



Vivo Drug Delivery Pharma Consulting ®

Numbers  Drugs ®

Excel data collection sheet User Manual

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Public use

The Excel sheet can be used commercially and privately with 2 exceptions:

- No change of the first page
- Always cite the originator company Vivo Drug Delivery GmbH if you make a reference

Purpose of the data sheet

During the development of a drug product many data are generated. This Excel sheet can systematically store, organize and share huge numerical data in an efficient and comprehensive way for ONE drug substance.

In addition this Excel sheet is organized for using it to simplify numerical input (copy / paste) into the simulation software Gastro plus V8 (trade mark of Simulations plus, USA).

You can share the data using a file server, a SharePoint, a Notes database or in the Cloud (e.g. dropbox) etc.

You can test the functions of the datasheet using the example file on the drug metoprolol after you have installed it and the support files according to *Getting started* section.

Getting started

Download this user manual and the Numbers4Drugs-Excel.zip from the web (<http://www.vivodrugdelivery.com/download>)

There is one Excel files as example using metoprolol as drug. The metoprolol data sheet comprises a lot of numerical data and you can explore the value of such type of data collection (for more information see Metoprolol data sheet section in this manual).

As a first step the Excel sheet must be placed on a file server or your computer in a special subdirectory e.g. C:\\Products\\Metoprolol. **All** source documents must be stored in **one** subfolder to this folder e.g. C:\\Products\\Metoprolol**Data**.

To use this Excel sheet efficiently hyperlinks are mandatory. There are 2 types of hyperlinks:

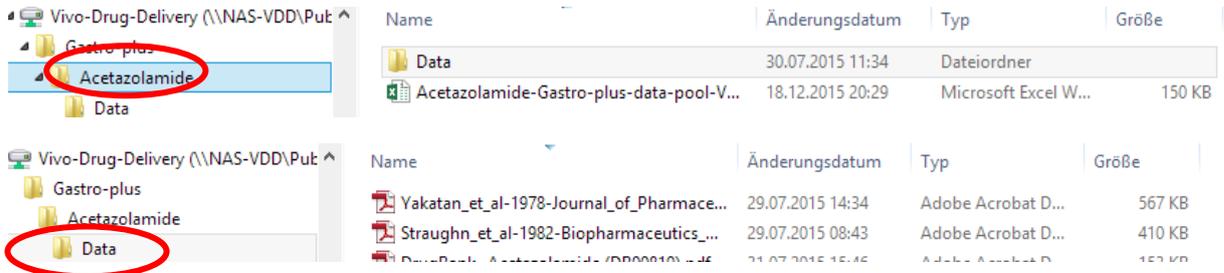
- External
- Internal

To directly access documents containing the numerical data e.g. pdf files from the Excel sheet you need to store it in your 'file' system. The easiest example would be your computer



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e.g. C:\Products\Acetazolamide\data. In the Data subfolder *ALL* source documents must be stored *without* any subfolder!



For a new drug product you need to store the path as a hyperlink to the source documents subfolder only once on the following location in Excel on the overview tap e.g. [\\serverpath\Acetazolamide\data](#) (on a server) or C:\products\Acetazolamide\data (on your PC, Laptop). Don't forget the slash at that end!

Drug	Species	Study n°	Adm route	Food	Dose	DF	Release	DS salt/ polymorph	Cp Mean	Cp Individual	PK mean	PK individual	Compound	Physiology	Pharmacokinetics	Dissolution	G+ results
Acetazolamide																	
Acetazolamide	Human	Straughn1982	po		250 solution			IR									
Acetazolamide					250 tablet			IR									

Place the cursor on cell B1 and click right mouse button and select hyperlink. The following window will appear:



Select Existing file... and click on the appropriate Data subfolder to create the path in the address field.

Press OK – and it's done.

From now on all external hyperlinks – and you can have hundreds of them – are working because the cell B1 is assigned to the name PATH. This name is part of all external hyperlinks. The advantage is if you have to change the directory or server – no problem just fill in the new data path on cell B1 and all external hyperlinks in the Excel sheet will work again!!

External hyperlink instruction

If you want to hyperlink an information in Excel to a particular file stored on your computer or



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company network, you need to create an **external** hyperlink.

1. In the target cell (here R3), copy/paste this formula:

```
=HYPERLINK(Path&"Yakatan_et_al-1978-Journal_of_Pharmaceutical_Sciences-acetazolamide-BAV.pdf"; "Yakatan1978")
```

where

"Yakatan_et_al-1978-Journal_of_Pharmaceutical_Sciences-acetazolamide-BAV.pdf" is the file name of the source document that is in the subdirectory DATA

and "Yakatan1978" is the description that should show up in the Excel sheet cell. In this case it is the paper that contains the human PK study data on acetazolamide.

	A	Q	R	S	T	U	V	W	X	Y	Z	AA	AB	AC	AD
1	Mean Cp/ti														
2															
3	Doc 1		Yakatan1978												
4	Doc 2														
5	Doc 3														
6	Doc 4														
7	Doc 5														
8															
9	Study		Yakatan1978												
10	Data ref.		Tablet A				Tablet B				Tablet C				Tablet D

When clicking on the Yakatan1978 hyperlink the pdf file will open and you can check the original document that contain the data of the Excel sheet.

Internal hyperlink instruction

On the overview sheet of the Excel file, there are hyperlinks (represented by [X](#)) to open directly a particular study in different sheets of the same Excel file e.g Mean CP, Indiv. CP, Compound,...

	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T
1	Path :	\\naa-xdf\public\vivo-drug-delivery\gastro-plus\Acetazolamide\data																		
2																				
3																				
4	Drug	Species	Study n°	Adm satme	Food	Dose	DF	Release	DS salt/ polymorph	CP mean	Individual	PK mean	PK individual	Compound	Physiology	Pharmacokinetics	Dissolution	G+ results		
5	Acetazolamide									X	X	X	X	X	X	X	X	X	X	
6																				
7																				
8																				
9	Acetazolamide	Human	Straightn1982	po		250 solution			IR											
10	Acetazolamide					250 tablet			IR											

Before you can create a hyperlink you have to define a name for the place you want to jump directly.

1. Go to Mean Cp tap



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2. Mark cell R10
3. Formulas
4. Define Name
5. Fill in the Name field: Mean_Cp_Yakantan1978_tab_A (only underscore allowed as special character)
6. OK (Name is created)
7. Go to overview tap
8. Mark cell L14 and insert character X
9. Click right mouse button and select hyperlink
10. Select : Mean_Cp_Yakantan1978_tab_A
11. Click OK done

Acetazolamide

FILE HOME INSERT PAGE LAYOUT FORMULAS DATA REVIEW VIEW ADD-INS

Function Library

Function Library: Insert Function, AutoSum, Recently Used, Financial, Logical, Text, Date & Time, Lookup & Reference, Math & Trig, More Functions

Defined Names: Name Manager, Define Name, Use in Formula, Create from Selection

Name: Cp_Yakatan1978_tab_A
Scope: Workbook
Comment:
Refers to: =Mean Cp_PK!ISR\$10

	A	R	S	T	U	V	W	X	Y
1	Mean Cp/tir								
2									
3	Doc 1	Yakatan1978							
4	Doc 2								
5	Doc 3								
6	Doc 4								
7	Doc 5								
8									
9	Study	Yakatan1978							
10	Data ref.	Tablet A							
11	Species	human							
12	Gender	male							
13	Pre-treatment								
14	Food	fasted							
15	Dose	250							
16	Route								
17	Admin.	po							
18	Release	IR					IR		
19	DF	Tablet					Tablet		
20	Water mL	240,00					240,00		
21	Day								
22	Drug salt	free base					free base		



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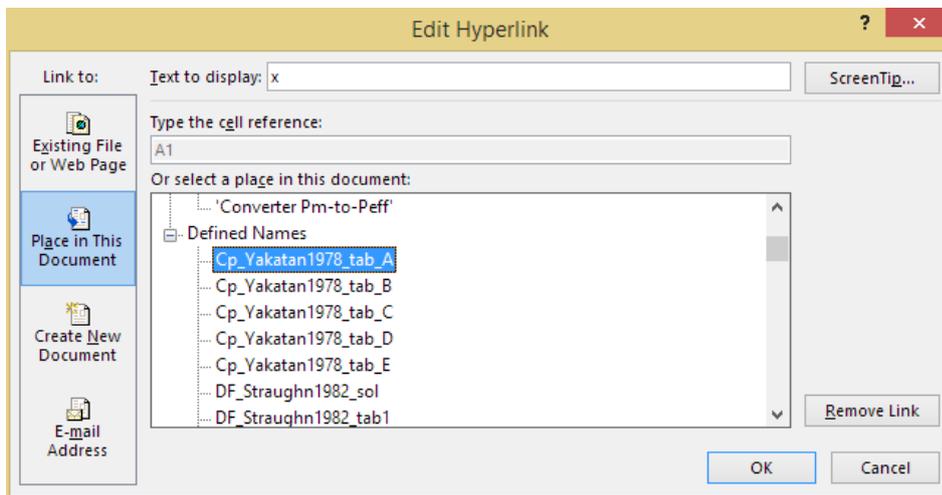
Acetazolamide-Gastro-plus-data-pool-V1.xlsx - Excel

FILE HOME INSERT PAGE LAYOUT FORMULAS DATA REVIEW VIEW ADD-INS

Function Library: Insert Function, AutoSum, Recently Used, Financial, Logical, Text, Date & Time, Lookup & Reference, Math & Trig, More Functions, Name Manager, Define Name, Use in Formula, Create from Selection, Defined Names, Trace Precedents, Trace Dependents, Remove Arrows, Show Formulas, Error Checking, Evaluate Formula, Formula Auditing

Path: \\nas-vdd\public\vivo-drug-delivery\gastro-plus\Acetazolamide\data\

Drug	Species	Study n°	Adm	eatme	Food	Dose	DF	Release	DS salt/ polymorph	Cp Mean	Indi
Acetazolamide								x		x	
Acetazolamide	Human	Straughn1982	po			250 solution	x	IR	Na/Batch A (Diamox, Led	x	
Acetazolamide						250 tablet	x	IR	Base/Batch B (Diamox, L	x	
						250 tablet	x	IR	Base/ Batch C (Warner L	x	
						250 tablet	x	IR	Base/ Batch D (Diamox, I	x	
Acetazolamide	Human	Yakatan1978	po	A		250 tablet	x	IR	Base/ Diamox	x	
				B		250 tablet	x	IR	Base/ Diamox	x	
				C		250 tablet	x	IR	Base/ Diamox	x	
				D		250 tablet	x	IR	Base/ Diamox	x	
				E		250 tablet	x	IR	Base/ Diamox	x	



The taps in the Excel sheet:

First Page	Disclaimer
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Overview	A list of study arms hyperlinked (X) to the mean Cp, Ind. Cp, dosage form used in study arm, dissolution of dosage form and properties of the drug (compound, PK) and physiology
Mean Cp_PK	Mean plasma drug concentration – time profile
Ind Cp_PK	Individual plasma drug concentration – time profile (for one or more subjects)
Dosage form	Dosage form used in the study arm and its properties like drug substance particle size, composition,...
Compound	Properties of the drug substance like solubilities, Log P, pKa, Papp, ...
Physiology	for simulation software to store which physiological model has been used
PK	Pharmacokinetic properties of the drug substance like first pass, clearance, Fa, metabolic enzymes, transporters,...
Dissolution	Dissolution data of the drug product used in the study arm
G-plus-results	If Gastro plus is used the results of the simulation can be stored
Notes	For comments
User manual	Hyperlink to user manual
#4Drugs	
Ref	List of references to all data stored in the sheet

Metoprolol data sheet

This data sheet comprises of 35 scientific articles. An overview on animal and human trials using several dosageforms and investigating food effect, transports, metabolism and the like is given in the following table and on tab #4Drugs in the file. The referenes to articles in the data sheet using an abbreviation like Söderlind2015. At the end of the tab list you find the abbreviation and the full citation and open access articles are marked.

Adm.	Dosage Form	Release	Gut segment	Physiology	Human	Dose mg	Dog	Dose mg	Rat	Dose mg	Dissol.	Dose mg	Enzym metab.	Dose mg	Transporter	Dose mg	Individual Cp	Dose mg	Food	Dose mg
iv	Solution	IR			Regardh1980	10	Borg1975	6,75	Ni2006											
po	Solution	IR	all		Söderlind2015	50	Borg1975	27	Ni2006		Söderlind2015				Dudley2000		Söderlind2015			
					Regardh1974	5														
			jejunum		Nyberg2007	25														
			ileum		Nyberg2007	25														
			colon		Nyberg2007	25	Kerckhof2014	35	Masaoka2006											
				fast metabolizer	Eddington1998	50					Eddington1998									
po	Suspension	IR	all																	
po	Tablet	IR	all		Grainiger1985	100	Löbenberg2005		Masaoka2006											
		IR	all		Al-Saidon2004	100					Al-Saidon2004									
	OROS	MR	all		Grainiger1985	19/285			N/A				Stout2013				Söderlind2015			
					Lecaillon1985	19/190													Lecaillon1985	
	Tablet	MR	all		Sandberg1988	200	Albin1993	200	N/A		Albin1993									
		MR	all				Löbenberg2005	100										Albin1993		
	Tablet	MR fast	all	fast metabolizer	Eddington1998	100			N/A		Eddington1998									
		MR med.	all	fast metabolizer	Eddington1998	100					Eddington1998									
		MR slow	all	fast metabolizer	Eddington1998	100					Eddington1998									
	Capsule	MR pulse	all				Löbenberg2005	100	N/A											
		IR (pure DS)	all				Löbenberg2005	100												



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Vivo Drug Delivery GmbH
Erwinstr. 21
79102 Freiburg
Germany

Disclosure: