pharmrep – A LaTeX package for Medical Reports*

Barbara Bredner† Barbara Jentges‡ Martin Sievers§

Released 2016/01/12

Abstract

The class PharmRep packages provides a set of tools for authors of submission-relevant documents in a consistent way. The package has an extended set of configuration options to make it possible to .....

The class pharmrep helps users to write standardised scientific pdf documents which have to be sent (electronically) to authorities. The class setups a layout (page layout, fonts etc.) and different properties of the resulting output file (bookmarks, hyperlinks, tagging, fast web view etc.) to match given requirements. In addition a template can be used as a starting point for new documents.

1 Introduction and Scope

¡hier weitere Hintergrundinformationen einfgen, z.B. strukturierte Dokumente / bookmarks in PDFs; ICH M4R3; eCTD Spec; FDA-PDF-Spec¿ The current manual is structured and formatted according to a typical submission file that is planned to be included into an electronic dossier (either NeeS or eCTD) in portable document format (PDF). When creating a file by using LaTex, the manual should be read in connection with the respective LaTex-Template. If any specific formatting or style settings are required in the document in question (e.g. the need to create a table) the correct LaTex settings can be copy-pasted from the manual directly into this document. The manual will be amended and updated on a regular basis.

1.1 Formal Requirements for Submission-relevant Documents

Minimum general requirements for layout and formatting of submission-relevant documents that form part of the Common Technical Document (CTD) are given in the internationally harmonized document ICH M4 (R3) ¡Referenz einfgen¿ and the Q-A document:

1.2 Basic Requirements for Layout and Format

- Text and tables should be prepared using margins that allow the document to be printed on both A4 paper (E.U. and Japan) and 8.5 x 11 paper (U.S.)
- The left-hand margin should be sufficiently large that information is not obscured by the method of binding
- Font sizes for text and tables should be of a style and size that are large enough to be easily legible, even after photocopying. Times New Roman, 12-point font, is recommended for narrative text
- Every page should be numbered be starting at page one, except for individual literature references, where the existing journal page numbering is considered sufficient.

*This file describes version v2.0BETA, last revised 2016/01/12.

†Email: bredner@bb-sbl.de

‡Email: barbara.jentges@phact.ch

§E-Mail: martin.sievers@schoenerpublizieren.de

- Acronyms and abbreviations should be defined the first time they are used in each module.
- References should be cited in accordance with the current edition of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, International Committee of Medical Journal Editors (ICMJE)"
- each page of a document should include a unique header or footer that briefly identifies its subject matter, an abbreviation of the full section number and title can be used. The applicant is free to put his logo on top of the CTD. However, logos are not acceptable in CTD sections' titles.
- In order to avoid 5th, 6th etc. level subheading numbering (e.g. 2.6.6.3.2.1) within a document, the applicant can use a shortened numbering string. In this case, the document number and the name (e.g. 2.6.6 Toxicology Written Summary) should appear in page headers or footers and then section numbering within the document can be used, for example, 1, 1.1, 2, 3, 3.1, 3.2 etc. Use of the full numbering string (e.g. 2.6.6.3.2.1) is also considered acceptable.

1.3 Additional Settings that need to be considered for Portable Document Files

With the eCTD becoming the mandatory format of a dossier in the major industrial regions of the world, specific settings in the PDF documents as addressed in the ICH eCTD specification ¡include reference here¿ need to be considered in the submission-relevant documents. Additional regional settings may need to be considered as addressed in the region-specific Module 1 eCTD specifications.

2 Short Description about the Features of PharmRep

PharmRep is a 'ready-to-use' package for creating eCTD-compliant PDFs with high-level layout that is harmonized all over the submission files created with PharmRep. PharmRep uses the format settings as required for submission relevant documents with view to becoming eCTD-PDFs. Once compiled, only minor PDF-settings need to be completed in ADOBE (e.g. 'initial view, etc as addressed in chapter xx of the present document). The PharmRep package was especially developed for Latex beginners. It has been developed with view to optimizing the creation of submission-relevant documents in a time-efficient way with focus on content without loosing time

3 Installation

¡include general description about the package here¿.

3.1 Specific Packages included into PharmRep

The PharmRep package includes a number of other packages that facilitate edit scientific texts and guarantee a level of harmonization throughout the complete submission-relevant documentation.

3.1.1 siunitx – A Comprehensive (SI) Units Package

package `siunitx`

"Physical quantities have both numbers and units, and each physical quantity should be expressed as the product of a number and a unit. Typesetting physical quantities requires care to ensure that the combined mathematical meaning of the number-unit combination is clear. In particular, the SI units system (International System of Units) lays down a consistent set of units with rules on how these are to be used. However, different countries and publishers have differing conventions on the exact appearance of numbers (and units). The 'siunitx' package provides a set of tools for authors to typeset

quantities in a consistent way.The package has an extended set of configuration options which make it possible to follow varying typographic conventions with the same input syntax. The package includes automated processing of numbers and units, and the ability to control tabular alignment of numbers."

In addition, numbers are automatically formatted.

Example:

3.1.2 hyperxmp - Creating PDF 1b Format

¡Hier kurze Beschreibung zum Package einfgen¿.

4 Instructions for the Users of PharmRep Package

¡hier kurze allgemeine Erluterung einfgen; inbesondere der Hinweis, dass das Package fr LaTex-Anfnger gedacht ist, die ohne erfahrene LaTex-User zu sein, mit Hilfe des Packages hochwertig formatierte Zulassungsdokumente erzeugen wollen. In diesem Sinne mgen Hinweise aus dem Kapitel Instructrions for the Users of PharmRep - insbesondere auch die im Anhang bereitgestellte short list of comman commands berflssig erscheinen.

4.1 Section Levels and Section Numbering

Numbering of sections, subsections and subsubsections is added automatically during the compilation.

The numbering is indicated by the command 'section' for title level 1, 'subsection' for level 2, 'subsubsection' for level 3, and 'paragraph' for level 4. Please note: Only the 'section', 'subsection',... titles will be automatically converted to bookmarks during the PDF creation. For paragraphs, text is usually in the same layout as the title, but a paragraph is not numbered. The unnumbered 'paragraph' levels will not be converted to bookmarks during the PDF creation.

- Level 1 Title 1: sections: `\section{Title}`
- Subtitle 1.1 level 2 - Sub-Title 1.1: subsections: `\subsection{Title}`
- Section level 3 - Subsub-Title 1.1.1: subsubsections: `\subsubsection{Title}`
- Section level 4 - ParagraphTitle : paragraph: `\paragraph{Title}`
- Section level 5 - Sub-ParagraphTitle : subparagraph: `\subparagraph{Title}`

4.2 Page Orientation: Portrait and Landscape

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper.

4.2.1 Landscape

`\landscapeformat`

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper.

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper.

4.2.2 Back to Portrait

`\portraitformat`

Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Etiam lobortis facilisis sem. Nullam nec mi et neque pharetra sollicitudin. Praesent imperdiet mi nec ante. Donec ullamcorper, felis non sodales commodo, lectus velit ultrices augue, a dignissim nibh lectus placerat pede. Vivamus nunc nunc, molestie ut, ultricies vel, semper in, velit. Ut porttitor. Praesent in sapien. Lorem ipsum dolor sit amet, consectetuer adipiscing elit. Duis fringilla tristique neque. Sed interdum libero ut metus. Pellentesque placerat. Nam rutrum augue a leo. Morbi sed elit sit amet ante lobortis sollicitudin. Praesent blandit blandit mauris. Praesent lectus tellus, aliquet aliquam, luctus a, egestas a, turpis. Mauris lacinia lorem sit amet ipsum. Nunc quis urna dictum turpis accumsan semper.

4.3 Common Formatting Functions

4.3.1 Paragraphs and Line Breaks

- new paragraph: insert 1 or more blank line(s) (more than 1 will be ignored during the compilation
- new line or linebreak: `\newline`

4.3.2 Hyphenation

- separate words: 1 or more blanks (more than 1 will be ignored during the compilation)
- no break between two words: `~`
- enable hyphenation at specific locations of a word: `\-` (e.g. `reac\-tion`) Usually not necessary since hyphenation is already enabled by the loaded packages

4.3.3 Quotation Marks

- quotation mark ("double") ``` ``double'' ```
- quotation mark ('single')Fett un `` `single' ``

4.3.4 Font Style

- **bold** text: `\textbf{text}`
- *italic* text: `\textit{text}`
- small text: `{\small small text}`
- footnotesize text: `{\footnotesize footnotesize text}`
- tiny text: `{\tiny tiny text}` (usually too small)Inhalt...

4.3.5 Special Characters

In most cases a backslash (\) directly in front of a special character will work, e.g.

- % (percent): `\%`
- & (ampersand): `\&`

4.4 Annotations in a tex-file

Annotations in the tex-file may be used for explanatory purposes – or as a reminder that specific information is still missing and needs to be included into the document. Annotations only appear in the tex-file, the are not converted into the PDF.

Symbol for annotations in the tex-file is `%` (everything in a line after a % is ignored)

4.5 Tables

In LaTeX, 'table' is the name for a floating object (see p.**??**), whereas 'tabular' provides the environment for tables. In a 'tabularx' environment, the table width can be set (e.g. to textwidth) and page breaks are enabled [1]. Creating tables with LaTex require some experience. In the following, basic instructions on how to create tables are described. Alternatively, tables can be created in MS Excel and converted into LaTex-tables by installing the Excel-add-in Excel2Latex. Tables can also be included as objects.

4.5.1 Caption of Tables

Every table included into a document requires a brief, informative title ('caption') that describes its contents in nonsentence format ¡Let.Ref. ACS Style Guide¿. Tables are numbered sequentially with arabic numerals. Please make sure that every table needs to be discussed within the text, whereas the tables should be discussed sequentially, so that Table 1 is discussed before Table 2, Table 2 before Table 3, and so on ¡ACS Style Guide¿.

A table caption should be placed at the beginning of the table.

Please note that the word "Table" is only capitalized when it is followed by the table number - and in the beginning of the table caption that starts with Table, followed by its numeral.

Each table with a caption is automatically listed in the list of tables.

4.5.2 General layout options for tables

```
The instructions as given below create a basic table with two columns and three row. In general
are separated by the symbol \& (ampersand) and rows are ended by using the command
\textbackslash\textbackslash (double backslash). The column format is defined at the beginning o
table, e.g. \verb|{rr}| for two right-aligned columns (more options see \autopageref{tab:TabGenL

\captionof{table}{first tabular}\label{tab:FirstTab}
\begin{tabular}{rr}
a & 1 \\
b & 2 \\
c & 3 \\
\end{tabular}
```

As an example, the instructions as given above create **??** with two columns and three rows.

a	1
b	2
c	3

The layout of a table can be modified with a huge number of commands and tools. The major characteristics of a table are the number and type of columns and lines. **??** shows some of the options using the following code:

```
\begin{minipage}{\linewidth}%
\captionof{table}[xyz]{Some Options for tables}\label{tab:TabGenLayout}
\begin{tabularx}{\linewidth}{rlcp{10mm}S}\toprule
\textbf{Col 1} & \textbf{ Col 2} & \textbf{Col 3} &
\textbf{Col 4} & \textbf{ Col 5} \\ \cmidrule{1-4}
right & left & centered & fixed width &
\text{justified at decimal separator} \\ \midrule
& & & & 12.97 \\
& & & & 0.4 \\
& & & & 10000.3 \\ \bottomrule
\end{tabularx}
\end{minipage}%
```

[1] for PharmRep the package `ltablex` is used

that results in the following PDF-printout:

Col 1 `r`	Col 2 `l`	Col 3 `c`	Col 4 `p`	Col 5 `S`
right	left	centered	fixed width	justified at decimal separator
				12.97
				0.4
				10 000.3

4.5.3 General Commands for Table Layout

In the follwing, general commands for typical table layout is given.

Column without and with Linebreak

Column formats

without linebreak

`r` aligned right

`l` aligned left

`c` centered

`S` justified at decimal separator

with linebreak

`p<width>` parbox ('paragraph box') with predefined width

`X` only in `tabularx` environment: parbox with flexible width to meet the predefined tablewidth (e.g. `{\linewidth}`)

Header and footer (example see p.??ff.)

`\endhead` [optional argument] table content before this command will be used for the header on every page of a table

`\endfoot` [optional argument] table content between `\endhead` and `\endfoot` will be used for the footer on every page of a table. The footer is defined at the beginning of a table!

Lines Use horizontal lines rarely and avoid vertical lines always. Reasons and examples see e.g. http://ctan.org/pkg/booktabs

horizontal lines (avoid whenever possible)

`\toprule` first horizontal line at the top of the table

`\midrule` horizontal line within the table

`\cmidrule{a-b}` horizontal line starting at column `a` and ending at column `b`

`\cmidrule(lr){a-b}` horizontal line starting at column `a` and ending at column `b` shortened left (`l`) and right (`r`)

`\bottomrule` last horizontal line at the end of the table

vertical lines Vertical lines in tables should be avoided in general. (They are easy to use in LaTeX, but a huge challenge regarding the readability and usability of any document.)

4.5.4 Long Table - Portrait Format

Table generated by Excel2LaTeX from sheet 'Tabelle2'

Col 1	**Col 2**	**Col 3**	**Col 4 with very long header using some more superfluous additional text**
the	1	a	more and more text
quick	2	b	some more text
brown	3	c	some more text (in addition)
fox	4	d	more text
jumps	5	e	more text
over	6	f	more text
the	7	g	more text
lazy	8	h	more text
dog	9	i	more text
.	10	j	more text
the	11	k	more and more text
quick	12	l	some more text
brown	13	m	some more text (in addition)
fox	14	n	more text
jumps	15	o	more text
over	16	p	more text
the	17	q	more text
lazy	18	r	more text
dog	19	s	more text
.	20	t	more text
the	21	u	more and more text
quick	22	v	some more text
brown	23	w	some more text (in addition)
fox	24	x	more text
jumps	25	y	more text
over	26	z	more text
the	27	a	more text
lazy	28	b	more text
dog	29	c	more text
.	30	d	more text
Foot 1	*Foot 2*	*Foot 3*	*Foot 4*

4.5.5 Long Table - Landscape Format

Table generated by Excel2LaTeX from sheet 'Tabelle2'

Col 1	Col 2	Col 3	Col 4 with very long header using some more superfluous additional text and extra words to stretch the tabular width to textwidth
the	21	u	more and more text
quick	2	b	some more text
brown	3	c	some more text (in addition)
fox	4	d	more text
jumps	5	e	more text
over	6	f	more text
the	7	g	more text
lazy	8	h	more text
dog	9	i	more text
.	10	j	more text
the	11	k	more and more text
quick	12	l	some more text
brown	13	m	some more text (in addition)
fox	14	n	more text
jumps	15	o	more text
over	16	p	more text
the	17	q	more text
lazy	18	r	more text
dog	19	s	more text
.	20	t	more text
the	21	u	more and more text
quick	22	v	some more text
brown	23	w	some more text (in addition)
fox	24	x	more text
jumps	25	y	more text
over	26	z	more text
the	27	a	more text
lazy	28	b	more text
dog	29	c	more text
.	30	d	more text
Foot 1	Foot 2	Foot 3	Foot 4

4.5.6 Table Footnotes

¡include instructions here¿

4.5.7 Positioning of Tables - Floating versus Manually

In LaTex, tables and figures can basically be positioned in two different ways: They are included manually and appear exactly at this place (like in word processing software, e.g. Microsoft Word) or they can be included as a floating object.

Floating Table Floating objects are included where they are in the code if there is enough space for a eye-friendly layout. In case the place is too small floating objects are positioned automatically near the original insertion. 'Near' can be on the same page, the next page or farer away depending on the amount of text and/or other floating objects. Floating provides a more professional layout and should be used if possible to increase the readability.

A	B	C
1	has	6
2	a yellow	4
3	car	2

Table 3: Table as a floating object

Code for table **??** (page **??**)

```
\begin{table}[hbpt]
\begin{tabular}{ccc}\toprule
A & B & C \\\midrule
1 & has & 6 \\
2 & a yellow & 4 \\
3 & car & 2 \\\bottomrule
\end{tabular}
\caption[short caption table]{Table as a floating object}%
\label{tab:tableFloatingObject}
\end{table}
```

printed in list of tables as "**??** short caption table" . The optional short title `[short caption table]` in squared brackets is used for LOT. If no short title is given the whole caption is printed in the list of tables.

referred to by using:
`table \ref{tab:tableFloatingObject}` (result: table **??**) or
`\autoref{tab:tableFloatingObject}` (result: **??**)

page number:
`page \pageref{tab:tableFloatingObject}` (result: page **??**) or
`\autopageref{tab:tableFloatingObject}` (result: page **??**)

4.5.8 In-Text References to Tables

In general, the instruction `\label{key}` is used for names and references of tables, figures and everything else (e.g. sections, paragraphs).

If a table or figure is included directly at a specific place a caption is included by
`\captionof{figure}[short]{title}\label{fig:figurelabel}` or
`\captionof{figure}[short]{title}\label{tab:tablabel}`

For floating tables or figures in a floating environment `\begin{table}...\end{table}` (see **??**) or `\begin{figure}...\end{figure}` (see **??**):

`\caption[short]{title}\label{fig:figurelabel}` or
`\caption[short]{title}\label{tab:tablabel}`

`[short]`: optional 'shortcaption' being printed in the list of figures or list of tables, respectively, and 'title' used for the figure or table itself. The label is used for reference purposes, e.g.

`\ref{fig:figurelabel}` or `\ref{tab:tablabel}`

Label names do not work with special characters (except ':') or blanks.

4.5.9 MS Excel Add-in 'Excel2LaTeX'

Excel spreadsheets can be converted into a LaTeX tabular structure manually or using third party software, e.g. Excel2Latex (available on http://www.ctan.org/pkg/excel2latex).

Excel2Latex works for Windows, Mac OS X and Excel 2000 up to Excel 2010. For Excel 2007 and Excel 2010 the add-in has to be activated within the options menu in Excel. After a restart of Excel and the activation of 'Excel2Latex' as a secure macro the add-in excel2latex is available in the ribbon 'Add-In'. ¡diese Angaben mssen noch auf Korrektheit geprft werden; ggfs. hier keine weiteren Angaben, sondern nur Referenz auf das package, wo in der readme alle weiteren Details beschrieben sind¿.

Instead of converting Excel or Word tables (and other parts) into LaTeXthe part could be included using `\includegraphics` (see p.**??**). ¡hier: Hinweis auf Vorgehensweise, wenn PDF/A-1b gefordert ist¿.

4.6 Figures

Figures are not directly inserted into the tex file, but are created as separate files which are included during the compilation. For PDF generation, file formats png, jpg or pdf are allowed, all others will produce an error.The figure-files need to be stored in the same folder as the tex file (alternatively, the complete file-path has to be provided).

4.6.1 Caption of Figures

Every figure included into a document requires a brief, informative title ('caption') that describes its contents in nonsentence format ¡Let.Ref. ACS Style Guide¿. Figures are numbered sequentially with arabic numerals. Please make sure that every figure needs to be discussed within the text, whereas the figures should be discussed sequentially, so that Figure 1 is discussed before Figure 2, Figure 2 before Figure 3, and so on ¡ACS Style Guide¿.

A fiugre caption should be placed below the figure.

Please note that the word "Figure" is only capitalized when it is followed by the figure number - and in the beginning of the figure caption that starts with Figure, followed by its numeral.

Each figure with a caption is automatically listed in the list of figures.

4.6.2 Positioning of Figures – Floating versus Manual

Figure 1: Figure as a floating object. CTAN lion drawing by Duane Bibby; thanks to www.ctan.org

Automatic Insertion of Figures ('Floating Figures') Code for figure **??** (page **??**)

```
\begin{figure}[hbpt]
\includegraphics[width=0.2\linewidth]{ctanlion}
\caption[short caption figure]{Figure as a floating object. CTAN lion drawing by Duane Bibby; th
\label{fig:figureFloatingObject}
\end{figure}
```

printed in list of tables as "**??** short caption figure" . The optional short title in squared brackets `[short caption figure]` is used for LOF. If no short title is given the complete caption is printed in the list of figures.

referred to by using:
`figure \ref{fig:figureFloatingObject}` (result: figure **??**) or
`\autoref{fig:figureFloatingObject}` (result: **??**)

page number:
`page \pageref{fig:figureFloatingObject}` (result: page **??**) or
`\autopageref{fig:figureFloatingObject}` (result: page **??**)

Manual Insertion of Figures

Figure 2: example of a manually inserted figure

Code for figure ?? (page ??)

```
\begin{minipage}[t]{\linewidth}%
\includegraphics[width=0.2\linewidth]{ctanlion}
\captionof{figure}{example of a manually inserted figure}%
{\label{fig:figureManuallyInserted}}
\end{minipage}%
```

Note: It is recommended to end the `\begin{minipage}` and `\end{minipage}` line with a percent sign (%) to avoid spurious blanks.

4.6.3 In-Text References to Figures

`\label{key}` is used for names and references of tables, figures and everything else (e.g. sections, paragraphs).

If a table or figure is included directly at a specific place a caption is included by

`\captionof{figure}[short]{title}\label{fig:figurelabel}` or
`\captionof{figure}[short]{title}\label{tab:tablabel}`

A table caption should be placed at the beginning of the table whereas a figure caption is usually beneath the figure.

For floating tables or figures in a floating environment `\begin{table}...\end{table}` (see ??) or `\begin{figure}...\end{figure}` (see ??):

`\caption[short]{title}\label{fig:figurelabel}` or
`\caption[short]{title}\label{tab:tablabel}`

`[short]`: optional 'shortcaption' being printed in the list of figures or list of tables, respectively, and 'title' used for the figure or table itself. The label is used for reference purposes, e.g.

`\ref{fig:figurelabel}` or `\ref{tab:tablabel}`

Label names do not work with special characters (except ':') or blanks.

4.7 Footnotes in Text

Footnotes are set by including `\footnote{text}` directly behind the word, where the footnote should be added. No space should be placed between word and instruction. THe footnote will be automatically numbered and placed at the end of the page.

4.8 Lists and Enumeration Items

Lists can be described with different enumeration items. Generally, bullet points, numbered and description are used.

Reference of lists (only useful for pagenumber reference since lists do not have a number/internal counter): Define unique label using
`\label{list:listdescription}`
Label names do not work with special characters (except ':') or blanks.

4.8.1 Bullet Point Lists

- item 1
- item 2

Code for bullet point list:

```
\begin{itemize}
\item item 1
\item item 2
\end{itemize}
```

4.8.2 Numbered List

1. item 1
2. item 2

Code for numbered list:

```
\begin{enumerate}
\item item 1
\item item 2
\end{enumerate}
```

4.8.3 Description List

description label 1 item 1

description label 2 item 2

Code for description list:

```
\begin{description}
\item[description label 1] item 1
\item[description label 2] item 2
\end{description}
```

4.8.4 List in a List

Lists can be combined arbitrarily and levels are automatically formatted, e.g. bullet point and numbered list:

- item 1
  1. subitem 1
  2. subitem 2
     - subsubitem 1
     - subsubitem 2
  3. subitem 3
- item 2

Code for the combined list:

```
\begin{itemize}
\item item 1
\begin{enumerate}
\item subitem 1
\item subitem 2
\begin{itemize}
\item subsubitem 1
\item subsubitem 2
\end{itemize}
\item subitem 3
\end{enumerate}
\item item 2
\end{itemize}
```

4.9 Splitting Large Documents

Large documents can be split into several `*.tex` files. Special characters should be avoided in the PDF file name!. For an example see below:

- three files: `master.tex`, `part1.tex` and `part2.tex`
- `master.tex`: usual LaTeXfile with definition of styles, commands, etc.
- `part1.tex`, `part2.tex`: two files with content which is copy-pasted into `master.tex` using `\input`

Typical commands for splitting documents are the following: ¡Kommandozeilen sind nicht klar, sollten besser erlutert werden¿.

```
%%% master.tex file:

% preamble, styles, etc.
[...]

\begin{document}
some text
\input{part1.tex}
more text
\input{part2.tex}
some more text
\end{document}
```

4.10 Including Figures from external PDFs into the LaTeX File

Pictures, figures, tables and any other objects that are provided in PDF-files can be included into LaTeX by using the command `\includegraphics[`⟨*options*⟩`]{`⟨*filename*⟩`}`. Special characters and spaces should be avoided in the PDF file name!

Example

- The figure of the PDF-file `pdfexample.pdf` is planned to be included into the file `master.tex`
- `master.tex`: usual LaTeXfile with definition of styles, commands, etc.
- `pdfexample.pdf`: pdf file

```
%% master.tex file:

 preamble, styles, etc.
         [...]

 \begin{document}
   some text
   \begin{minipage}{\linewidth}%
      \captionof{figure}{example including pdf}
      \includegraphics[page=1, trim=60mm 170mm 90mm 40mm, clip]{pdfexample.pdf}
   \end{minipage}%
   more text
 \end{document}
```

4.10.1 Clipping of PDF Page

Clipping of PDF pages is done via `trim=<left> <top> <right> <bottom>` (with arbitrary units, e.g. mm, pt) and (mandatory!) `clip`.

¡nicht klar, was hier passiert¿.

¡NOTE: if a PDF/A-1b document is required, the external PDF needs to be PDF/A-1b compliant itself. This can be created from other files (e.g. MS WORD, MS VISIO,etc) by using the 'print as' function and choosing in the PDF-properties the setting to create a PDF/A-1b-compatible PDF¿.

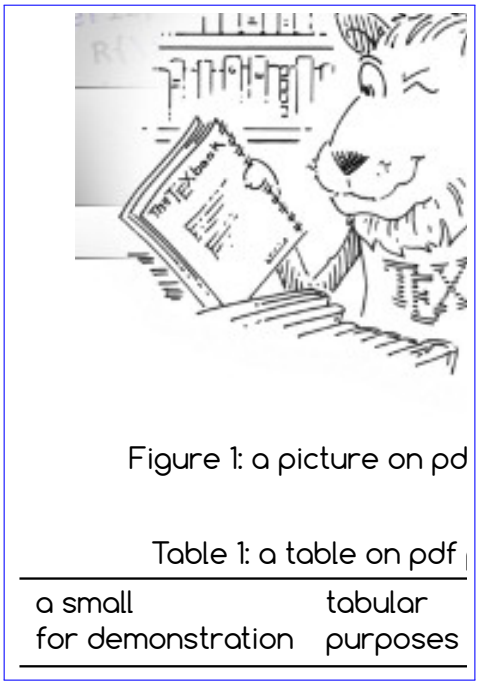


Figure 1: a picture on pd

Table 1: a table on pdf

a small	tabular
for demonstration	purposes

Figure 3: example including pdf (colored box for demonstration purposes)

4.11 Commenting in TEX files

A practical tool during the creation of a document is the inclusion of comments into the tex-files. This may serve as reminders, remaining action items or comments required during document review.

```
\todo{a comment in the margin}
\todo[inline, color=green]{a green inline comment}
```

If at least one `\todo`-command is present in the text the list of todonotes will be printed using `\listoftodos`.

4.12 Bibliography with JabRef and Citations

4.12.1 Extenal Bibliography with JabRef

External sources (books, papers, websites, etc.) are stored in a separate file `literatur.bib`. bib-files can be created using JabRef (jabref.sourceforge.net/), online and versions for local installation available). Example `literatur.bib`:

```
...
@ELECTRONIC{Q1E,%
   author = {{International Conference on Harmonization}},%
   shorthand = {{International Conference on Harmonization (2004)}},%
   month = {6},%
   year = {2004},%
   title = {Guidance for Industry: Q1E Evaluation of Stability Data.},%
   url = {http://www.fda.gov/RegulatoryInformation/Guidances/ucm128092.htm},%
   urldate = {2014-06-28},%
   owner = {Jane Doe},%
}%
```

```
@BOOK{Krishnamoorthy,%
    title = {Statistical Tolerance Regions},%
    shorthand = {Statistical Tolerance Regions (2009)}%
    publisher = {Wiley},%
    year = {2009},%
    author = {Kalimuthu Krishnamoorthy and Thomas Mathew},%
    isbn = {9780470380260},%
    owner = {Jane Doe},%
    timestamp = {2014-05-13},%
    totalpages = {461}%
}
...
```

The bibliography entries are sorted during the compilation of the bibliography. This has to be done separately and in addition to the text compilation (e.g. in TeXstudio key `F11` for bibliography and key `F6` for text compilation). Tool for generating BibTeX-entries, e.g. http://lead.to/amazon/en/ (uses Amazon data base) and http://literatur-generator.de/ (uses google). It doesn't matter if the bib-file contains more bibliography entries than the tex-file; only cited sources are listed in the bibliography.

Test: Amazon.com

Note: The configuration for TeXstudio has to be changed that biber is used for the bibliography (see figure **??**).

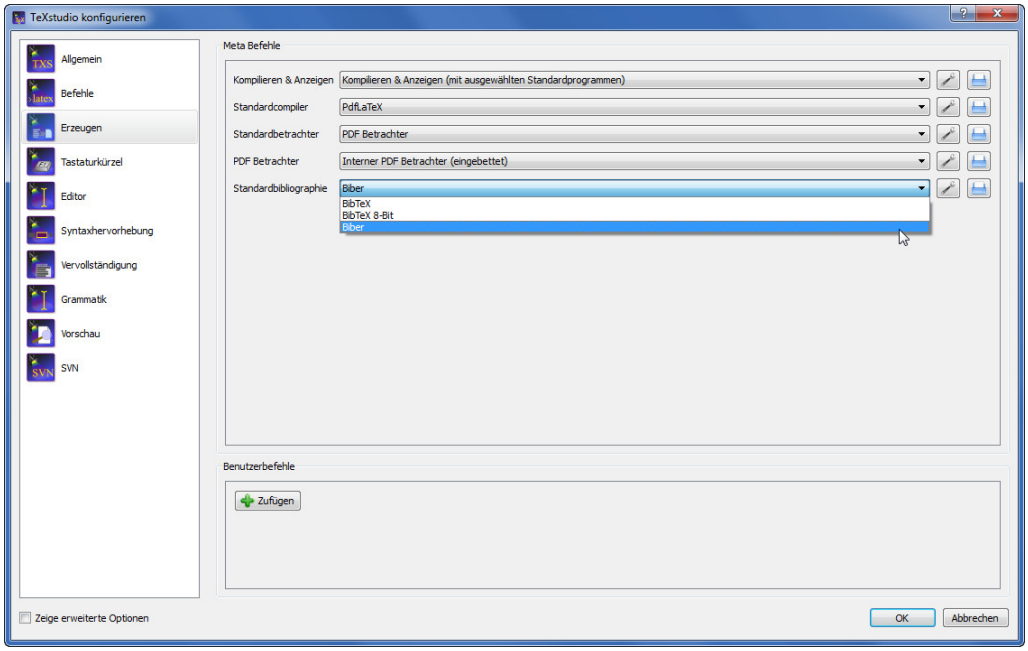


Figure 4: Configuration for biber in TeXstudio

4.12.2 Citations

All citations use the unique key for a bibliographical entry, e.g. `Q1E` or `Krishnamoorthy`.
using `\cite{Q1E}`: [International Conference on Harmonization (2004)]
using `\cite[123]{Q1E}`: [International Conference on Harmonization (2004), p. 123]
using `\cite[123--125]{Q1E}`: [International Conference on Harmonization (2004), pp. 123–125]
using `\autocite{Q1E}`: [International Conference on Harmonization (2004)]
using `text\footcite{Q1E}`: text[2]
using `\fullcite{Q1E}`: International Conference on Harmonization. *Guidance for Industry: Q1E Evaluation of Stability Data.* June 2004. URL: `http://www.fda.`

[2] International Conference on Harmonization (2004).

gov / downloads / Drugs / GuidanceComplianceRegulatoryInformation / Guidances / UCM073380.pdf (visited on 06/28/2014)
Print all bibliographic entries used in the text (indepedent of the entries in the bibliography file) with a numbered section: `\printbibliography]`

References

[International Conference on Harmonization (2004)] International Conference on Harmonization. *Guidance for Industry: Q1E Evaluation of Stability Data.* June 2004. URL: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM073380.pdf (visited on 06/28/2014).

4.12.3 In-text Use of Universal Resource Locators (URLs)

A Universal Resource Locator URL (which is the path to a certain file on the World Wide Web) can be included directly into the text on two different ways:

- by including the instruction `\url{URL}` Inhalt...
- with differnt descriptive text or url: `\href{URL}{text}`

Examples: `\url{http://ctan.org}` http://ctan.org
`\href{http://ctan.org}{ctan.org}` ctan.org

4.13 Creating a 'List Abbreviations, Acronmys and Symbols'

Abbreviations, acronyms and symbols that are used within the text need to be predefined in the preamble ¡where exactly?¿, e.g.

```
\newglossaryentry{abb:eCTD}
    {name={eCTD},
    description={electronic Common Technical Document}}
```

After an abbreviation has been defined in the preamble, it can be used in the following text, e.g. using `\gls{abb:eCTD}`: eCTD
using `\gls{abb:CTD}`: CTD
using `\gls{abb:ICH}`: ICH
Used abbreviations, their explanation and page number(s) where they are used within the text are automatically listed if a glossary is printed:
`\printnoidxglossary[title={List of Abbreviations}]`

4.14 Setting intra-text Cross-References

Define unique label using
`\label{sec:secdescription}`
Label names do not work with special characters (except ':') or blanks.
Labels can be used everywhere (sections, paragraphs, figures, tables,...)

5 Handling Specific Issues

5.1 How to create PDF/A-1b Files

6 Organization of Different Types of Files used by LaTex in an eCTD File and Folder Structure

LaTeX uses a number of file types. For details, reference is made to relevant LaTeX publications, e.g. Frank Mittelbach, Michel Goossens, Der LaTeX Begleiter. Some basic

information about the different types of files, however, is required, in order to correctly organize these files when creating documents that are planned to be organized in an eCTD file-and folder structure.

¡hier: Auszug aus Tab. 1.1 von Mittelbach/Goossens einfgen¿.

With reference to different 'texwelt' discussions in this field,the question on how to handle the auxiliary files that are created when creating tex- and the corresponding PDF-files, shall be addressed in this subsection. In summary, and in order to enable a correct and smooth PDF creation, it can be concluded that the auxiliary files are recommended to be listed together with the tex-files in one and the same folder and or subfolder. For further information, please find the respective discussions listed below:
http://texwelt.de/wissen/fragen/2530/was-sind-hilfsdateien-und-wo-finde-ich-diese
http://texwelt.de/wissen/fragen/5501/wie-kann-ich-mit-latex-dateien-hilfsdateien-or
http://tex.stackexchange.com/a/11125 http://tex.stackexchange.com/a/24787

In this respect, it is recommended to created sub-folders for each CTD-related submission-file as given in Figure 1.

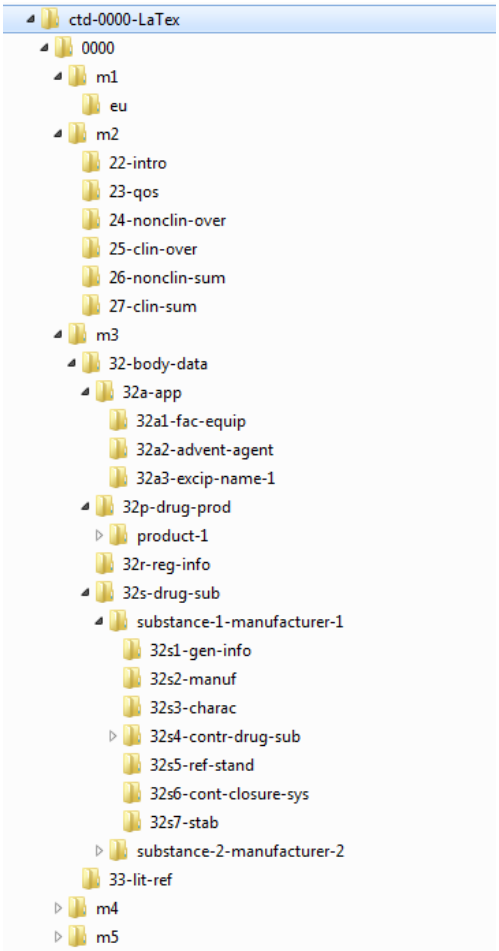
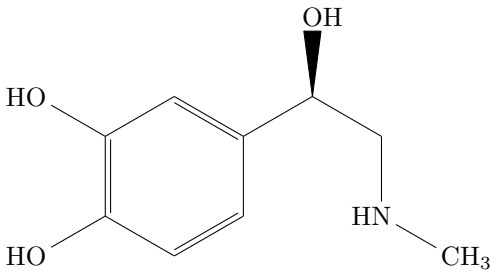


Figure 5: Organizing of LaTeX Files in an eCTD File and Folder Structure

7 Extra Packages which are recommended, but which are not included into PharmRep

7.1 Structural Formula of Chemicals with Package chemfig

To draw molecules and reaction schemes different packages can be used, e.g. with package ChemFig something like that:



7.2 Graphs and Plots with Package TikZ

One of the most powerful packages to create graphs and plots is TikZ which can be used for nearly every kind of graphical representation, e.g. flowcharts, mathematical graphs, 3D visualization, etc. See http://www.texample.net/tikz/examples/ for a gallery of examples.

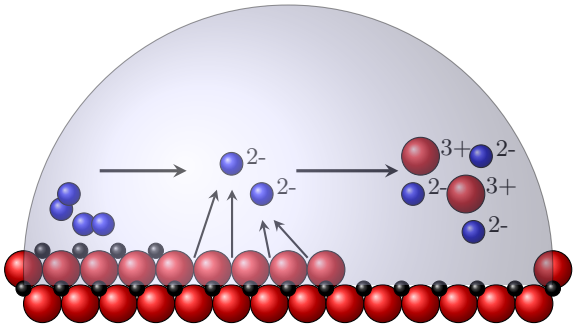


Figure 6: TikZ example graph rusting iron, http://www.texample.net/tikz/examples/rusting-iron/

8 Dealing with Typical Problems by using PharmRep

One typical problem that may occur when using Latex respectively the PharmRep package may occur, when the PDF that was successfully compiled remains opened when further editing the tex-file. With the PDF opened, the compilation process cannot be performed and the following error message apprears: MedRepStyle¡xx¿.tex: Fehler; Zeile 30: I can't write on file 'MedRepManual23.pdf' .. Once the PDF is closed, compilation can be performed without any problems.

9 User Feedback and Reporting Bugs

Feedback on PharmRep is always welcome and will help us in improving the package and correct any problems. ¡is there an 'official' chanel for reporting problems?

10 Thanks

We would like to express our particular thanks to Martin Sievers, who supported the development of the PharmRep with valuable input and tested the beta version, including identifying any incorrect output, bad documentation and spelling mistakes in the documentation. His specific focus was the support in solutions on how to create PDF/A-1b compatible files with the PharmRep package.

11 zu behebende Probleme

- Einbindung von externen Grafiken bzw. Tabellen macht Probleme, siehe Test-Page.pdf (in der Praxis: Einbindung von Plots, HPLC-Chromatogrammen, etc.)
- Excel2Latex bei umfangreichen Tabellen mit Text ber mehrere Zeilen ergibt Probleme

A Short List of Common Commands

Table generated by Excel2LaTeX from sheet 'Tabelle1'

Command	**Result**
\section{⟨*title*⟩}	starts a new section
\subsection{⟨*title*⟩}	starts a new subection
\subsubsection{⟨*title*⟩}	starts a new subsubsection
\paragraph{⟨*title*⟩}	starts a new paragraph
\label{⟨*key*⟩}	defines label (must be unique throughout document)
\ref{⟨*key*⟩}	references label
\autoref{⟨*key*⟩}	references label and type of reference
\pageref{⟨*key*⟩}	references pagenumber of label
\autopageref{⟨*key*⟩}	references pagenumber of label and type of reference
\textbf{⟨*text*⟩}	bold text
\textit{⟨*text*⟩}	italic text
\small{⟨*text*⟩}	small text
\footnotesize{⟨*text*⟩}	footnotesize text
\%	percent (%)
\&	ampersand (&)
\url{⟨*URL*⟩}	url
\href{⟨*URL*⟩}{⟨*text*⟩}	text instead of url
\landscape	page orientation landscape
\portrait	page orientation portrait
\captionof{table}{⟨*title*⟩}	caption of table
\captionof{figure}{⟨*title*⟩}	caption of figure
\begin{tabular}	simple table
\begin{tabularx}	table with automatic width and optional pagebreaks
\begin{figure}	figure environment (floating)
\includegraphics{⟨*filename*⟩}	include 'figure' (format png, jpg or pdf)
\begin{itemize}	bullet point list
\begin{enumerate}	numbered list
\item text	item in list
\begin{description}	description list
\item[label] text	item with label (description list only)
\input{⟨*filename.tex*⟩}	copy-paste contents of tex-file
\todo{⟨*text*⟩}	comment or todo
\cite{⟨*bibkey*⟩}	citation of source stored with 'bibkey' (in 'filename'.bib)
\newglossaryentry{⟨*glskey*⟩}{⟨...⟩}{⟨...⟩}	define new glossary entry (at the beginning of the TEX file)
\gls{⟨*glskey*⟩}	use abbreviation stored with 'glskey'

B Implementation

```
1 ⟨*class⟩
2 \RequirePackage{kvoptions}
3 \SetupKeyvalOptions {
4    family  = pharmrep,%
5    prefix  = pharmrep@,%
6    setkeys = \kvsetkeys,%
7 }
8
9 \DeclareStringOption[utf8]{inputenc}
10 \DeclareStringOption[sRGB_IEC61966-2-1_black_scaled.icc]{colorprofile}
11 \DeclareBoolOption[true]{pdfa}
12 \DeclareBoolOption[false]{letter}
13 \DeclareVoidOption{US}{\pharmrep@lettertrue}
14 \ProcessKeyvalOptions*\relax
15 \PassOptionsToPackage{\pharmrep@inputenc}{inputenc}
```

```
\RequirePackage{etoolbox}
```
For pdf 1.4 output and xml metadata
```
\RequirePackage{pdf14}
\input glyphtounicode.tex
\input glyphtounicode-cmr.tex
\pdfgentounicode=1
\pdfobjcompresslevel=0
\pdfinclusioncopyfonts=1
```
Load KOMA documentclass scrartcl with required options
```
\ifpharmrep@letter
   \PassOptionsToPackage{paper=letter,pagesize}{typearea}
\fi%
\LoadClass[parskip=half,fontsize=12bp,%
      bibliography=totoc,listof=totoc,%
      numbers=noendperiod]{scrartcl}
```
pdf 1b format
```
\RequirePackage{hyperxmp}
```
Input encoding
```
\RequirePackage{inputenc}
```
Font encoding
```
\RequirePackage[T1]{fontenc}
   \hyphenchar\font=\string"7F
```
Language definition, typesetting and hyphenation
```
\RequirePackage[english]{babel}
   \addto{\captionsenglish}{\renewcommand*{\contentsname}{Table of Contents}}
```
Font evtl. TeXGyre einbinden, z.B. ber eine Option
```
\RequirePackage{mathptmx} % times font
\RequirePackage{couriers} % monospace fonts
\RequirePackage{helvet}   % for sans serif fonts (\textsf{...} or \sffamiliy)
\RequirePackage{pifont}   % symbols
\RequirePackage{textcomp} % symbols
\RequirePackage{microtype}% microtypographic extensions
\RequirePackage{xspace}   % automatic spacing with own commands
```
Graphic extensions
```
\RequirePackage{graphicx}
\RequirePackage{grffile}
```
Color profile
```
\RequirePackage[rgb]{xcolor}
\ifpharmrep@pdfa
   \IfFileExists{\pharmrep@colorprofile}
      {\immediate\pdfobj stream attr{/N 3}  file{\pharmrep@colorprofile}
      \pdfcatalog{%
      /OutputIntents [ <<
      /Type /OutputIntent
      /S/GTS_PDFA1
      /DestOutputProfile \the\pdflastobj\space 0 R
      /OutputConditionIdentifier (\pharmrep@colorprofile)
      /Info(\pharmrep@colorprofile)
      >> ]
      }}{\ClassError{pharmrep}{Color profile \pharmrep@colorprofile not found!}{Please check y
\else
   \ClassInfo{pharmrep}{PDF/A support is disabled!}
\fi%
```
SI number formatting
```
\RequirePackage{siunitx}
```
Page layout, header and footer
```
\RequirePackage{geometry}
    \geometry{textheight=600pt,head=50pt,left=60pt,right=60pt,includeheadfoot}
    \setlength{\footheight}{38pt}
\RequirePackage[section]{placeins}
```

```
\RequirePackage{lastpage}
\RequirePackage{totcount}
   \regtotcounter{figure}
   \regtotcounter{table}
\IfFileExists{scrlayer-scrpage.sty}
   {\RequirePackage[headsepline,footsepline]{scrlayer-scrpage}}%
   {\RequirePackage[headsepline,footsepline]{scrpage2}}%
   \setkomafont{pageheadfoot}{\small}
   \setkomafont{pagenumber}{\small}
   \clearscrheadfoot
    \ihead{\begin{minipage}[b][16mm]{0.48\textwidth}Applicant: \@Applicant\\Drug Product:
    \@DrugProduct\hspace{0pt}\end{minipage}}
    \ohead{\begin{minipage}[b][16mm]{0.48\textwidth}\raggedleft\@PharmRepTitle\hspace{0pt}\end
    \ifoot{\begin{minipage}[t][10mm]{0.3\textwidth}\vspace{0pt}\@eCTDno\end{minipage}}
    \cfoot{\begin{minipage}[t][10mm]{0.3\textwidth}\vspace{0pt}\centering\jobname{}\end{minipa
    \ofoot{\begin{minipage}[t][10mm]{0.3\textwidth}\vspace{0pt}\flushright\pagemark/\upshape\p
    \pagestyle{scrheadings}
```

Portrait- and Landscape-Format

```
\newcommand{\landscapeformat}{%
   \clearpage%
   \pdfpagewidth=\paperheight%
   \pdfpageheight=\paperwidth%
   \newgeometry{textwidth=600pt,left=50pt,top=60pt,bottom=60pt,includeheadfoot}}
\newcommand{\portraitformat}{%
   \clearpage%
   \pdfpagewidth=\paperwidth%
   \pdfpageheight=\paperheight%
   \restoregeometry}
```

Tables and figures

```
\RequirePackage[justification=RaggedRight,singlelinecheck=false,labelfont=bf,hypcap=false]{cap
\RequirePackage{rotating}
\RequirePackage{booktabs}
\RequirePackage{multirow}
\RequirePackage{ltablex}
```

Lists

```
\RequirePackage{enumitem}
   \setlist[1]{parsep=4pt}
```

Notes and comments

```
\RequirePackage[backgroundcolor=orange!40,%
    linecolor=black!20!orange,%
    textsize=footnotesize,%
    colorinlistoftodos]{todonotes}
   \reversemarginpar
   \setlength{\marginparwidth}{20mm}

\RequirePackage[babel]{csquotes}
```

Bibliography

```
\RequirePackage[backend=biber,%
   style=authoryear,%
   ]{biblatex}
\RequirePackage{xpatch}% author bold
   \xpretobibmacro{author}{\mkbibbold\bgroup}{}{}
   \xapptobibmacro{author}{\egroup}{}{}
   \xpretobibmacro{bbx:editor}{\mkbibbold\bgroup}{}{}
   \xapptobibmacro{bbx:editor}{\egroup}{}{}
   \renewcommand*{\labelnamepunct}{\mkbibbold{\addcolon\space}}
\AtEndPreamble{%
   \ifdefempty{\@BibFileName}{%
      \ClassError{pharmrep}{You have to provide a bib file!}{Please use the macro
      \string\BibFileName{<MYFILE.bib>} in the preamble}}%
      {\addbibresource{\@BibFileName}}%
}%
```

Internal and external links, pdf meta data

```
\RequirePackage[pdftex,pdfa]{hyperref}%
   \AtEndPreamble{%
   \hypersetup{%
      pdftitle       = {\@PharmRepTitle},%
      pdfauthor      = {\@Applicant},%
      pdfsubject     = {\@eCTDno},%
      pdfkeywords    = {},%
      pdflang        = en,%
      bookmarks      = true,%
      pdfdisplaydoctitle = true,%
      colorlinks         = true,%
      plainpages     = false,%
      hypertexnames  = false,%
      pdfpagelabels  = true,%
      hyperindex     = true,%
      unicode        = true,%
      pdfmetalang    = {en},%
      pdfpagemode    = UseOutlines,%
      bookmarksopen  = true,%
      bookmarksnumbered  = true, %
      bookmarksopenlevel = 2,%
      colorlinks         = true,%
      allcolors          = blue,%
      breaklinks         = true,%
      linktoc            = all,%
   }}%
\apptocmd{\UrlBreaks}{\do\f\do\m}{}{}
   \setcounter{biburllcpenalty}{9000}%
   \setcounter{biburlucpenalty}{9000}%
```

Glossary

```
\RequirePackage[nopostdot,nonumberlist,toc]{glossaries}
   \setlength{\glspagelistwidth}{\linewidth}
\RequirePackage{glossary-list}
   \setglossarystyle{list}
   \makenoidxglossaries
%      \renewcommand{\glsnamefont}[1]{\bfseries #1}
\setcounter{tocdepth}{4}
\setcounter{secnumdepth}{4}

\newcommand*{\@Applicant}{}
\newcommand*{\@DrugProduct}{}
\newcommand*{\@PharmRepTitle}{}
\newcommand*{\@eCTDno}{}
\newcommand*{\@BibFileName}{}
\newcommand*{\Applicant}[1]{\renewcommand*{\@Applicant}{#1}}
\newcommand*{\DrugProduct}[1]{\renewcommand*{\@DrugProduct}{#1}}
\newcommand*{\PharmRepTitle}[1]{\renewcommand*{\@PharmRepTitle}{#1}}
\newcommand*{\eCTDno}[1]{\renewcommand*{\@eCTDno}{#1}}
\newcommand*{\BibFileName}[1]{\renewcommand*{\@BibFileName}{#1}}

\AtBeginDocument{%
   \listoftodos % List of ToDo's if at least 1 \todo{xxx} is present in the document
   \clearpage

   \pdfbookmark[1]{\@PharmRepTitle}{Sec:Title}
   \section*{\@PharmRepTitle}
   \bigskip

   \tableofcontents
   \clearpage
   \ifnum\totvalue{table}>0
      \listoftables
      \clearpage
```

```
    \fi%
    \ifnum\totvalue{figure}>0
       \listoffigures
       \clearpage
    \fi%
    \cleardoubleemptypage
}%
```

⟨/class⟩