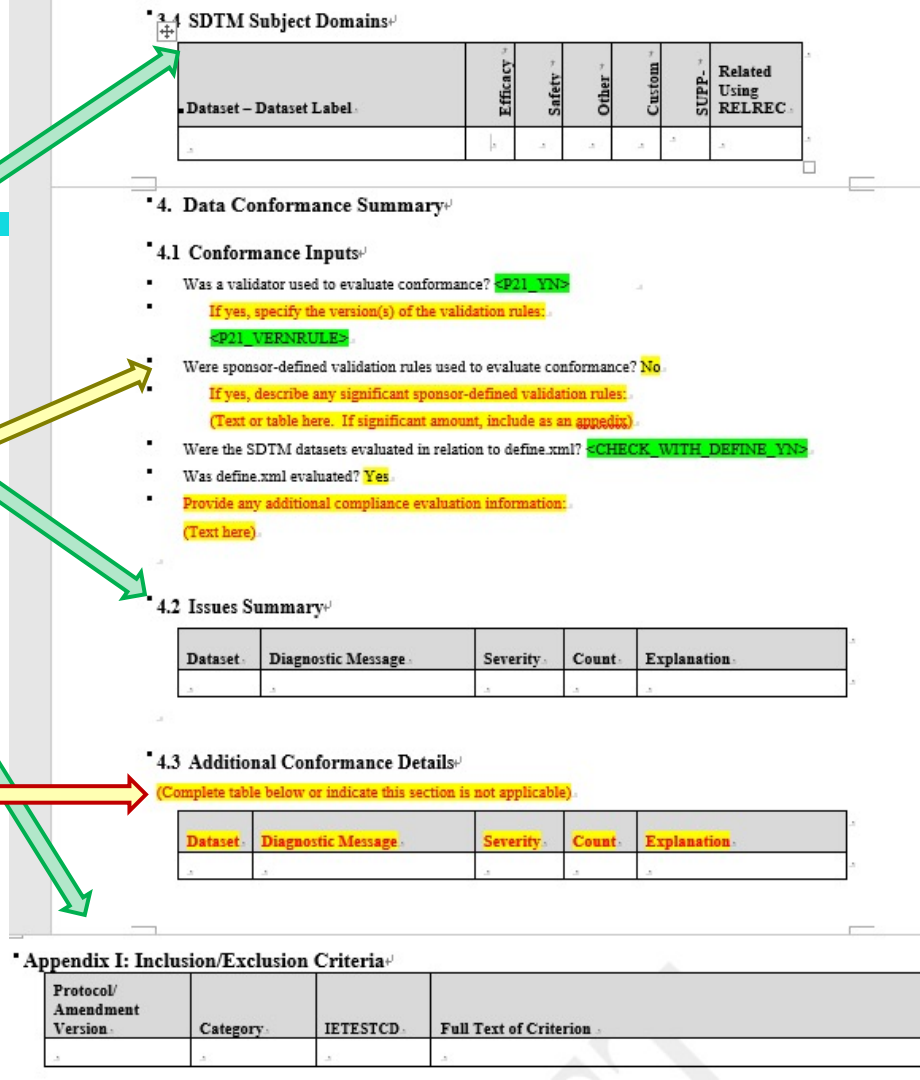
XR

SDRG EN Template

This is where the automation process occurs.

This is where you perform manual modification.

You may delete this note.



3.4 SDTM Subject Domains

Dataset – Dataset Label	Efficacy	Safety	Other	Custom	SUPP-	Related Using RELREC

4. Data Conformance Summary

4.1 Conformance Inputs

- Was a validator used to evaluate conformance? <P21_YN>
- If yes, specify the version(s) of the validation rules:
  <P21_VERNRULE>
- Were sponsor-defined validation rules used to evaluate conformance? No
- If yes, describe any significant sponsor-defined validation rules:
  (Text or table here. If significant amount, include as an appendix)
- Were the SDTM datasets evaluated in relation to define.xml? <CHECK_WITH_DEFINE_YN>
- Was define.xml evaluated? Yes
- Provide any additional compliance evaluation information:
  (Text here)

4.2 Issues Summary

Dataset	Diagnostic Message	Severity	Count	Explanation

4.3 Additional Conformance Details

(Complete table below or indicate this section is not applicable)

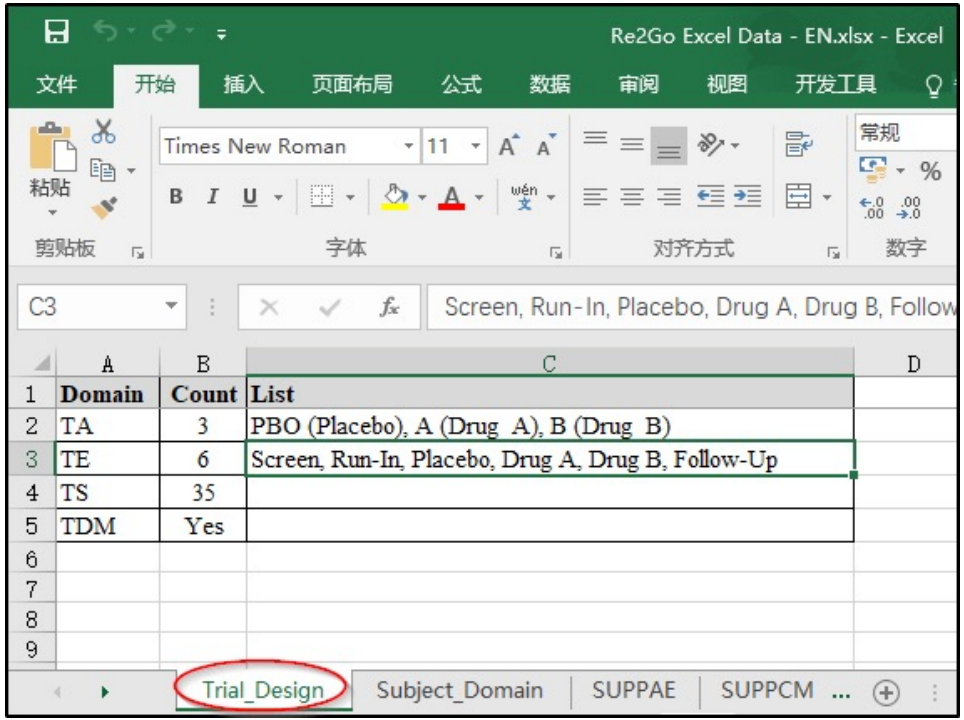
Dataset	Diagnostic Message	Severity	Count	Explanation

Appendix I: Inclusion/Exclusion Criteria

Protocol/ Amendment Version	Category	IETESTCD	Full Text of Criterion

SDTM/ADaM Construct Excel Data File (SAS Macro)

For Section 2.3 Trial Design Datasets



	A	B	C	D
1	**Domain**	**Count**	**List**	
2	TA	3	PBO (Placebo), A (Drug A), B (Drug B)	
3	TE	6	Screen, Run-In, Placebo, Drug A, Drug B, Follow-Up	
4	TS	35		
5	TDM	Yes		
6				
7				
8				
9				

SDTM/ADaM Construct Excel Data File (SAS Macro)

For Section 3. Subject Data Description

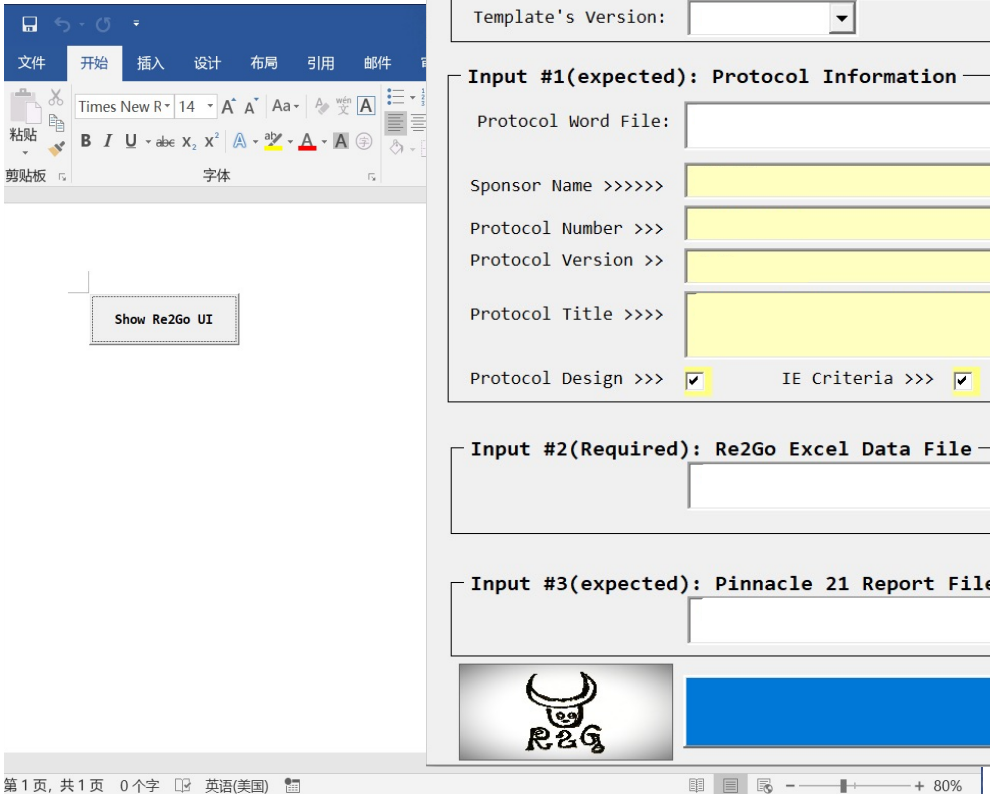
	A	B	C	D	E	F	G	H	I
1	Dataset – Dataset Label	Efficac	Safet	Othe	Custor	SUPF	Related Using RELREC	Screen Failure Data?	Null Dataset
2	AE - Adverse Events		X			X		X	
3	CM - Concomitant/Prior Medications		X			X		X	
4	CO - Comments			X					
5	CV - Cardiovascular System Findings			X				X	
6	DM - Demographics			X		X			
7	DS - Disposition			X		X		X	
8	DV - Protocol Deviations			X		X			
9	EC - Exposure as Collected			X					
10	EG - ECG Test Results		X			X		X	
11	EX - Exposure			X		X			
12	IE - Inclusion/Exclusion Criteria Not Met			X				X	
13	LB - Laboratory Test Results		X			X		X	
14	MB - Microbiology Specimen			X					
15	MH - Medical History			X		X		X	
16	MI - Microscopic Findings			X					
17	PE - Physical Examination		X					X	
18	PR - Procedures			X		X		X	
19	QS - Questionnaires		X					X	
20	RE - Respiratory System Findings		X					X	
21	RS - Disease Response and Clin Classification	X					TR		
22	SE - Subject Elements			X				X	
23	SS - Subject Status		X						
24	SU - Substance Use			X				X	
25	SV - Subject Visits			X				X	
26	TR - Tumor/Lesion Results	X				X	TU, RS		
27	TU - Tumor/Lesion Identification	X				X	TR		
28	VS - Vital Signs		X					X	
29	XJ - Genetic Mutations			X	X				
30	XR - Pregnancy Report			X	X				X
31									

Trial_Design | Subject_Domain | SUPPAE | SUPPCM ...

	A	B
1	QNAM	Description
2	AEACNKB	Action Taken with Carboplatin
3	AEACNYT	Action Taken with Etoposide
4	AECMNO	Related CM ID
5	AECOM	AE Note
6	AEDIS	Leading to Discontinue
7	AEHORMYN	Hormone Treatments for irAE YN?
8	AEIRAEYN	irAE YN?
9	AEPRIOR	Prior AE?
10	AERELKB	Causality with Carboplatin
11	AERELYT	Causality with Etoposide
12	AESIEYN	Special AE?
13	AESOURCE	AE Source
14	DICTVER	Dictionary Version
15	FENRLOBS	Records from First Enrollment (Y/null)
16	IRAECAT	irAE Cluster
17	IRAESCAT	irAE Sub-cluster
18	LABAE	Related Lab
19		

... | Subject_Domain | SUPPAE | SUPPCM

Automatic Generation of SDRG
Re2G



Re2Go (An Automation Tool for Generating Reviewer's Guide)

Input #0(Required): Reviewer's Guide Setting

RG's Type: SDTM ADaM

RG's Template File: Browse | Clear Highlights

Template's Version:

Input #1(expected): Protocol Information

Protocol Word File: Browse

Sponsor Name >>>>>>

Protocol Number >>>

Protocol Version >>

<<<<< Extract Protocol Information

Clear All

Protocol Title >>>>

Protocol Design >>> IE Criteria >>> Protocol Acronyms >>>

Input #2(Required): Re2Go Excel Data File

Browse

Input #3(expected): Pinnacle 21 Report File

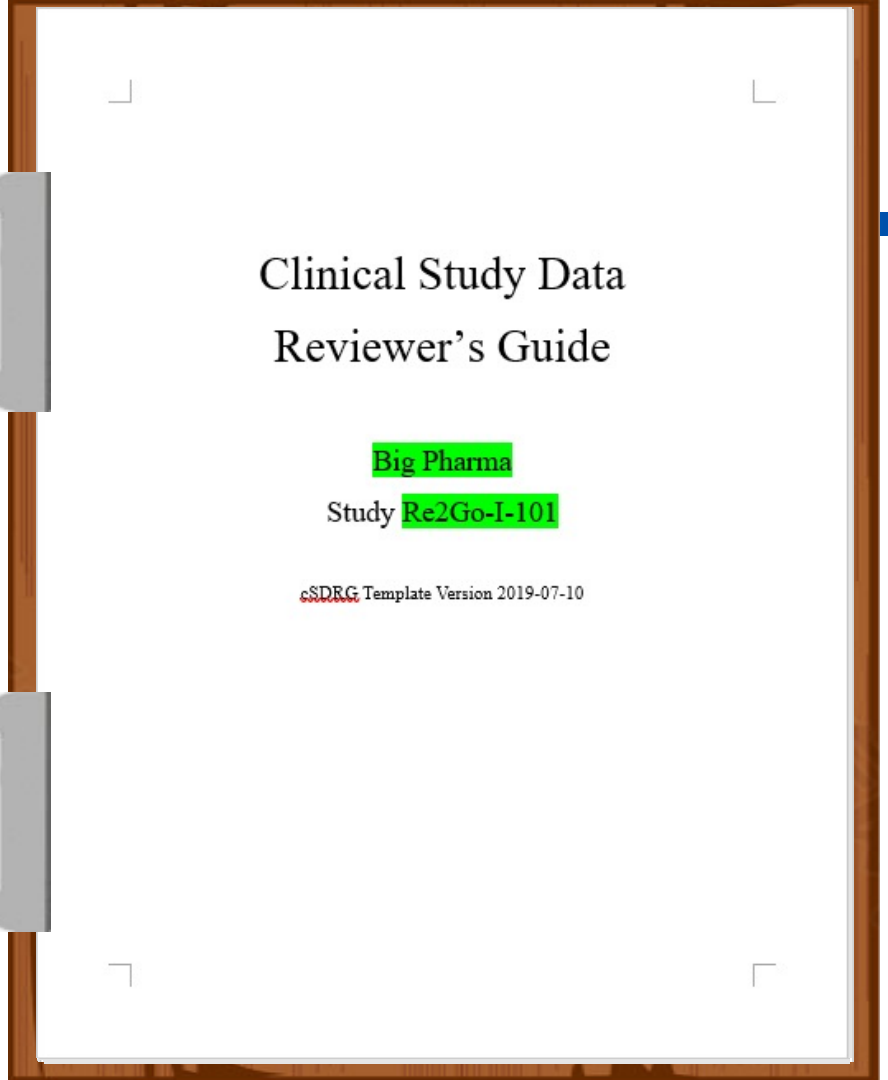
Browse

R2G

Press me to start >>>>>

Re2Go Output

- ✓ Sponsor Name
- ✓ Acronym
- ✓ Protocol Number, Title, Version, Design
- ✓ Information of Trial Design Datasets (eg. TA, TE, TS)
- ✓ Information of Subject Datasets (eg. Screen Failure, Null Datasets, SUPP-)
- ✓ Data Conformance Summary (Validator, Issues)
- ✓ Inclusion/Exclusion Criteria



Automatic Generation of ADRG

ADRG

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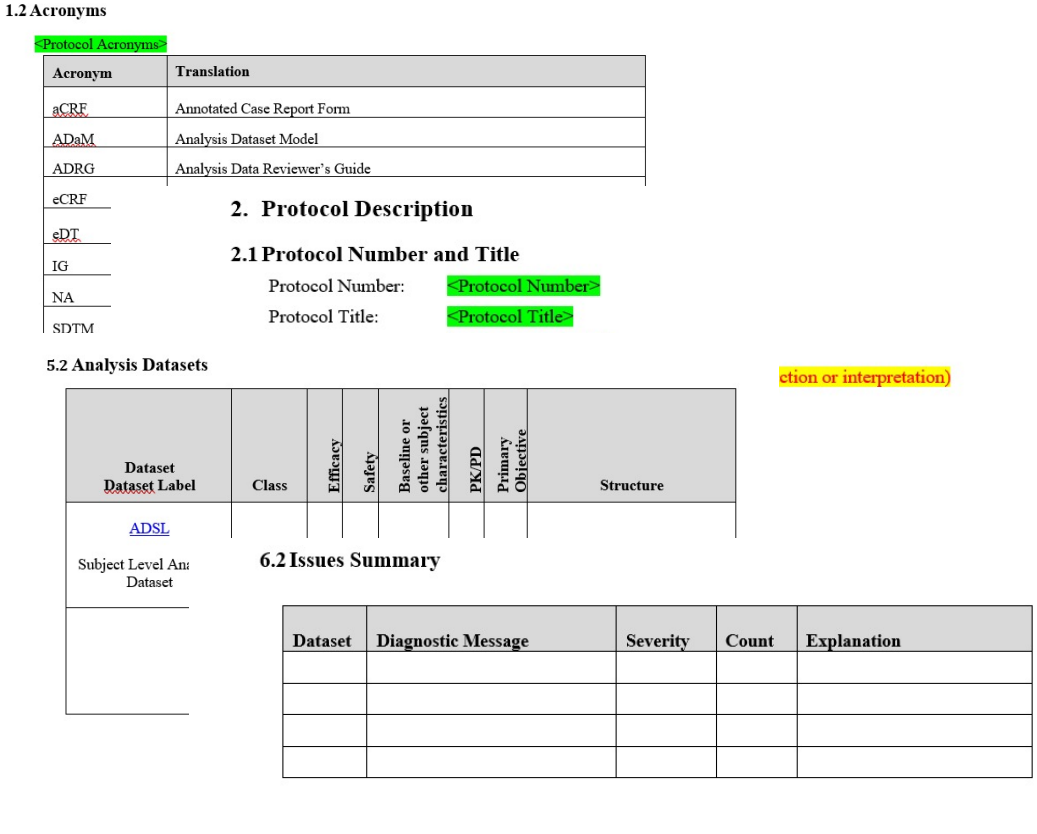


1.2 Acronyms

<Protocol Acronyms>

Acronym	Translation
aCRF	Annotated Case Report Form
ADaM	Analysis Dataset Model
ADRG	Analysis Data Reviewer's Guide
eCRF	
eDT	
IG	
NA	
SDTM	

2. Protocol Description

2.1 Protocol Number and Title

Protocol Number: <Protocol Number>

Protocol Title: <Protocol Title>

5.2 Analysis Datasets

ction or interpretation)

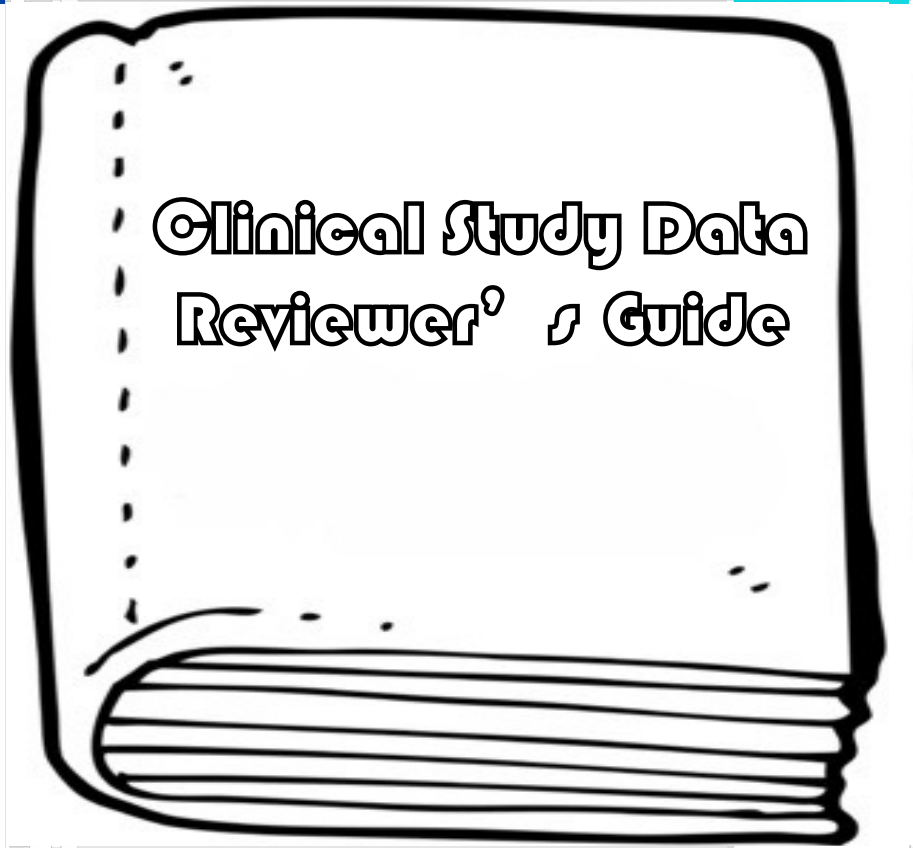
Dataset Dataset Label	Class	Efficacy	Safety	Baseline or other subject characteristics	PK/PD	Primary Objective	Structure
ADSL Subject Level Ana Dataset							

6.2 Issues Summary

Dataset	Diagnostic Message	Severity	Count	Explanation

Preparing Multilingual SDRG - Flowchart

Preparing Multilingual SDRG - Flowchart



Advantages of Using Re2Go

- ✓ Only four input sources:
  - a) *DRG Template*
  - b) *Study Protocol*
    - Information directedly extracted from protocol (e.g. study design, inclusion/exclusion criteria) is more accurate.
  - c) *SDTM/ADaM Datasets*
    - Key dataset information can be matched to the corresponding sections.
  - d) *Pinnacle 21 Report*
- ✓ Automatically identifying DRG language while reading in template
- ✓ Efficient operating process
- ✓ Updating DRG with ease in response to new release of template

Q & A

Thank You!

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The Global Healthcare
Data Science Community