



Single Day Event

PHUSE Japan OST Working Group Activity Report

2021/12/10

Open Source Technology Working Group



Open Source Technology (OST) Working Group

- **Goal**
 - To broaden the acceptance and general level of comfort with these technologies in our industry to assist in increasing their level of adoption in Japan.
- **Objective**
 - Understand industry needs and HA requirements to Open Source Technology (OST).
 - Develop general guidance including implementation, use case and possible solution for clinical study / PMS for adoption of OST.
 - Learn OST and suggest the way to implement OST in our industry.

Members

- Ippei Akiya, A2 Healthcare Corporation
- Masashi Aonuma, Astellas Pharma Inc.
- Tomoyuki Namai, Chugai Pharmaceutical Co., Ltd.
- Masashi Tanaka, EPS Corporation
- Yutaka Morioka, EPS Corporation
- Naoko Izumi, Novartis Pharma K.K.
- Yuichi Nakajima, Novartis Pharma K.K.
- Yasutaka Moriguchi, GlaxoSmithKline K.K.



Open Source Technology (OST) Working Group

Two teams have been active in OST Working Group

- OST in Regulatory Submissions
- OST Use Case



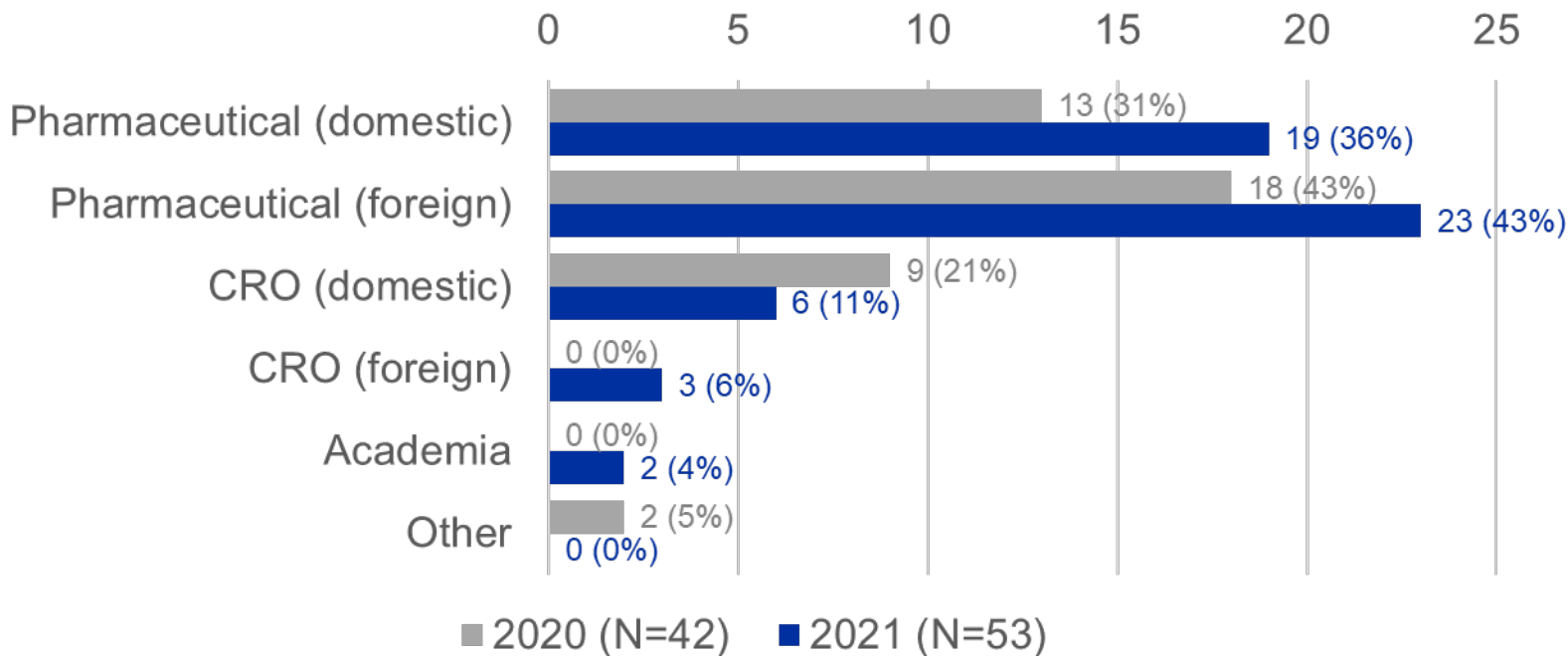
OST in Regulatory Submissions

Team Activities in 2021

- Presentation at domestic / global conferences.
 - SAS user group in Japan
 - PHUSE EU Connect 2021
- Survey for OST use in Japan
 - We conducted a survey in July 2021 to grasp the actual situation of OST usage and expectations for OST in Japan.
 - The result shows that the interest in OST is growing compared to 2020.

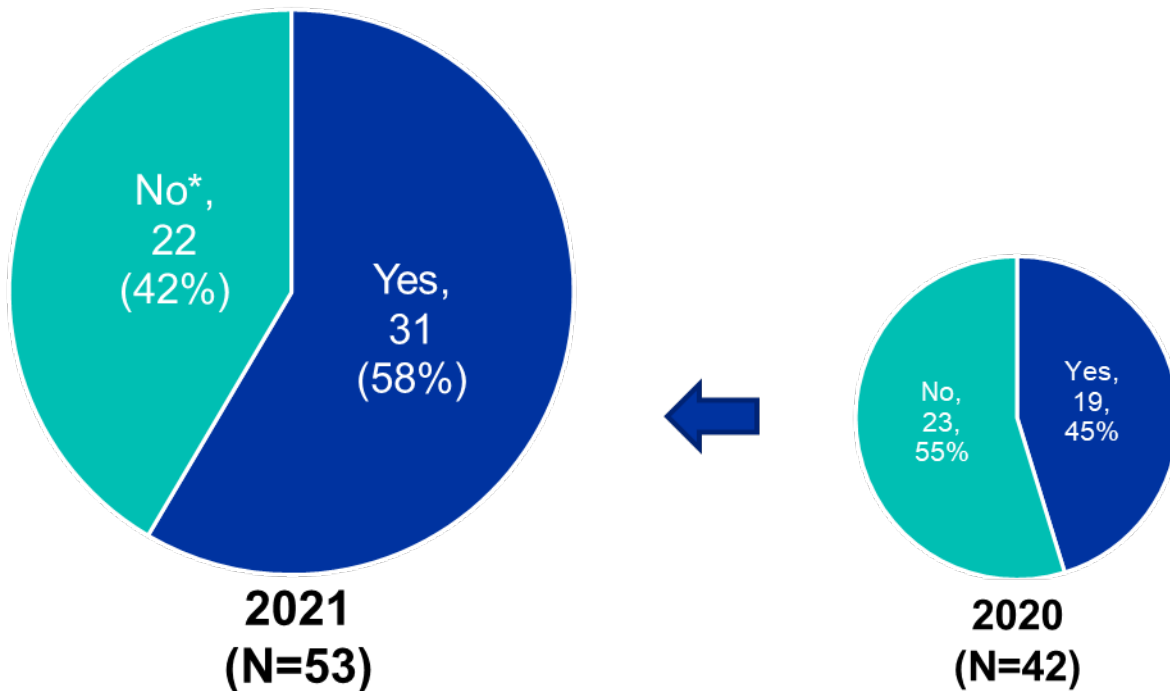
Survey for OST use in Japan

Q1: Which type of company are you currently working for?



Survey for OST use in Japan

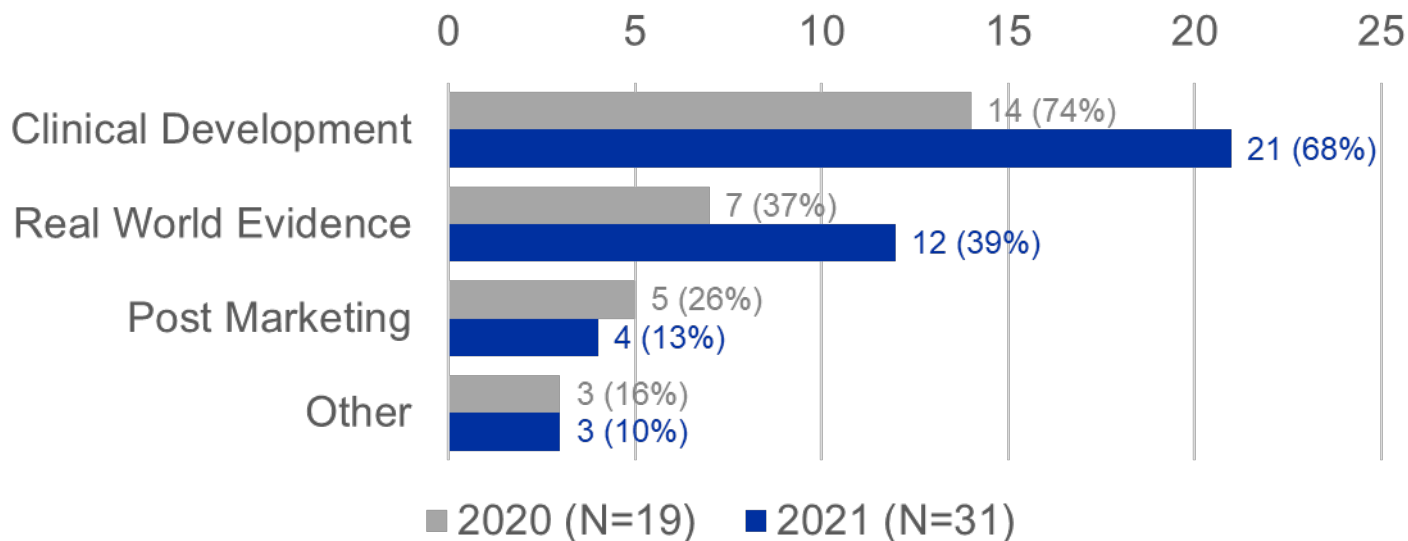
Q2: Do you utilize OST such as R/Python at work? (including work efficiency)



* including personal use only

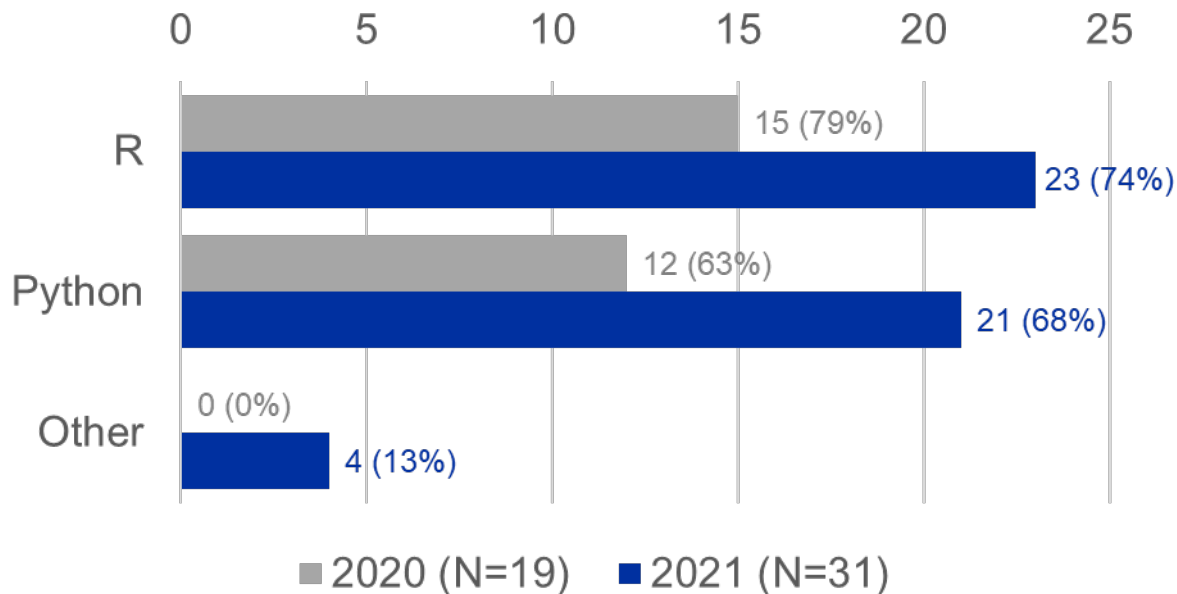
Survey for OST use in Japan

Q3: If you answered “Yes” to the question 2, which phase of clinical development or post marketing do you utilize OST? (multiple answers)



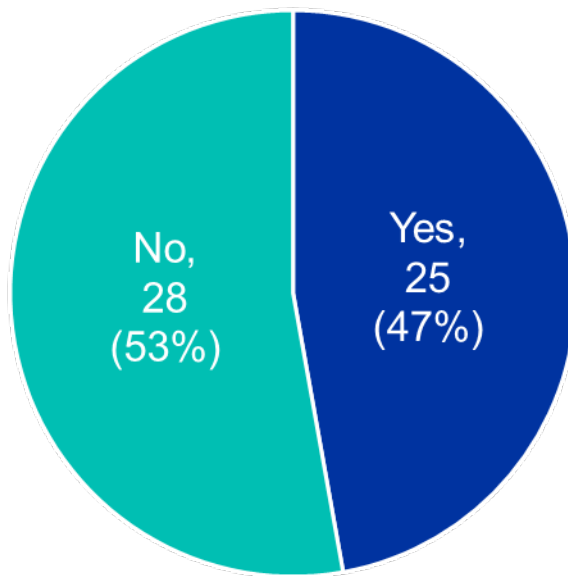
Survey for OST use in Japan

Q4: If you answered “Yes” to the question 2, which programming language do you utilize? (multiple answers)

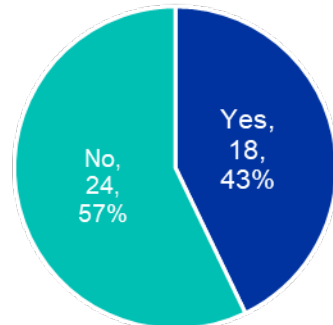


Survey for OST use in Japan

Q5: Does your company have a function/group which administers and introduces OST?



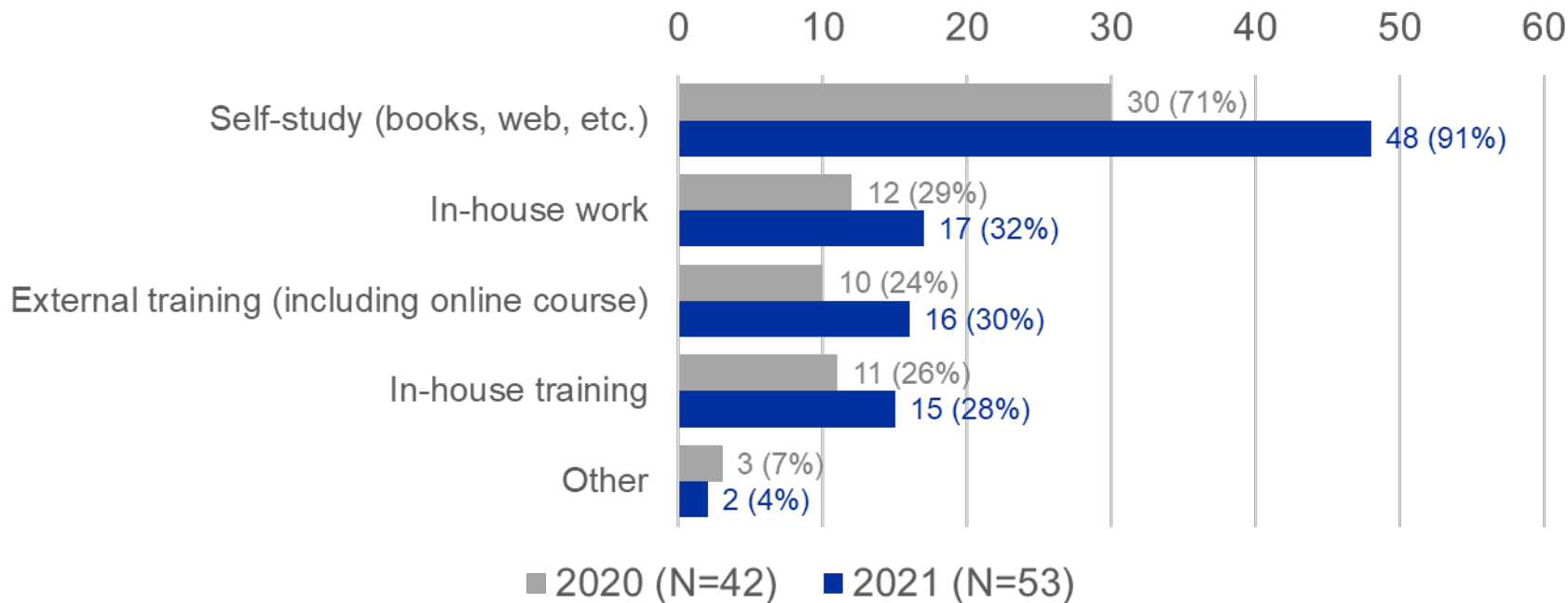
2021
(N=53)



2020
(N=42)

Survey for OST use in Japan

Q6: What opportunities do you have to learn OST? (multiple answers)



Survey for OST use in Japan

Q7: Expectations in pharmaceutical industry in terms of usage of OST.

- **Summary**

- Sharing knowledge, experiences and program code about OST among industries, academia, and health authorities.
- Standardization of the program code.
- Statistical methods which are NOT implemented in SAS.
- Work efficiency and cost reduction.
- Encouraging personnel acquisition from other industries.

Survey for OST use in Japan

Q8: What do you expect regulatory authorities to do?

- **Summary**

- Providing guidance for applicants submitting the results analyzed by OST.
- Presenting acceptance criteria/validation policy for OST usage.
- Presenting recommended way of validation.
- Understanding submitted R/Python code correctly and use it for reviews.
- Reducing inquiries by sharing and standardizing program codes with companies.
- Set up a forum/symposium for exchanging opinions with industries regarding OST usage.

Survey for OST use in Japan

Q9: Any other comments

- **Summary**

- It will be easier to use If the characteristics of OST tools (when it is convenient to use, etc.) are presented.
- I want to use OST tools, but I do not have a chance to use them due to the restrictions in the company.
- Using OST cannot be promoted by pharmaceutical companies alone, it is necessary for them to expand their knowledge of OST together with CROs that have actual programming resources.



OST Use Case Team Activities in 2021

Activities

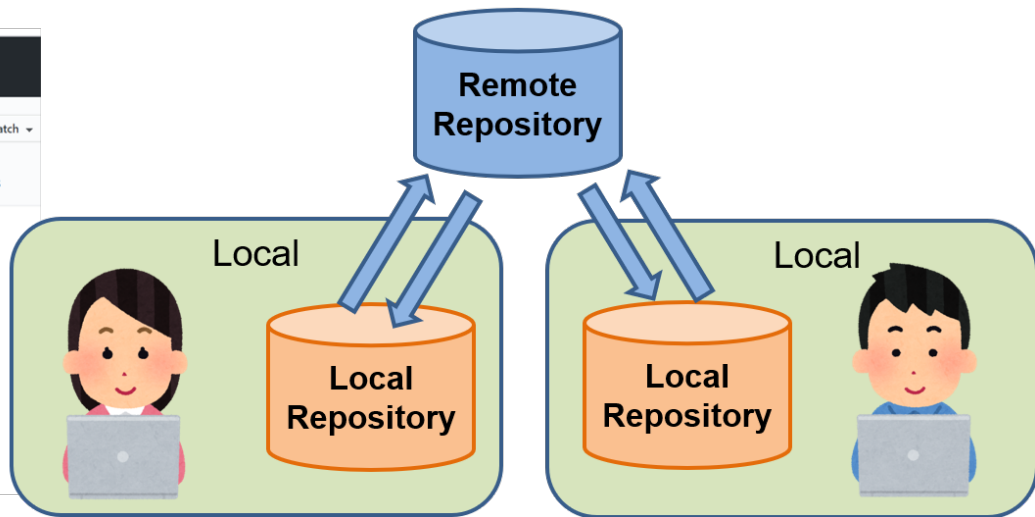
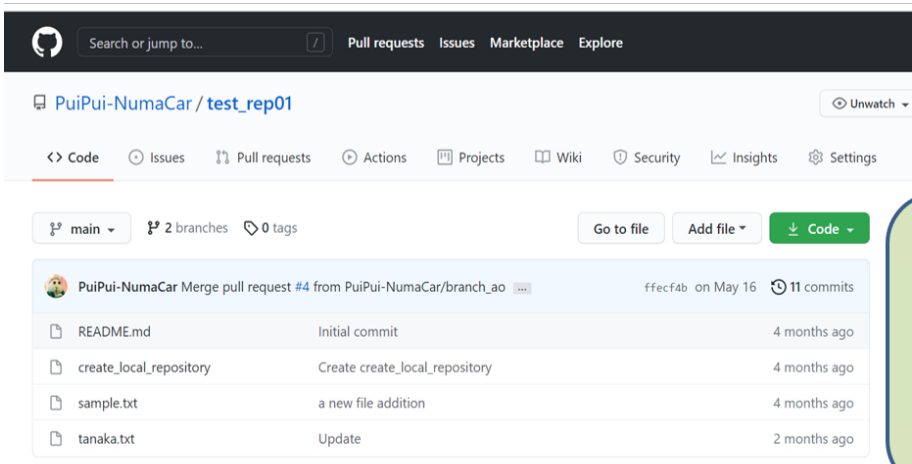
- Learn and use GitHub
- Learn and use the programming language 'R'
- Explore ways to utilize GitHub and R in our industry

OST Use Case Team Activities in 2021

Activity 1: Learn and use GitHub

- Create GitHub account and remote repository
- Modify a file by multiple users through GitHub Desktop

GitHub (Remote Repository)





OST Use Case Team Activities in 2021

What we have learned from this activity 1

- GitHub is a useful tool to manage source code
- Enable multiple users to modify the same file at the same time
- GitHub is also communication tool



OST Use Case Team Activities in 2021

Challenges

- Is it possible to use GitHub in terms of information security policy of my company?
 - GitHub is secure like Box and OneDrive unless you disclose your files on purpose.
 - GitHub provides enterprise version

OST Use Case Team Activities in 2021

Activity 2: Learn and use the programing language 'R'

- Create a TEAE table which is often developed
- Use R Markdown to develop a table and report

OST Use Case Team Activities in 2021

What is R-markdown?

- a file format for making dynamic documents with R

R Markdown script

YAML sets title, date, and output type

Code chunk loads packages and data

```
1 ---
2 title: "Outbreak Situation Report"
3 date: "4/24/2021"
4 output: word_document
5 ---
6
7 ```{r setup, echo=FALSE}
8 pacman::p_load(r10, here, tidyverse, janitor, incidence2, flextable)
9 linelist <- r10::import(here("data", "case_linelists", "linelist_cleaned.rds"))
10
11 This report is for the Incident Command team of the fictional outbreak of Ebola cases.
12 **As of 'r format(max(linelist$date_hospitalisation, na.rm=T), "%d %B")' there have
13 been 'r nrow(linelist)' cases reported as hospitalized.**
14
15 ## Summary table of cases by hospital
16
17 ```{r, echo=F, out.height="75%"}
18 linelist %>%
19   filter(!is.na(hospital)) %>%
20   group_by(hospital) %>%
21   summarise(cases = n(),
22             deaths = sum(outcome == "Death", na.rm=T),
23             recovered = sum(outcome == "Recover", na.rm=T)) %>%
24   adorn_totals() %>%
25   flextable()
26
27 ## Epidemic curve by age
28
29 ```{r, echo=F, warning=F, message=F, out.height = "75%", out.width="100%"}
30 # create epi curve
31 age_outbreak <- incidence(
32   linelist,
33   date_index = date_onset, # date of onset for x-axis
34   interval = "week", # weekly aggregation of cases
35   groups = age_cat)
36
37 # plot
38 plot(age_outbreak, n_breaks = 3, fill = age_cat, col_pal = muted, title = "Epidemic
39 curve by age group")
40
```

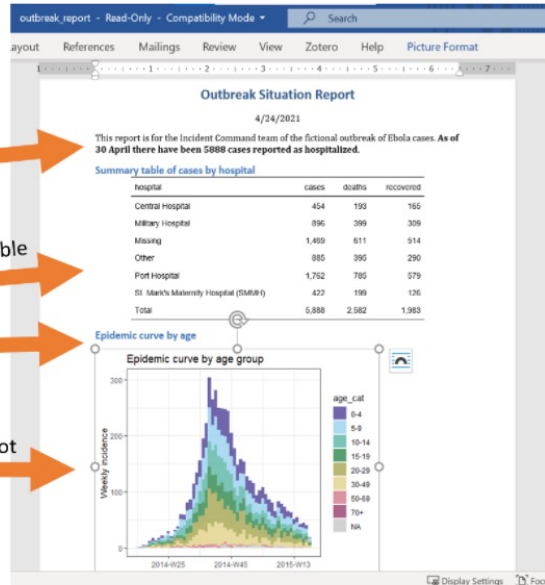
Text and in-line code

Code chunk makes table

Headings

Code chunk makes plot

Output (e.g. Word document)





OST Use Case Team Activities in 2021

```
admiral - RStudio
File Edit Code View Plots Session Build Debug Profile Tools Help
Go to file/function
teae_tables_blue.Rmd x adae.j x
1 ---
2 title: "TEAE Table"
3 author: "PuiPui_NumaCar"
4 date: "r format(Sys.time(), '%Y/%m/%d')""
5 output: html_document
6 ---
7
8 {r setup, include=FALSE}
9 knitr::opts_chunk$set(echo = TRUE)
10
11
12 ## Introduction
13
14 Phuse Japan open source technology working group are learning R and R-markdown.
15 A following Treatment Emergent Adverse Event (TEAE) table was developed by R and R-markdown.
16 This R program was made referring to the following URL.
17 <https://www.r-bloggers.com/2020/02/how-to-make-nice-publishable-adverse-event-tables-using-tidyverse/>.
18
19
20 {r message=FALSE, , echo=FALSE}
21 library(foreign)
22 library(tidyverse)
23 # Importing ADaM Datasets
24 adsl <- read.xport("adsl.xpt")
25 # adae <- read.xport("adae.xpt")
26 adae_j <- read.xport("adae_j.xpt")
27
28 # Develop Header
29 pre_header_ae <- adsl %>%
30   filter(SAFFL == "Y") %>%
31   group_by(TRT01AN) %>%
32   summarise(n=n()) %>%
33   ungroup() %>%
34   mutate(armtxt = case_when(
35     TRT01AN == 0 ~ "Placebo",
36     TRT01AN == 54 ~ "Low_Dose",
37
38 14:79 Introduction
```

TEAE Table

PuiPui_NumaCar

2021/11/17

Introduction

Phuse Japan open source technology working group are learning R and R-markdown. A following Treatment Emergent Adverse Event (TEAE) table was developed by R and R-markdown. This R program was made referring to the following URL.
<https://www.r-bloggers.com/2020/02/how-to-make-nice-publishable-adverse-event-tables-using-tidyverse/>.

Treatment Emergent Adverse Events by System Organ Class and Preferred Term

System Organ Class	System Organ Class (日本語)	Preferred Term	Preferred Term (日本語)	Placebo (N=86)	Low Dose (N=84)	High Dose (N=84)
CARDIAC DISORDERS	心疾患	#Total	#合計	12 (14%)	13 (15.5%)	15 (17.9%)
		ATRIAL FIBRILLATION	心房細動	1 (1.2%)	1 (1.2%)	3 (3.6%)
		ATRIAL FLUTTER	心房粗動		1 (1.2%)	1 (1.2%)
		ATRIAL HYPERTROPHY	心房性高血圧	1 (1.2%)		
		ATRIOVENTRICULAR BLOCK FIRST DEGREE	第1度房室ブロック	1 (1.2%)	1 (1.2%)	
		ATRIOVENTRICULAR BLOCK SECOND DEGREE	第2度房室ブロック	1 (1.2%)		
	BRADYCARDIA	徐脈		1 (1.2%)		

OST Use Case Team Activities in 2021

- **What we have learned from this activity 2**
 - R Markdown is useful when you develop reports
- **Challenges**
 - It is ok to submit TFLs developed by R to Regulatory authority?
 - PMDA does not require use of any specific software for statistical analyses
 - Guidelines are released (see the slide “Reference”)
 - Learning a new language requires time and effort
 - Let’s share our knowledge and experiences!



OST Use Case Team Activities in 2021

Activity 3: Explore ways to utilize GitHub and R in our industry

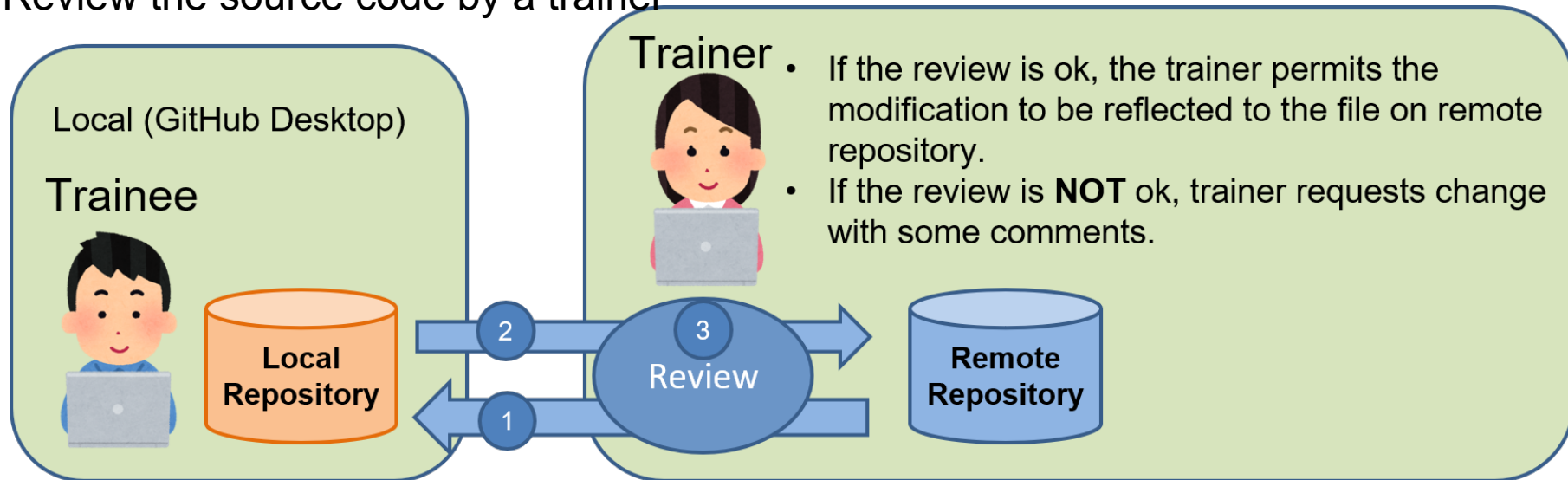
- 3.1: Source code review for new employees on GitHub
- 3.2: Collaborate with medical writing to shorten timeline of Clinical Reports

OST Use Case Team Activities in 2021

3.1 Source code review for new employees on GitHub

When a trainee modifies a program file:

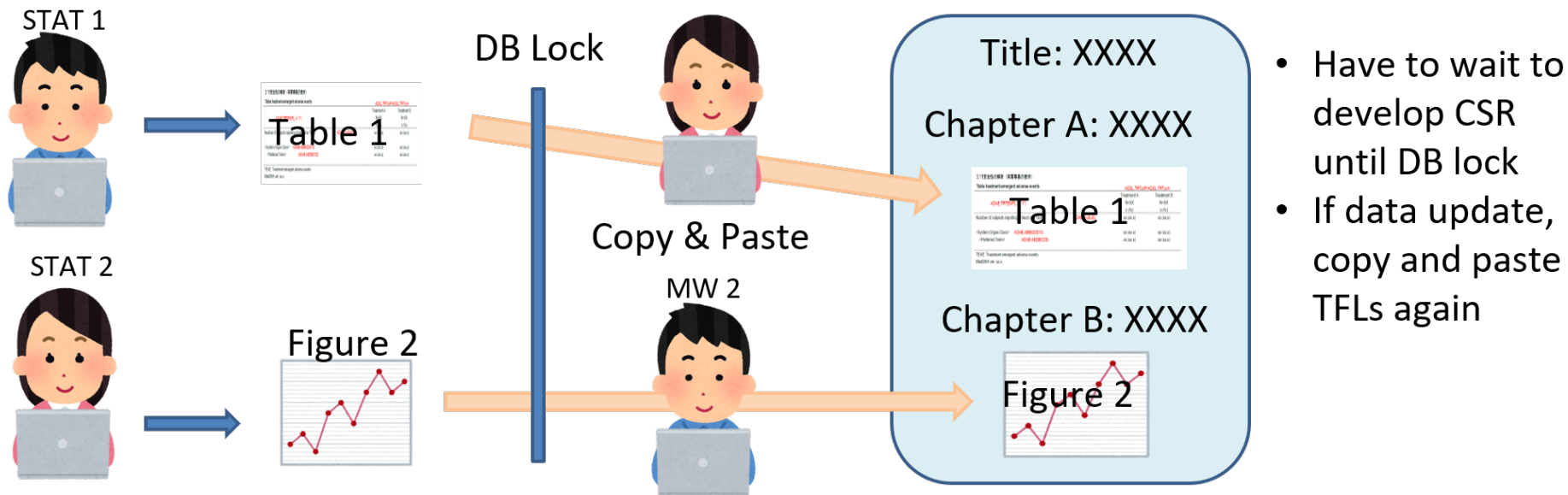
1. Get the file from remote repository to local
2. Upload the modified file to remote repository
3. Review the source code by a trainer



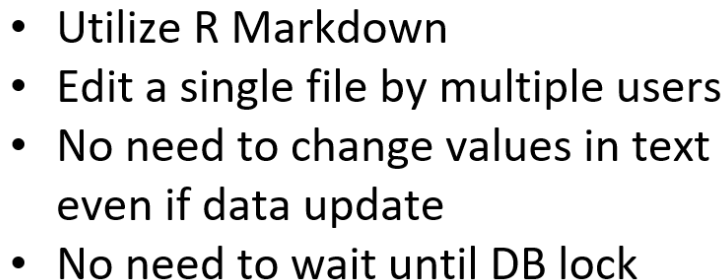
OST Use Case Team Activities in 2021

3.2 Collaborate with medical writing to shorten timeline of Clinical Reports

Present Flow



New Flow



Reduce repetitive process

Shorten timeline!

Reference

- [The Epidemiologist R Handbook](#)
- (You)R programs for health authorities in Japan, PHUSE Japan OST WG, PHUSE EU Connect 2021
- “医薬品・医薬部外品製造販売業者等におけるコンピュータ化システム適正管理ガイドラインについて”, https://www.mhlw.go.jp/web/t_doc?dataId=00tb6573&dataType=1&pageNo=1
- “医薬品等の承認または許可等に関わる申請等における電磁的記録及び電子署名の利用について(Use of Electronic Records and Electronic Signatures in Applications for Approval or License of Pharmaceuticals, etc.), 01-Apr-2005, MHLW
<https://www.pmda.go.jp/files/000158308.pdf>

Thank you for your attention!



**The Global Healthcare
Data Science Community**

Contact Channels

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▶️ [/phusetube](https://youtube.com/phusetube)
🌐 [/company/phuse](https://linkedin.com/company/phuse)