# CFO suite User Guide

## Contents

1	CFC	) desig	gns for phase I clinical trial		<b>2</b>
	1.1	Real to	rial: Dose determination for next cohort		2
		1.1.1	Step-by-step instructions		2
		1.1.2	Result Analysis		5
	1.2	Real to	rial: MTD selection		6
		1.2.1	Step-by-step instructions		6
		1.2.2	Results Analysis		7
	1.3	Simula	ation		8
		1.3.1	Step-by-step instructions		8
		1.3.2	Result Analysis	•	11
<b>2</b>	Oth	er not	es regarding the use of the CFO suite	-	13
	2.1	CFO d	design for Phase I/II trial		13
	2.2	Use CI	FO2d to conduct a phase I trial		13

## 1 CFO designs for phase I clinical trial

The CFO suite is designed to perform real trials and single or multiple simulations. For real trials, it provides functions to determine the next cohort dose. It also facilitates the selection of the maximum tolerated dose (MTD) upon completion of dose assignments in a real trial. In the context of simulation trials, the CFO suite executes one or multiple simulations of a CFO-type design, obtaining relevant operating characteristics.

## 1.1 Real trial: Dose determination for next cohort

Click **Dose for Next Cohort** (shown in Figure 1), and enter design parameters (e.g., the target DLT rate, current dose level, .....).

Step 2: Set the parameters are observed data	ne trial nd record the n.	Step 1: Choose the Calibration-Free Odds (Cl	appropriate CF( FO) Design For F	O design Phase I T	ı. Trial		
manple strategies	Source Heat Contra		Communication of the second se				
	Trial Setting	Summary					
Target DLT rate	Current dose level		Expe	ected Toxicity Pr	obabilities		
0.2	3	Show 5 $\checkmark$ entries					Search:
DLTs at left, current, and right doses			Left Dose Level		Current Dose Level		Right Does Level
0, 1, 0		Toxicity Probability	0.076		0.342		
The part should be filled with NA if the	re is no data. Example: NA, 1, 2	Showing 1 to 1 of 1 entries					Previous 1 Next
Patients at left, current, and right do	oses		NOTE: No estimates are av	vailable for the	doses with no patien	its treated.	
3, 6, 0							
The part should be filled with NA if the	re is no data. Example: NA, 9, 12						
alpha.prior	beta.prior	All tested doses are not overly t	toxic.				
0.2	0.8	Dose movement for next cohor	t: Stay				
		Dose level for next cohort: Dose	e Level 3				
S	afety Control						
Safety cutoff	Early stopping	Step 3: Set safety c	control paramet	ers			
0.95	0.95		one paramot				
	Run						

Figure 1: Main Interface of CFO Suite

#### 1.1.1 Step-by-step instructions

(1) Choose the appropriate CFO design.

The App can be used in two scenarios: with late-onset toxicity or without late-onset toxicity. For scenarios without late-onset toxicity, the **Dose for Next Cohort** tab follows the standard CFO design, which offers two variants: aCFO and rCFO. For scenarios considering late-onset toxicity, the **Dose for Next Cohort (with Late-onset)** tab provides an appropriate adjustment.

- (2) Set the trial parameters and record the observed data.
  - (2a) The CFO and rCFO designs

Trial Setting						
Target DLT rate						
0.2	0.2					
Current dose level						
3						
DLTs at left, current, and right doses						
0, 1, 0						
The part should be filled with NA if there is no	data. Example: NA, 1, 2					
Patients at left, current, and right doses						
3, 6, 0						
The part should be filled with NA if there is no	data. Example: NA, 9, 12					
alpha.prior	beta.prior					
0.2	0.8					

Figure 2: Trial configuration interface under **Dose for Next Cohort (CFO)** tab and **Dose for Next Cohort (rCFO)** tab

Remark 1: **DLTs at left, current, and right doses** should be filled in with the observed DLT results at different dose levels. For example, 0,1,0 indicates that one DLT outcome has been observed so far at the dose level used for the current cohort (the third dose level in this example), with no DLT outcomes at the adjacent left (dose level 2) or right (dose level 4) doses. When there is no data available on the left or right of the current dose—for example, if the current cohort is treated at the first dose level, meaning there is no lower dose— use NA for the missing data. For instance, if the current dose is 1 (with no dose to the left), the data is filled in as NA,1,0, which means one DLT was observed at the current dose, no DLT was observed at the right dose, and there is no dose level on the left. **Patients at left, current, and right doses** is also set in a similar way.

Remark 2: **alpha.prior** and **beta.prior** are used to set the prior distribution for the DLT rate. The beta distribution Beta(alpha.prior, beta.prior) is used here.

(2b) The aCFO design

	Trial	Setting	
Target DLT rate		Current dose level	
0.2	٢	3	\$
DLTs at all doses			
0, 0, 1, 0, 0, 0, 0			
Example: 0, 0, 1, 0, 0, 0, 0			
Patients at all doses			
3, 3, 6, 0, 0, 0, 0			
Example: 3, 3, 6, 0, 0, 0, 0			
alpha.prior		beta.prior	
0.2	٢	0.8	¢

Figure 3: Trial configuration interface under the Dose for Next Cohort (aCFO) tab

The settings here are essentially the same as those in **Dose for Next Cohort.** The only difference is that you need to enter all observed data from the lowest to the highest dose level. As shown in the example in the figure 3, the vector 3, 3, 6, 0, 0, 0 indicates that seven doses to be tested in the entire trial. Results from the first to the

current cohort show that 3 patients were treated at dose level 1, 3 at dose level 2, and 6 at dose level 3. The vector 0, 0, 1, 0, 0, 0, 0 shows that one DLT outcome was observed at dose level 3, while no DLT outcomes were observed at the other dose levels.

(2c) Designs with late-onset toxicity

		Trial S	Setting		
Step A: Basic Setting	Type of CFO design		Target DLT rate		
of the trial.	TITE-CFO	-	0.2		
A 1 Salaat tha tura	Current dose level		Number of dose	level	
of CFO design	3	٢	7	٢	
	alpha.prior		beta.prior		
A.2 Enter the basic	0.2	٢	0.8	٢	
experimental					
settings.					
A 2 Enter the pro		Late-ons	et Setting		
A.S Effer the pre-	Participant entry tim	e			
distribution for the	0, 0.266, 0.638, 1.54,	2.48, 3.14, 3.3	2, 4.01, 4.39, 5.38, 5.7	76, 6.54, 6.66, 6.9	
DIT rate	Subject DLT time				Step B: Enter the
DET TURC.	0, 0, 0, 0, 0, 0, 0, 0, 0, 0,	0.610, 0, 2.98,	0, 0, 1.95, 0, 0, 1.48		experimental record
	Subject dose level				data.
	1, 1, 1, 2, 2, 2, 3, 3, 3,	4, 4, 4, 3, 3, 3,	4, 4, 4		
	Maximal assessment	window size			
	3			٢	
	Current time				
	9.41			•	

Figure 4: Trial configuration interface under the Dose for Next Cohort (late-onset) tab

The data encompasses all records from the first enrolled cohort up to the current cohort in the trial. This includes the entry time of each cohort and the dose level treated. If a DLT outcome occurs, the time from treatment to the observation of the DLT outcome should also be recorded.

(3) Set safety control parameters



Figure 5: Safety control interface

For safety, early stopping and dose elimination rules are adopted. Any dose level identified as overly toxic, as well as all the higher dose levels, are eliminated. If the lowest dose level is overly toxic, the trial will be terminated according to the early stopping rule. The **Safety cutoff** and **Early stopping** tabs respectively set the thresholds for removing over-toxic doses from the trial and stopping the entire trial due to excessive drug toxicity.

#### 1.1.2 Result Analysis

Summary	6					
		Expec	ted Toxic	ity Probabilities		
Show 5	∼ entries					Search:
		Left Dose Level	÷	Current Dose Level	÷	Right Does Level
	Toxicity Probability	0.076		0.342		
Showing 1 to	o 1 of 1 entries	NOTE: No estimates are ava	ilable fo	r the doses with no patients	reated.	Previous 1 Next

All tested doses are not overly toxic. Dose movement for next cohort: Stay Dose level for next cohort: Dose Level 3

Figure 6: An example of determining the dose level for the next cohort using the CFO suite

The results are presented in two parts: the expected toxicity probability and the dose recommendation. The first part provides the estimates of the probability of toxicity for each dose level, based on observed data. The second part displays the dose escalation or de-escalation decision, along with the recommended dose for the next cohort. For example, as shown in Figure 6, the trial is recommended to continue at dose level 3. Additionally, none of the tested dose levels may be identified as excessively toxic.

If a dose level is deemed excessively toxic, the result shown in Figure 7 indicates that dose level 3 and higher doses are too toxic and should be excluded from the trial.

Summary								
		Exped	cted Toxici	ty Probabilities				
Show 5 ~	entries					Search:		
		Left Dose Level	¢	Current Dose Level	\$	<b>Right Does Level</b>		\$
	Toxicity Probability	0.076		1.000				
Showing 1 to 1	of 1 entries					Previous	1	Next
		NOTE: No estimates are ava	ailable for	r the doses with no patients t	reated.			

Dose level 3 and all levels above exhibit excessive toxicity. Dose movement for next cohort: De-escalation Dose level for next cohort: Dose Level 2

Figure 7: An example demonstrating an overly toxic scenario

## 1.2 Real trial: MTD selection

Step 2: En design and experimen	ter the experimental d the recorded ntal results. imulations Sectim Door For Nex Cohor Door	1: Choose "Sele Calibration-Free For Next Cohort (ACPO) Dose For Next	ct MTD" tab Odds (CFO) Design	For Phase I Trial		
Target DLT rate	Trial Setting	Summary Plot The MTD: Dose	level 3			
0.2				Statistical Results At Each Dose Level		
Patients at each dose		Show 7 $$				Search:
3, 3, 27, 3, 0, 0, 0			Posterior DLT Estimate	95% Credible Interval		Pr(toxicity > 0.2   data)
cample:3, 3, 27, 3, 0, 0, 0		1	0.05	(0.00,0.36)		0.08
0, 0, 4, 2, 0, 0, 0		2	0.05	(0.00,0.36)		0.08
cample: 0. 0. 4. 2. 0. 0. 0		3	0.15	(0.05,0.30)		0.21
Ipha.prior	beta.prior	4	0.55	(0.12,0.93)		0.93
0.2	0.8	5		()		
		6		()		
		7		()		
	Safety Control	Showing 1 to 7 of 7 entrie	95			Previous 1 Ne
afety cutoff			NOTE: No estimat	es are available for the doses with ne	o patients trea	ited.
0.95						
arly stopping		Sten 3: Set t	the safety control thr	eshold		
0.95		Step 5. Set	and survey control the	conora		
	Run					

Figure 8: Main interface

#### 1.2.1 Step-by-step instructions

(1) Choose **Select MTD** tab

Remark: Regardless of which CFO design is used, the final summarization of results is performed using the functionality provided in this tab for estimation.

(2) Enter the trial design and the recorded results

After the trial is completed, input the results for all tested doses, along with the pre-specified target and the prior distribution parameters for the DLT rate.

	Trial	Setting	
Target DLT rate			
0.2			٢
Patients at each d	ose		
3, 3, 27, 3, 0, 0, 0			
Example:3, 3, 27, 3,	0, 0, 0		
DLTs at each dose			
0, 0, 4, 2, 0, 0, 0			
Example: 0, 0, 4, 2,	0, 0, 0		
alpha.prior		beta.prior	
0.2	٢	0.8	٢

Figure 9: Trial configuration interface under the  ${\bf Select}~{\bf MTD}$  tab

(3) Set the safety control threshold



Figure 10: Safety control interface

### 1.2.2 Results Analysis

Summary	Select the "Summary" tab to view the statistical results.				
The MTD:	Dose level 3				
		Statistical Results At Each Dose Lev	el		
Show 7 ~ e	entries			Search:	
	Posterior DLT Estimate		Á.	Pr(toxicity > 0.2   data)	÷
1	0.05	(0.00,0.36)		0.08	
2	0.05	(0.00,0.36)		0.08	
3	0.15	(0.05,0.30)		0.21	
4	0.55	(0.12,0.93)		0.93	
5		()			
6		()			
7		()			
Showing 1 to 7 o	of 7 entries			Previous	1 Next

NOTE: No estimates are available for the doses with no patients treated.

Figure 11: An example of selecting the MTD based on complete trial data using the CFO suite

Select the **Summary** tab to view the estimation results based on the observed data, including the final MTD and the corresponding estimates of the DLT rate at different dose levels. The **Statistical Results At Each Dose Level** table displays the DLT rate-related results. For dose levels that are not administered to any patients, no results are displayed, and these levels are represented by <u>-----</u>. For a more intuitive visualization of the statistical results, relevant charts display the estimated DLT rate along with its confidence interval. To view this plot, select the **Plot** tab, as shown in Figure 12.

Summary Plot

Select "Plot" tab to view the plot



Figure 12: Plot displaying confidence intervals, mean estimates, and the target DLT rate indicated by a red dashed line

## 1.3 Simulation

Step 1: Select t	he type of simulation Calibi	ration-Free C	dds (CF)	0) Desi	gn F	or Ph	ase l'	Trial						
Single Simulation Multiple Simulations	Select MTD Dose For Next Cohort Dose For Next C	ohort (aCFO) Dose For Next Col	ort (Late-onset) Do	se For Next Cohort	(rCFO) G	Samma Table								
	1: Select the type of simulation Market Not Date for Nace Card Card Card Card Card Card Card Card													
Configur	ation for CFO Design	Selected MTD: Dos	e level 3											
CFO	•				Sim	ulation O	utcomes At	Each Dose	e Level					
True DLT rates		Show 5 $\checkmark$ entries										Search:		
0.05, 0.15, 0.30, 0.40, 0.65				r	Dose1		Dose2		Dose3		Dose4		Dose!	5
Example: 0.05, 0.15, 0.30, 0.40, 0.65		Number o	Patients		3		33		24		0		0	
Target DLT rate:	Initial dose level:	Number o	f Toxicity		0		6		7		0		0	
0.3	1	Showing 1 to 2 of 2 entries											Previous	l Next
Number of cohorts	Cohort size					Dose Level	Assigned T	o Each Coh	nort					
20	3	Show 5 $\checkmark$ entries										Search:		
Safety cutoff	Early stopping	Cohort1 🕴 Co	hort2 🕴 Cohort3 🕴	Cohort4	Cohort5	Cohort6	Cohort7	Cohort8 🕴	Cohort9	Cohort10 🕴	Cohort11 🕴	Cohort12	Cohort13	Cohort
0.95	0.95	Number												
alpha.prior	beta.prior	of 1 Patients	2 2	2	2	2	2	2	2	2	2	3	3	2
0.3	0.7	4								-				
Set seed:		Showing 1 to 1 of 1 entries											Previous	Next
1					SI	tatistical <b>R</b>	tesults At E	ach Dose L	.evel					
	Run	Show 5 v entries										Search:		
			Posterior DLT Estima	ate			95% Credibl	e Interval			Pr(to	xicity > 0.3	data)	
		1	0.07				(0.00	.0.43)				0.06		
		2	0.19				(0.08	.0.33)				0.06		
Chain 0: Ca	A survey of the stand of the standard of the	3	0.29				(0.14	.0.48)				0.44		
Step 2: Se	t up the trial scenario	4					(	)						
and CFO o	design	5					(	)						
		Showing 1 to 5 of 5 entries											Previous 1	l Next
			NO	OTE: No est	imates a	are availa	ble for th	e doses w	vith no pi	atients tre	eated.			

Figure 13: Main interface

### 1.3.1 Step-by-step instructions

(1) Select the type of simulation

Several simulation scenarios are available, including **Single Simulation** and **Multiple Simulation**, each corresponding to different needs. **Single Simulation** allows the use of the CFO design and its variants to perform a single simulation without late-onset toxicity. To conduct multiple simulations for a more comprehensive analysis, select the **Multiple Simulation** tab.

(2) Set up the trial scenario and CFO design

The CFO design parameter configuration interfaces under the **Multiple Simulation** and **Single Simulation** tabs are nearly identical, except that the "Number of simulations setting" is not required in the **Single Simulation** tab. The following instructions use the **Multiple Simulation** tab as an example.

	Configuration	for CFO Design				
Step 1:	Type of CFO design					
Select the 🛛 🛑	CFO	•				
type of CFO	Number of simulations					
	5					
	True DLT rates					
	0.05, 0.15, 0.30, 0.40, 0.65					
	Example: 0.05, 0.15, 0.30, 0.40, 0.65					
	Target DLT rate:	Initial dose level				
	0.3	1				
	Number of cohorts:	Cohort size:				
	20	3				
	Safety cutoff	Early stopping				
	0.95	0.95				
	alpha.prior	beta.prior				
	0.3	0.7				
	Set seed:					
	1					
	R	In				

Figure 14: CFO design parameter configuration interface under the Multiple Simulation tab

In the first step, select the CFO design you wish to use. This includes CFO designs that account for late-onset toxicities. Then, set the **seed** to initialize the random number generator, ensuring the reproducibility of the random process. Finally, specify the parameters for the prior distribution of the DLT rate, which follows a Beta distribution. When choosing CFO, aCFO, or rCFO, the CFO settings interface will appear as shown in Figure 15.

	Configuration for CFO Design							
	Type of CFO design							
	CFO 🔹							
	Number of simulations	·						
	5							
	True DLT rates							
	0.05, 0.15, 0.30, 0.40, 0.65							
	Example: 0.05, 0.15, 0.30, 0.40, 0.65							
	Target DLT rate:	Initial dose level						
Step 2: Set the	0.3	1						
design	Number of cohorts:	Cohort size:						
	20	3						
	Safety cutoff	Early stopping						
	0.95	0.95						
	l alpha.prior	beta.prior						
	0.3	0.7						
	Set seed:							
	1							
		Run						

Figure 15: CFO design parameter configuration interface under the **Multiple Simulation** tab

If you select  $\boxed{\text{TITE-CF0}}$ ,  $\boxed{\text{TITE-aCF0}}$ ,  $\boxed{\text{fCF0}}$ , or  $\boxed{\text{f-aCF0}}$ , additional settings will be required. In this case, the CFO settings interface will appear as shown in the figure 16.



Figure 16: CFO design parameter configuration interface under the Multiple Simulation tab

Remark: Explanation of the option of **Patient arrival distribution**. When set to **fix**, patients in each cohort arrive simultaneously at a given rate. When set to **unif**, arrivals follow a uniform distribution, and when set to **exp**, they follow an exponential distribution.

#### 1.3.2 Result Analysis

### (a) Single Simulation

```
When choosing CFO, aCFO, or rCFO
```

Select "Summary"	Summary	Plot											
simulation	Selected	d MTD: Do	ose level 3	3									
results					Simula	tion Ou	comes At Ea	ch Dose Le	vel				
results.	Show 5	entries									Search:		
					Dose1	+	Dose2	Dose3	+	Dose4	Dose5	+	
		Nur	mber of Patien	ts	3		33	24		0	0		
		Nur	mber of Toxicit	y	0		6	7		0	0		
	Showing 1 to	o 2 of 2 entries									Previous	1	Next
					Dose	Level A	ssigned To E	ach Cohort	:				
	Show 5	entries									Search:		
		Cohort1 🔶	Cohort2 🔶	Cohort3 🔶	Cohort4 🔶	Cohort5	Cohort6 🔶	Cohort7 🔶	Cohort8	Cohort9	Cohort10 🔶 C	ohort11 🔶	Coh
	Number of Patients	1	2	2	2	2	2	2	2	2	2	2	
	Showing 1 to	o 1 of 1 entries						_			Previous	1	Next
					Statis	tical Re	sults At Each	Dose Leve	el				
	Show 5	entries									Search:		
			Posterior	DLT Estimate	+	9	5% Credible Inte	rval		Pr(toxicity >	• 0.3   data)	+	
		1		0.07			(0.00,0.43)			0	.06		
		2		0.19			(0.08,0.33)			0	.06		
		3		0.29			(0.14,0.48)			0	.44		
		4					()						
		5					()						
	Showing 1 to	5 of 5 entries									Previous	5 1	Next
			NO	TE: no esti	mate is pro	vided fo	r the doses a	t which no	patient v	was treated.			

Figure 17: An example of performing a single CFO simulation using the CFO suite

When choo	osing TITE	-CFO, TITE-a	aCFO, 1	fCFO, or f	-aCFO				
Select "Summary" to view the simulation	Selected MTD: Do: Duration of the tri	se level 3 al: 31.500 months	Simu	lation Outcomes At E	ach Dose Level				
results.	show 5 v entries						Search:		
			Dose1	Dose2	Dose3	Dose4		Dose5	
	Number	of Patients	6	21	24	6		3	
	Number	or loxicity	U	5	5	3		3	Maria
	showing I to 2 of 2 entries		D	as I aval Assigned To	Each Cohort			Previous	Next
	Show 5 v entries			ose Level Assigned To	Each Conort		Search:		
	Cohort1 👌 C	Cohort2 🗄 Cohort3 着 Cohort4	Cohort5 Co	ohort6 🗄 Cohort7 🗄 Coh	ort8 🗄 Cohort9 着 Coh	ort10 🚔 Cohort11 🚔 Co	ohort12 👌 Co	ohort13 🖕 Coho	ort14 🗄
	Number of 1 Patients	2 3 2	1	2 2	2 2	2 3	3	4	5
	Showing 1 to 1 of 1 entries								
								Previous 1	Next
			Sta	itistical Results At Eac	h Dose Level			Previous 1	Next
	Show 5 ~ entries		Sta	ntistical Results At Eac	h Dose Level		Search:	Previous 1	Next
	Show 5 v entries	Posterior DLT Estimate	Sta	ntistical Results At Eac 95% Credible II	th Dose Level	Pr(to	Search: xicity > 0.3   da	Previous 1 ta)	Next
	Show 5 v entries	Posterior DLT Estimate	¢	ntistical Results At Eac 95% Credible I (0.00,0.2	th Dose Level	Pr(to	Search: xicity > 0.3   da 0.02	Previous 1	Next
	Show 5 v entries	Posterior DLT Estimate 0.04 0.22	\$	ntistical Results At Eac 95% Credible I (0.00,0.2 (0.09,0.4	th Dose Level	Pr(to	Search: xicity > 0.3   da 0.02 0.19	Previous 1	Next ¢
	Show 5 centries	Posterior DLT Estimate 0.04 0.22 0.22	\$	Stistical Results At Eac           95% Credible I           (0.00.0.7           (0.09,0.4           (0.08,0.3           (0.08,0.3	th Dose Level	Pr(to	Search: xicity > 0.3   da 0.02 0.19 0.19	Previous 1	Next ¢
	Show 5 ventries	Posterior DLT Estimate 0.04 0.22 0.22 0.47	¢	stistical Results At Eac           95% Credible In           (0.00,0,2           (0.09,0,4           (0.08,0,3           (0.15,0,8	th Dose Level	Prito	Search: xicity > 0.3   da 0.02 0.19 0.19 0.82	Previous 1	Next ∲
	Show 5 v entries	Posterior DLT Estimate 0.04 0.22 0.47 0.82	\$	stistical Results At Eac           95% Credible II           (0.00,0,2           (0.09,0,4           (0.08,0,3           (0.15,0,8           (0.39,1,0,1	th Dose Level           nterval         0           260         4           390         311           300         300	Prito	Search: xicity > 0.3   da 0.02 0.19 0.19 0.82 0.99	Previous 1	Next
	Show 5 v entries	Posterior DLT Estimate 0.04 0.22 0.22 0.47 0.82	¢	At Eac           95% Credible I           (0.00,0,2           (0.08,0,3           (0.15,0,8           (0.39,1,0	th Dose Level	Prito	Search: xicity > 0.3   da 0.02 0.19 0.19 0.82 0.99	Previous 1	Next

Figure 18: An example of performing a single CFO simulation considering late-onset toxicity using the CFO suite.

## (b) Multiple Simulation

When choosing	CFO,	aCFO	, or	rCFO	
---------------	------	------	------	------	--

Select "Summary" to view the simulation results.

	oping was observe	d in	5 simulations	5.						
	Average S	Simul	ation Outcome	es At l	Each Dose Lev	el				
ihow 5 \$ entries							Searcl	h:		
	Dose1	+	Dose2	+	Dose3	+	Dose4	÷	Dose5	
Selection Percentage	0		0.2		0.6		0.2		0	
Number of Patients	3		21.6		25.2		10.2		0	
Number of Toxicity	0		4		8.6		3		0	
howing 1 to 3 of 3 entries								Previo	us 1	Ne
		Sun	nmary of the S	imula	ition					
ihow 5 💠 entries							Searc	h:		
	Correct MTD Selection	+	MTD allocation	+	Over Selection	*	Over Allocation	+	Average D	LT
Percentage of All Patients	Correct MTD Selection	÷	MTD allocation	÷	Over Selection	÷	Over Allocation	•	Avera	age D

Figure 19: An example of performing multiple CFO simulations using the CFO suite

When choosing <b>TIT</b>	E-CFO, TITE-aC	FO, fCFO, or	f-aCFO
--------------------------	----------------	--------------	--------

#### Select "Summary" to view the simulation results.

Summary Plot										
No instance of early stop Average trial duration: 3	oping was observed 1.5	d in 5	simulations.							
	Average S	imula	tion Outcomes	At E	ach Dose Lev	el				
Show 5 \$ entries							Searc	h:		
	Dose1	+	Dose2	+	Dose3	+	Dose4	÷	Dose5	+
Selection Percentage	0		0.4		0.4		0.2		0	
Number of Patients	4.2		21.6		22.8		10.2		1.2	
Number of Toxicity	0		4.2		7.4		3.4		1.2	
Showing 1 to 3 of 3 entries								Previous	1	Next
		Sum	mary of the Si	nulat	tion					
Show 5 ‡ entries							Searc	h:		
	Correct MTD Selection	*	MTD allocation	+	Over Selection	+	Over Allocation	÷ A	verage [	DLT 🕴
Percentage of All Patients	0.400		0.380		0.200		0.190		0.270	)
Showing 1 to 1 of 1 entries								Previous	1	Next

Figure 20: An example of performing multiple CFO simulations using the CFO suite.

## 2 Other notes regarding the use of the CFO suite

## 2.1 CFO design for Phase I/II trial

There is little operational difference between using the CFO suite to conduct a phase I/II trial and a phase I trial. You only need to add the additional parameters for the efficacy rate, which can be configured similarly to those for the DLT rate.

## 2.2 Use CFO2d to conduct a phase I trial

CFO2d is applied in dose-combination trials. Because the DLT rate is a matrix in this case, the process of setting the DLT rate-related parameters and the DLT outcome is slightly different. In **Single Simulation** and **Multiple Simulation**, the matrix is set in **DLT rates configuration**.

In CFO2d Select MTD and Dose For Next Cohort, the matrix is set in Observed data configuration. When configuring the matrix, please ensure that the number of rows is less than or equal to the number of columns.

	DLT rates configuration							
Step A: Set DLT	Number of rows:		Number of column	columns:				
rate matrix and	3	٢	3	٢				
generate the matrix	The number of rows sho	uld less than Generat	or equal to the numbe te Matrix	r of columns				

Figure 21: DLT rates matrix configuration interface for the CFO2d.

After setting the shape of the matrix, you can then access the input box for entering the DLT rate. Note that the elements in the DLT rate matrix must increase from left to right and from top to bottom.

		Input DLT Rates								
	Number of rows:		Number of columns:							
	3		3							
	The number of rows sho	The number of rows should less than or equal to the number of columns Generate Matrix Input True DLT Rates								
Step B: Enter	0.19 0.48	0.34	0.38							
	0.67	0.83	0.87							
	Doses increase from left	t to right, top to bottom								

Figure 22: DLT rates matrix configuration interface for the CFO2d.

After defining the DLT rate matrix, the rest of the usage follows a similar approach to that of CFO in Phase I trials. For more details, refer to Section 1.