PharmaSUG China 2025 - Paper SA-118

Using VBA to Calculate Agreement for Consistency Evaluation in Diagnostic Assays

Wen Chen, Sharon Cao, Yibo Zhu, Roche Diagnostics (Shanghai) Limited

A reproducibility study of a diagnostic assay for quantitating immunohistochemistry (IHC) biomarkers in tumor tissue specimens typically includes two study designs: a ring study and a reader precision study. These studies cover consistency evaluation with both reference results and paired results among the readers. In comparison with reference results, the main evaluation metrics are positive percent agreement (PPA), negative percent agreement (NPA), and overall agreement (OA). For pairwise comparison, consistency is evaluated by calculating the average positive percent agreement (APA), average negative percent agreement (ANA), and average overall agreement (OA).

INTRODUCTION <HEADING 1>

This paper presents the agreement for consistency evaluation in the reproducibility study, with calculations performed using Visual Basic (VB).

REPRODUCIBILITY STUDY <HEADING 1>

The reproducibility study evaluates the consistency among at least three clinical sites in processing, staining, and interpreting the same set of sample slides. Each slide is binned scored as positive or negative based on specific thresholds. This study includes two parts: the ring study and the reader precision study.

RING STUDY <HEADING 2>

In a ring study, identical pathological slides are provided by each site and distributed to all participating sites. Qualified pathologists at each site stain and interpret the slides according to the product instructions.

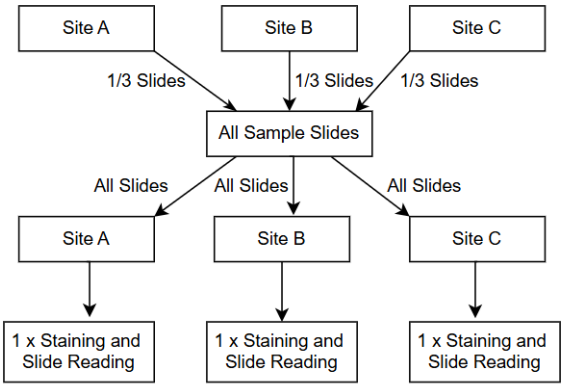


Figure 1. Ring Study Diagram

Table 1 shows the percent tumor membrane (%TC) staining, positive or negative results, and reference results for three sample slides. A cutoff of 70 is used: TC values <70 are negative, ⩾70 are positive. The reference result (i.e., PARAMCD=MODE) is defined as the outcome most frequently observed across the three sites. If multiple slide readings are available, the last valid reading is used for analysis.

Obs	SUBJID	SITE	ASEQ	ADT	PARAMCD	PARCAT1	ATEST	AVALC	EVAL	EVALSITE	ANL01FL
1	1001	Site 1	1	2022-05-02	TC	Ring Study		0	Pathologist C	Site 1	
2	1001	Site 1	2	2022-06-01	TC	Ring Study	Read 1	50	Pathologist C	Site 1	Y
3	1001	Site 1	3	2022-06-01	TC	Ring Study	Read 1	80	Pathologist C	Site 2	Y
4	1001	Site 1	4	2022-06-01	TC	Ring Study	Read 1	75	Pathologist C	Site 3	Y
5	1001	Site 1	5	2022-06-01	TCNP	Ring Study	Read 1	-	Pathologist C	Site 1	Y
6	1001	Site 1	6	2022-06-01	TCNP	Ring Study	Read 1	+	Pathologist C	Site 2	Y
7	1001	Site 1	7	2022-06-01	TCNP	Ring Study	Read 1	+	Pathologist C	Site 3	Y
8	1001	Site 1	8		MODE	Ring Study		+	Pathologist C	Site 1 2 3	Y
9	2001	Site 2	1	2022-05-02	TC	Ring Study		0	Pathologist C	Site 1	
10	2001	Site 2	2	2022-06-01	TC	Ring Study	Read 1	40	Pathologist C	Site 1	Y
11	2001	Site 2	3	2022-06-01	TC	Ring Study	Read 1	45	Pathologist C	Site 2	Y
12	2001	Site 2	4	2022-06-01	TC	Ring Study	Read 1	75	Pathologist C	Site 3	Y
13	2001	Site 2	5	2022-06-01	TCNP	Ring Study	Read 1	-	Pathologist C	Site 1	Y
14	2001	Site 2	6	2022-06-01	TCNP	Ring Study	Read 1	-	Pathologist C	Site 2	Y
15	2001	Site 2	7	2022-06-01	TCNP	Ring Study	Read 1	+	Pathologist C	Site 3	Y
16	2001	Site 2	8		MODE	Ring Study		-	Pathologist C	Site 1 2 3	Y
17	3001	Site 3	1	2022-05-02	TC	Ring Study		0	Pathologist C	Site 1	
18	3001	Site 3	2	2022-06-01	TC	Ring Study	Read 1	70	Pathologist C	Site 1	Y
19	3001	Site 3	3	2022-06-01	TC	Ring Study	Read 1	75	Pathologist C	Site 2	Y
20	3001	Site 3	4	2022-06-01	TC	Ring Study	Read 1	80	Pathologist C	Site 3	Y
21	3001	Site 3	5	2022-06-01	TCNP	Ring Study	Read 1	+	Pathologist C	Site 1	Y
22	3001	Site 3	6	2022-06-01	TCNP	Ring Study	Read 1	+	Pathologist C	Site 2	Y
23	3001	Site 3	7	2022-06-01	TCNP	Ring Study	Read 1	+	Pathologist C	Site 3	Y
24	3001	Site 3	8		MODE	Ring Study		+	Pathologist C	Site 1 2 3	Y

Table 1 Dataset of Readings in Ring Study

READER PRECISION STUDY <HEADING 2>

The reader precision study evaluates the consistency of slide interpretation by the same or different pathologists within sites and across different sites. This study includes three parts:

- Intra-site intra-pathologist consistency: the same pathologist interpreting the slides three times at each site, with each reading separated by an interval of more than two weeks. (see observations 1 - 3 in Table 2)
- Intra-site inter-pathologist consistency: three pathologists with different qualifications at each site interpret the same slides. (see observations 1, 4, and 7 in Table 2)
- Inter-site inter-pathologist consistency: three pathologists with same qualification at different sites interpreting the same slides. (see observations 4 - 6 in Table 2)

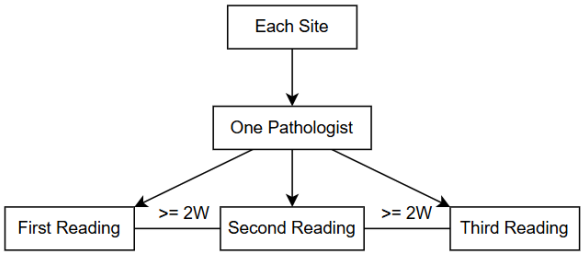


Figure 2. Intra-Site Intra-Pathologist Consistency in Reader Precision Study Diagram

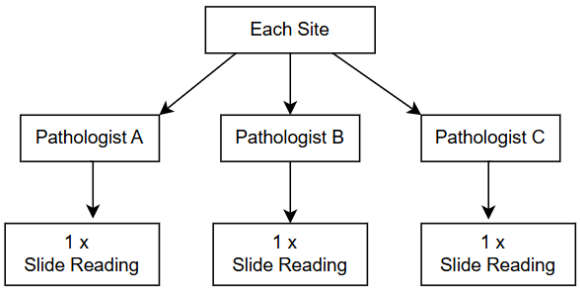


Figure 3. Intra-Site Inter-Pathologist Consistency in Reader Precision Study Diagram

Obs	SUBJID	SITE	ASEQ	ADT	PARAMCD	PARCAT1	ATEST	AVALC	EVAL	EVALSITE	ANL01FL
1	1008	Site 1	8	2022-07-01	TC	Reader Precision	Read 1	50	Pathologist A	Site 1	Y
2	1008	Site 1	9	2022-07-21	TC	Reader Precision	Read 2	80	Pathologist A	Site 1	Y
3	1008	Site 1	10	2022-08-10	TC	Reader Precision	Read 3	75	Pathologist A	Site 1	Y
4	1008	Site 1	11	2022-07-01	TC	Reader Precision	Read 1	80	Pathologist B	Site 1	Y
5	1008	Site 1	12	2022-07-01	TC	Reader Precision	Read 1	70	Pathologist B	Site 2	Y
6	1008	Site 1	13	2022-07-01	TC	Reader Precision	Read 1	80	Pathologist B	Site 3	Y
7	1008	Site 1	14	2022-07-01	TC	Reader Precision	Read 1	80	Pathologist C	Site 1	Y
8	1008	Site 1	15	2022-07-01	TCNP	Reader Precision	Read 1	-	Pathologist A	Site 1	Y
9	1008	Site 1	16	2022-07-21	TCNP	Reader Precision	Read 2	+	Pathologist A	Site 1	Y
10	1008	Site 1	17	2022-08-10	TCNP	Reader Precision	Read 3	+	Pathologist A	Site 1	Y
11	1008	Site 1	18	2022-07-01	TCNP	Reader Precision	Read 1	+	Pathologist B	Site 1	Y
12	1008	Site 1	19	2022-07-01	TCNP	Reader Precision	Read 1	+	Pathologist B	Site 2	Y
13	1008	Site 1	20	2022-07-01	TCNP	Reader Precision	Read 1	+	Pathologist B	Site 3	Y
14	1008	Site 1	21	2022-07-01	TCNP	Reader Precision	Read 1	+	Pathologist C	Site 1	Y
15	1008	Site 1	22		MODE	Reader Precision		+	Pathologist A	Site 1	Y
16	1008	Site 1	23		MODE	Reader Precision		+	Pathologist A B C	Site 1	Y
17	1008	Site 1	24		MODE	Reader Precision		+	Pathologist B	Site 1 2 3	Y

Table 2 Dataset of Readings in Reader Precision Study

AGREEMENT RATES ANALYSIS <HEADING 1>

Agreement rates analysis in consistency evaluation includes positive percent agreement (PPA), negative percent agreement (NPA), overall agreement (OA), average positive percent agreement (APA), and average negative percent agreement (ANA). The calculation formulas are as follows:

	Column Result	
Row Result	Positive (+)	Negative (-)
Positive (+)	a	b
Negative (-)	c	d

Table 3. One 2×2 table

$$Positive\ Percent\ Agreement\ (PPA) = \frac{a}{a + c}$$

$$Negative\ Percent\ Agreement\ (NPA) = \frac{d}{b + d}$$

$$Over\ Agreement\ (OA) = \frac{a + d}{a + b + c + d}$$

$$Average\ Positive\ Agreement\ (APA) = \frac{2a}{2a + b + c}$$

$$Average\ Negative\ Agreement\ (ANA) = \frac{2d}{2d + b + c}$$

BOOTSTRAP RESAMPLING <HEADING 1>

A nonparametric bootstrap procedure can be used to calculate the confidence interval for the agreement from a dataset with n observations. The steps are as follows:

1. Resample with replacement: randomly sample n observations with replacement from the original data to generate a simulated dataset.
2. Calculate the agreement: compute the agreement of the simulated dataset.
3. Repeat resampling: repeat steps 1 and 2 a total of B times to obtain B simulated agreement.
4. Compute the confidence interval: take the 2.5th and 97.5th percentiles.

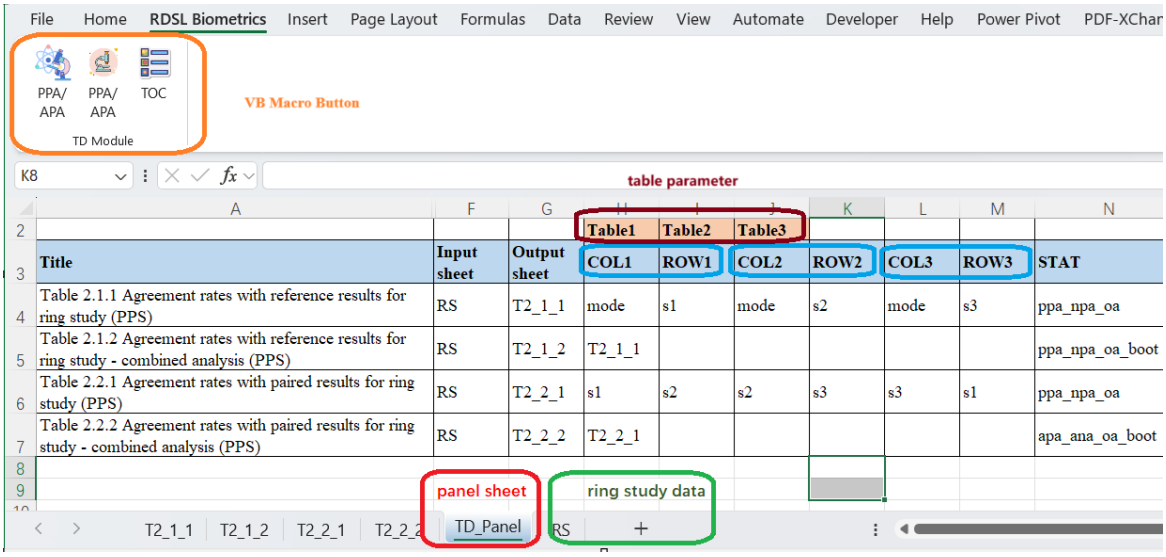
VBA FOR AGREEMENT <HEADING 1>

AGREEMENT: PPA NPA OA <HEADING 2>

Step 1: Prepare the data and parameters<Heading 3>

Taking Table 2.1.1 as an example in Display 1, input the necessary parameters including the input sheet, output sheet, rows and columns, and statistical measures into the panel sheet, and ensure that the corresponding ring study data are ready for agreement analysis.

- Column F: represents the input sheet containing the dataset of slide readings.
- Column G: represents the output sheet, i.e., the table to be generated.
- Columns H - M: correspond to the rows and columns of a 2×2 contingency table.
- Column N: contains the calculated statistical measures.



Display 1. Parameters for VBA Macro

Transpose the slide reading data in the Table 1, and recode positive results as 1 and negative results as 0. This is done to facilitate the calculation of frequencies in the 2×2 contingency table.

	A	B	C	D	E	F	G	H
1	subjid	s1	s2	s3	mode			
2	1001	0	0	0	0		0	negative
3	1002	1	1	1	1		1	positive
4	1003	0	0	0	0			
5	1004	1	1	1	1			
6	1005	1	1	1	1			
7	1006	0	0	0	0			
8	1007	0	0	0	0			
9	1008	1	1	1	1			
10	1009	0	0	0	0			
11	1010	1	1	1	1			
12	1011	0	0	0	0			
13	1012	1	1	1	1			
14	1013	0	0	0	0			
15	1014	1	1	1	1			
16	1015	0	0	0	0			

RS

Display 2. Slide Readings for Ring Study in Excel

To align the column names between the panel sheet and the slide reading data, the function stores the positions of the matched columns in the array, thereby facilitating the identification of row and column variables for the fourfold table.

(General) match_colname

```
    ReDim arr_nox(1, cnt_var)
    If InStr(LCase(Sheets(tocsht).Cells(row, 14)), "boot") = 0 Then
        'save the column no in arr_no()
        'match toc_colname with insht_colname
        For L = 1 To cnt_var
            For m = 1 To insht_last_c
                If LCase(Sheets(tocsht).Cells(row, L + 7)) = LCase(Sheets(insht).Cells(1, m)) And Sheets(tocsht).Cells(row, L + 7) <> "" Then
                    arr_nox(1, L) = m
                    Debug.Print "L=" & L & ", arr_nox=" & arr_nox(1, L) & ",var=" & Sheets(insht).Cells(1, m)
                End If
            Next m
        Next L
    End If

    'Output Array
    match_colname = arr_no
```

Immediate

```
cnt_var=6
L=1, arr_nox=5,var=mode
L=2, arr_nox=2,var=s1
L=3, arr_nox=5,var=mode
L=4, arr_nox=3,var=s2
L=5, arr_nox=5,var=mode
L=6, arr_nox=4,var=s3
```

Step 2: Obtain Frequency<Heading 3>

Based on the 2×2 contingency table, recode each record and store it in an array.

```
    'how many pairs for row and col
    loop_no = UBound(arr_nox, 2) / 2

    For i = 1 To loop_no
        a = 0: b = 0: c = 0: d = 0
        'remember to empty arr_a, arr_b, arr_c, arr_d before each loop
        ReDim arr_rng(loop_no, max_row, 3), arr_freq(3, 3)
        ReDim arr_a(max_row), arr_b(max_row), arr_c(max_row), arr_d(max_row)
        ReDim arr_id(max_row)

        For j = 1 To max_row
            arr_rng(i, j, 1) = Sheets(insht).Cells(j + 1, arr_nox(1, 2 * i - 1))
            arr_rng(i, j, 2) = Sheets(insht).Cells(j + 1, arr_nox(1, 2 * i))
            arr_rng(i, j, 3) = "site" & i & "_" & Sheets(insht).Cells(j + 1, 1)

            'get abcd=col vs row
            If arr_rng(i, j, 1) = 1 And arr_rng(i, j, 2) = 1 Then
                arr_a(j) = 1
            ElseIf arr_rng(i, j, 1) = 1 And arr_rng(i, j, 2) = 0 Then
                arr_c(j) = 1
            ElseIf arr_rng(i, j, 1) = 0 And arr_rng(i, j, 2) = 1 Then
                arr_b(j) = 1
            ElseIf arr_rng(i, j, 1) = 0 And arr_rng(i, j, 2) = 0 Then
                arr_d(j) = 1
            End If

            arr_id(j) = arr_rng(i, j, 3)
        Next j

        a = WorksheetFunction.Sum(arr_a)
        b = WorksheetFunction.Sum(arr_b)
        c = WorksheetFunction.Sum(arr_c)
        d = WorksheetFunction.Sum(arr_d)

        Debug.Print "i=" & i & ",a=" & a & ",b=" & b & ",c=" & c & ",d=" & d
```

mmediate

```
i=1,a=50,b=0,c=0,d=50
i=2,a=50,b=0,c=0,d=50
i=3,a=46,b=1,c=4,d=49
```

Step 3: Estimate the Agreement and 95% Confidence Intervals<Heading 3>

Estimate the agreement based on the formulas.

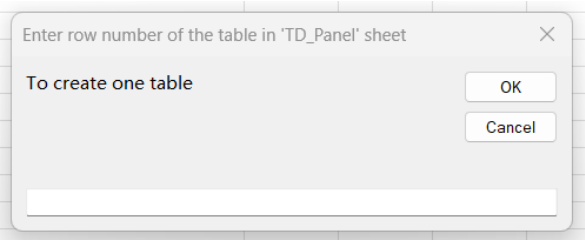
```
        a = arr_freq(1, 1): b = arr_freq(1, 2)
        c = arr_freq(2, 1): d = arr_freq(2, 2)

        'pct=numerator/denominator
        'APA_ANA_OA
        arr_num(1) = 2 * a: arr_den(1) = 2 * a + b + c
        arr_num(2) = 2 * d: arr_den(2) = 2 * d + b + c
        arr_num(3) = a + d: arr_den(3) = a + b + c + d

        'PPA_NPA_OA
        arr_num(4) = a: arr_den(4) = a + c
        arr_num(5) = d: arr_den(5) = b + d
        arr_num(6) = arr_num(3): arr_den(6) = arr_den(3)

        'pct(num/den)*100
        For i = 1 To 6
            If arr_den(i) <> 0 Then arr_pct(i) = Round((arr_num(i) / arr_den(i)) * 100, 1)
            arr_pctnd(i) = arr_pct(i) & " (" & arr_num(i) & "/" & arr_den(i) & ")"
        Next i
        arr_pctx = arr_pct: arr_pctndx = arr_pctnd
```

Calculate the corresponding confidence intervals.

```
    'for apa-ana-oa : Transformed Wilson Score
    arr_nn(1) = a + b + c: arr_nn(2) = d + b + c: arr_nn(3) = a + b + c + d

    'for ppa-npa-oa: wilson score
    arr_nn(4) = a + c: arr_nn(5) = d + b: arr_nn(6) = a + b + c + d

    'alpha two side
    alpha = 0.05
    Z = Application.NormSInv(1 - alpha / 2)

    'get 95% ci---wilson and transformed wilson
    For j = 1 To 6
        'pct for wilson score
        If arr_wn(j) <> 0 Then arr_wpct(j) = arr_wx(j) / arr_wn(j)

        low = (2 * arr_nn(j) * arr_wpct(j) + Z ^ 2 - Z * Sqr(Z ^ 2 + 4 * arr_nn(j) * arr_wpct(j) * (1 - arr_wpct(j)))) / (2 * (arr_nn(j) + Z ^ 2))
        upper = (2 * arr_nn(j) * arr_wpct(j) + Z ^ 2 + Z * Sqr(Z ^ 2 + 4 * arr_nn(j) * arr_wpct(j) * (1 - arr_wpct(j)))) / (2 * (arr_nn(j) + Z ^ 2))

        'ci 1=low 2=upper, percent *100
        If j <= 2 Then
        'ana apa --Transformed Wilson
           arr_wci(j, 1) = Round((2 * low / (1 + low)) * 100, 1)
           arr_wci(j, 2) = Round((2 * upper / (1 + upper)) * 100, 1)
        End If

        'ppa-npa-oa-oa--wilson
        If 3 <= j Then
           arr_wci(j, 1) = Round(low * 100, 1)
           arr_wci(j, 2) = Round(upper * 100, 1)
        End If

        arr_wci2(j) = "(" & arr_wci(j, 1) & ", " & arr_wci(j, 2) & ")"

'        Debug.Print "arr_nn=" & arr_nn(j) & ",low=" & low & ",upper=" & upper
'        Debug.Print "arr_wci2: j= " & j & "=" & arr_wci2(j)
    Next j
    arr_wcix = arr_wci2
    get_pct_wci = arr_wci2
End Function
```

Step 4: Output the Table<Heading 3>

In Display 1, by clicking the first button and entering the corresponding row number of the table in the panel sheet, the required table can be generated automatically.



Display 3. An Input Box

Table 2.1.1 Agreement rates with reference results for ring study (PPS)

		+	-	Total
mode VS s1	+	50	0	50
	-	0	50	50
	Total	50	50	100
	PPA% (n/N) [95% CI]	100 (50/50)	(92.9, 100)	
	NPA% (n/N) [95% CI]	100 (50/50)	(92.9, 100)	
	OA% (n/N) [95% CI]	100 (100/100)	(96.3, 100)	
		+	-	Total
mode VS s2	+	50	0	50
	-	0	50	50
	Total	50	50	100
	PPA% (n/N) [95% CI]	100 (50/50)	(92.9, 100)	
	NPA% (n/N) [95% CI]	100 (50/50)	(92.9, 100)	
	OA% (n/N) [95% CI]	100 (100/100)	(96.3, 100)	
		+	-	Total
mode VS s3	+	46	1	47
	-	4	49	53
	Total	50	50	100
	PPA% (n/N) [95% CI]	92 (46/50)	(81.2, 96.8)	
	NPA% (n/N) [95% CI]	98 (49/50)	(89.5, 99.6)	
	OA% (n/N) [95% CI]	95 (95/100)	(88.8, 97.8)	

Display 4. A Sample Table in Ring Study

AGREEMENT: APA ANA OA <HEADING 2>

Taking Table 2.1.2 as an example in Display 1, the previous steps can be referenced from Table 2.1.1.

Estimate the 95% CI Using the Bootstrap Resampling <Heading 3>

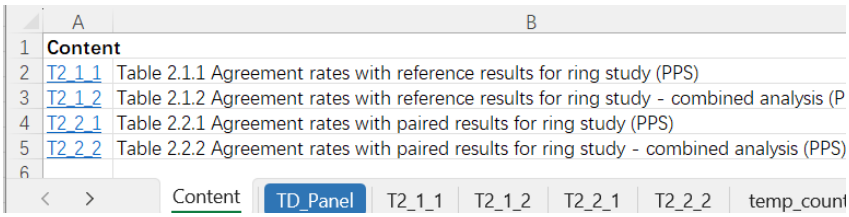
Perform 2,000 resampling iterations to calculate the confidence intervals of the agreement.

```
Randomize 1236
For bt = 1 To 2000
    a = 0: b = 0: c = 0: d = 0

    For i = 1 To tot_row
        rnd_no = Int(Rnd * tot_row + 1)
        'Debug.Print rnd_no
        a = a + arr_a(rnd_no)
        b = b + arr_b(rnd_no)
        c = c + arr_c(rnd_no)
        d = d + arr_d(rnd_no)
    Next i

    'get stat for each sampling
    If (2 * a + b + c) <> 0 Then arr_apa(bt) = 2 * a / (2 * a + b + c)
    If (2 * d + b + c) <> 0 Then arr_ana(bt) = 2 * d / (2 * d + b + c)
    If (a + b + c + d) <> 0 Then arr_oa(bt) = (a + d) / (a + b + d + c)

    'ppa & pna, same as sen-spe-oa
    If (a + c) <> 0 Then arr_ppa(bt) = a / (a + c)
    If (b + d) <> 0 Then arr_npa(bt) = d / (b + d)
Next bt

alpha = 0.05
p_1 = alpha / 2
p_2 = 1 - alpha / 2

'bootstrap --get Percentile 2.5-97.5%
arr_pct2(1, 1) = WorksheetFunction.Percentile(arr_apa, p_1)
arr_pct2(1, 2) = WorksheetFunction.Percentile(arr_apa, p_2)

arr_pct2(2, 1) = WorksheetFunction.Percentile(arr_ana, p_1)
arr_pct2(2, 2) = WorksheetFunction.Percentile(arr_ana, p_2)
```

CREATE ALL TABLES AND TOC <HEADING 2>

In Display 1, clicking the second icon generates all tables sequentially using a for loop, while clicking the last icon creates the table of contents.

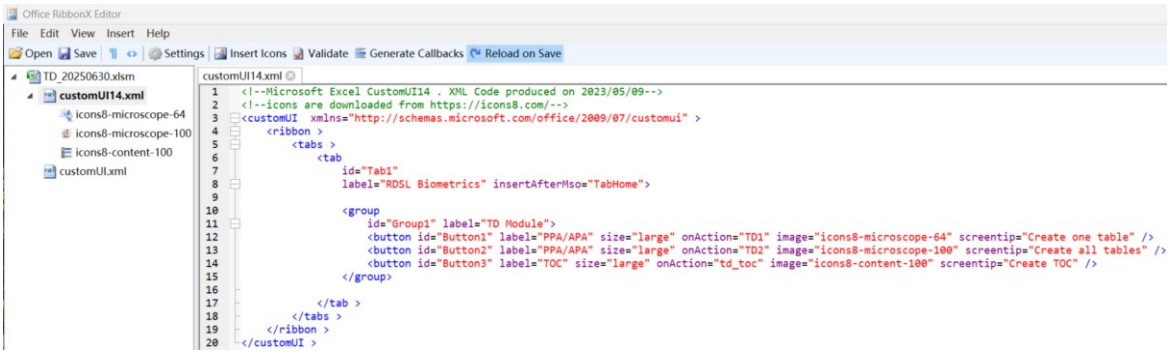
```
Sub td_loop()
    '*********************************************************************
    '*** Code is partially omitted for clarity
    '*********************************************************************
    prompt_s1 = "To create all tables"
    prompt_s2 = "Enter two numbers separated by a comma, e.g., 4,6"

    Title_s = "Enter start and end row numbers of the tables in 'TD_Panel' sheet"
    response = InputBox(prompt:=prompt_s1 & vbCr & vbCr & prompt_s2, Title:=Title_s)
    rowParts = Split(response, ","): start_row = Val(Trim(rowParts(0))): end_row = Val(Trim(rowParts

    For row = end_row To start_row Step -1
        Set outsheet = Worksheets.Add(Before:=Worksheets(1))
        ActiveSheet.Name = outsht

        '*************************************************************************************
        '***1.prepare Data: match colname between td_panel and reading data
        '*************************************************************************************
        arr_no = match_colname(tocsht, insht, row, toc_last_r, insht_last_c, arr_nox)
        loop_no = UBound(arr_no, 1)
        tot_row = max_row * 3 * loop_no

        If InStr(LCase(Sheets(tocsht).Cells(row, 14)), "boot") > 0 Then
            '*************************************************************************************
            '***2.prepare Data: append Data or read source data
            '*************************************************************************************
            Call append_row_col(tocsht, insht, max_row, arr_no, arr_a, arr_b, arr_c, arr_d, arr_id)
            '*************************************************************************************
            '***3.table part1: get frequency
            '*************************************************************************************
            arr_freq = get_freq(outsht, arr_a, arr_b, arr_c, arr_d)
            '*************************************************************************************
            '***4.table part2: get npct & wilson or transformed wilson ci
            '*************************************************************************************
            arr_wci = get_pct_wci(outsht, str, arr_freq, arr_pctx, arr_pctndx, arr_wcix)
            '*************************************************************************************
            '***5.table part3: get bootstrap ci
            '*************************************************************************************
            arr_pct2 = get_boot_ci(tot_row, outsht, str, arr_a, arr_b, arr_c, arr_d, arr_id)
            '*******************************************
            '***6.table part4: output ci
            '*******************************************
            Call output_ci(outsht, str, arr_pctx, arr_wci, arr_pct2, arr_pctndx)
        End If
        Call table_format(outsht, tocsht, row) 'table format
    Next row
End Sub
```



Display 5. Content of the Tables

CUSTOMIZE THE OFFICE RIBBON <HEADING 2>

You can use the Office RibbonX Editor to customize the office ribbon by adding buttons with icons that are linked to VB macros.



Display 6. Office RibbonX Editor

CONCLUSION <HEADING 1>

This paper describes the use of VBA to calculate the agreement rates in tissue diagnostic trials. The results are validated using SAS.

REFERENCES <HEADING 1>

[1] PD-L1 检测试剂临床试验一结果重现性研究注册审查指导原则. 2022. https://www.cmde.org.cn//flfg/zdyz/zdyzwbk/20220711100645123.html

[2] Jeffrey R. Budd, PhD; Karl De Vore, BA, SSBB. 2023. CLSI EP12 Evaluation of Qualitative, Binary Output Examination Performance. https://clsi.org/shop/standards/ep12/

[3] Yu SL, Hsiao YJ, Cooper WA, Choi YL, Avilés-Salas A, Chou TY, Coudry R, Raskin GA, Fox SB, Huang CC, Jeon YK, Ko YH, Ku WH, Kwon GY, Leslie C, Lin MC, Lou PJ, Scapulatempo-Neto C, Mendoza Ramírez S, Savelov N, Shim HS, Lara Torres CO, Cunha IW, Zavalishina L, Chen YM. The Ring Study: an international comparison of PD-L1 diagnostic assays and their interpretation in non-small cell lung cancer, head and neck squamous cell cancer and urothelial cancer. Pathology. 2023 Feb;55(1):19-30. https://doi.org/10.1016/j.pathol.2022.07.016

[4] Barnes, M., Srinivas, C., Bai, I. et al. Whole tumor section quantitative image analysis maximizes between-pathologists' reproducibility for clinical immunohistochemistry-based biomarkers. Lab Invest 97, 1508–1515 (2017). https://doi.org/10.1038/labinvest.2017.82

[5] Jiangtang Hu. 2015. Confidence Intervals for Binomial Proportion Using SAS®: The All You Need to Know and No More…https://www.lexjansen.com/sesug/2015/103_Final_PDF.pdf

RECOMMENDED READING <HEADING 1>

- *SAS/STAT(R) 9.22 User's Guide*
  https://support.sas.com/documentation/cdl/en/statug/63347/HTML/default/viewer.htm#statug_surveys

elect_sect007.htm

- *Resampling https://www.coursera.org/learn/statistical-inference/home/module/4*
- *Office RibbonX Editor https://github.com/fernandreu/office-ribbonx-editor*
- *Icons8 https://icons8.com*

CONTACT INFORMATION <HEADING 1>

Your comments and questions are valued and encouraged. Contact the author at:

Wen Chen
Roche Diagnostics (Shanghai) Limited
wen.chen.wc2@roche.com
chenwen_23@163.com

Sharon (Xianwen) Cao
Roche Diagnostics (Shanghai) Limited
sharon.cao@roche.com

Yibo Zhu
Roche Diagnostics (Shanghai) Limited
yibo.zhu@roche.com