



# **An Analysis and Evaluation of the Development of the QRD Human Product Information Template used in Package Leaflets**

**Anna Wolf**

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# Focus of the project

- Development and implementation of the QRD template
- The use of templates for the package leaflet in European and non-European countries
- Readability test of the QRD template 8, its predecessor and a shorter model template



# 1. What is the QRD template?

- The QRD template is a text framework containing headings and standard statements
- Published by the EMA – first version in 1996
- Available in 23 EU languages + Icelandic and Norwegian
- It is a guidance document
- Provides unity in PIL structure in the EU

Text type	Meaning
{text}	Information to be filled in
text	Text which must be used
<text>	Text to be selected or deleted as appropriate
[Orange text]	Cross-refer to the section / information of the SmPC
[Green text]	Explanations

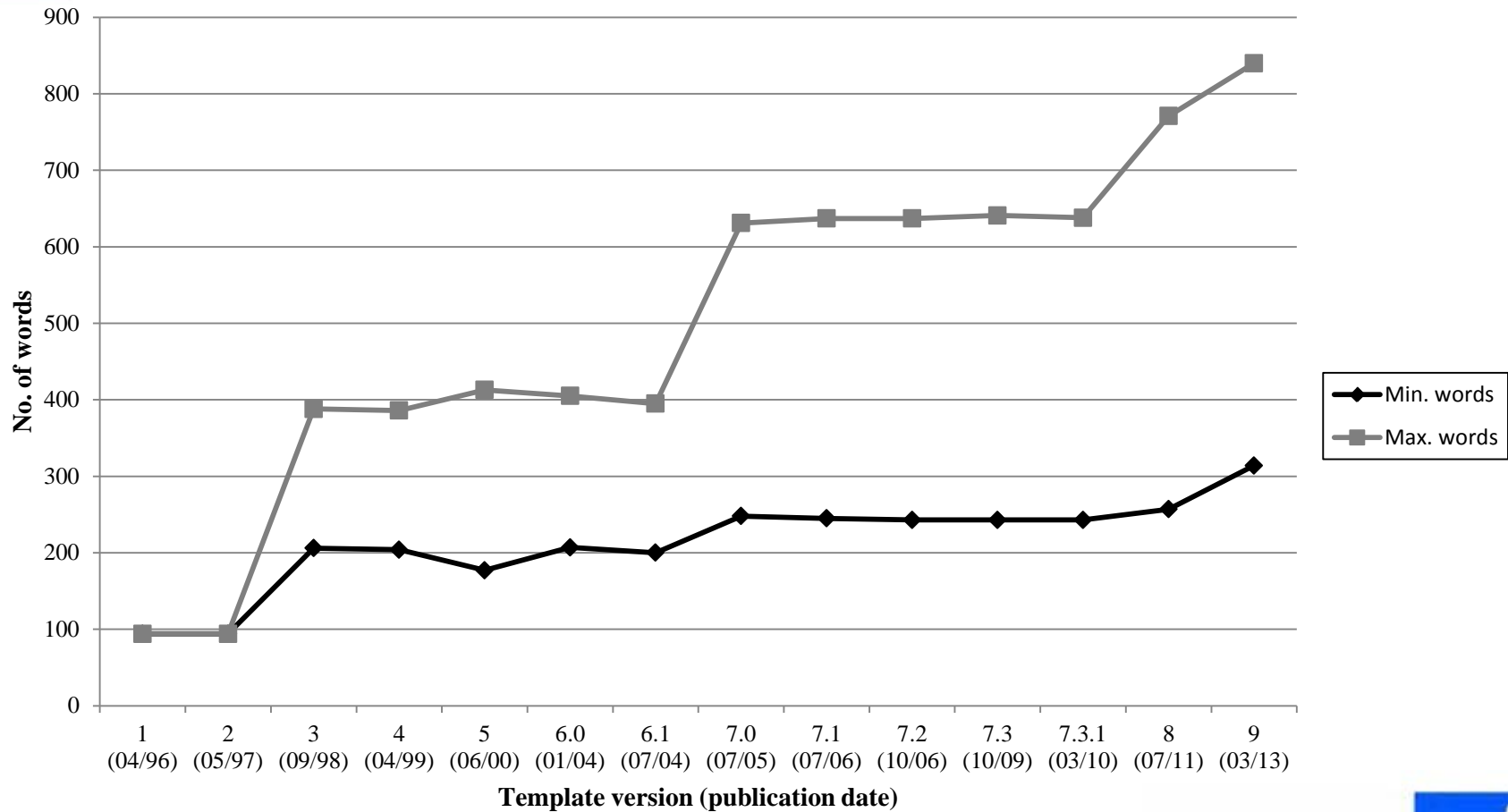


## Analysis of the text volume of the QRD template

- 14 versions of the QRD template have been published since 1996 – most recent version March 2013
- Word count tool in Microsoft Word was used to investigate the minimum and maximum number of words in each version of the template
- Maximum word count: All black mandatory template text
- Minimum word count: Bracketing convention was followed and optional text was deleted
- Number of QRD template words in package leaflets for medicines approved via a centralised procedure and available on the EMA website

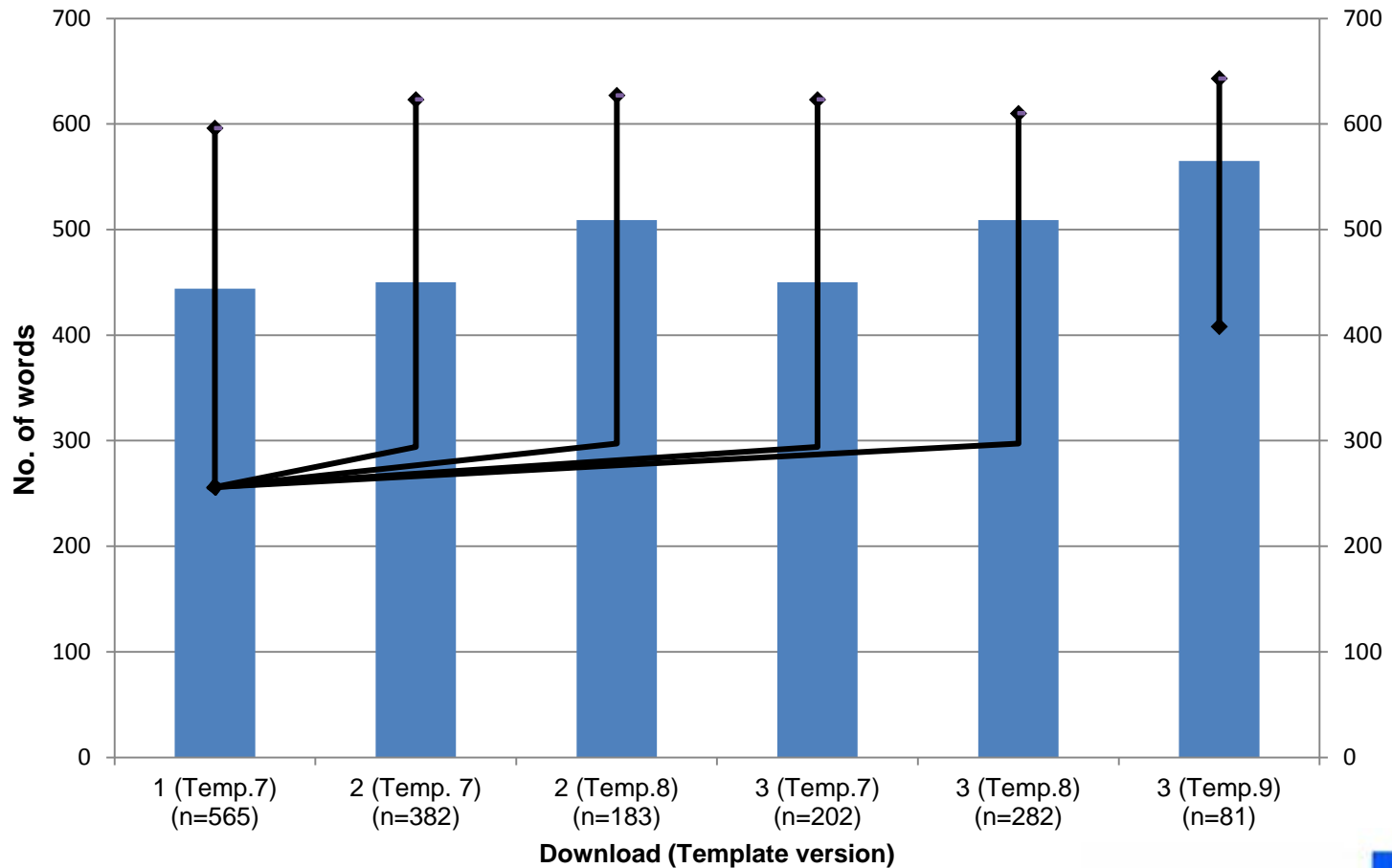


# Volume of text increase in the QRD template





# Words increase in package leaflets caused by the QRD template



Average no. of words with range of min. and max. words



## 2. Readability test

- Active ingredient enalapril - "Mustertext" from BfArM

Leaflet	Template version	Language	Text version
UK-Model-temp.-short	Model	English	Short
UK-QRD-temp.-7.3.1-short	QRD 7.3.1	English	Short
UK-QRD-temp.-8-short	QRD 8	English	Short
DE-Model-temp.-short	Model	German	Short
DE-QRD-temp.-7.3.1-short	QRD 7.3.1	German	Short
DE-QRD-temp.-8-short	QRD 8	German	Short
DE-Model-temp.-BfArM	Model	German	BfArM
DE-QRD-temp.-7.3.1-BfArM	QRD 7.3.1	German	BfArM
DE-QRD-template-8-BfArM	QRD 8	German	BfArM



## 2. Readability test

- Questionnaire to assess ease of finding of requested information and subjects opinion of the leaflet
- Cross-over design used – over 60 participants read all 3 versions of package leaflet separated by a time period of 6 months
- Data entered into and analysed using SPSS software





## Demographic data of participants at the start of the readability test

- 241 Participants (172 DE, 69 UK)

	<b>UK</b>	<b>Germany –Short text leaflet</b>	<b>Germany – Long text leaflet</b>
<b>No. participants</b>	69	76	96
<b>Age range (years)</b>	24 - 79	16 - 78	14 – 79
<b>Average age (years)</b>	52	42.2	36.4
<b>Gender of participants</b>	64.7 % Female 35.3 % Male	57.9 % Female 42.1 % Male	61.5 % Female 38.5 % Male
	<b>Level of education</b>		
<b>8th class</b>	0 %	9.2 %	43.8 %
<b>10th class</b>	7.2 %	35.5 %	12.5 %
<b>A-level</b>	10.1 %	11.8 %	10.4 %
<b>Polytechnic</b>	7.2 %	5.3 %	8.3 %
<b>University</b>	66.7 %	14.5 %	18.8 %
<b>Other</b>	8.7 %	23.7 %	6.3 %

## Percentages of correct, wrong and not found answers per package leaflet and the time needed to answer the 26 questions relating to package leaflet content

Package leaflet	No. of words per package leaflet	Calculated median				n
		Correct answers (%)	Wrong answers (%)	Not found answers (%)	Time to answer the 26 content questions (min)	
UK-Model-temp.-short	1221	95.0	1.3	3.6	17.8	67
UK-QRD-temp.-7.3.1-short	2169	83.4	11.6	3.4	19.7	65
UK-QRD-temp.-8-short	2227	91.5	5.2	3.0	19.3	65
DE-Model-temp.-short	1007	93.2	2.2	4.4	20.7	75
DE-QRD-temp.-7.3.1-short	2002	87.3	9.7	2.7	23.4	72
DE-QRD-temp.-8-short	2023	91.1	5.0	3.3	20.3	73
DE-Model-temp.-BfArM	2893	80.4	7.7	11.1	24.5	93
DE-QRD-temp.-7.3.1-BfArM	3890	76.2	15	7.6	29.2	93
DE-QRD-temp.-8-BfArM	3956	81.2	11.5	6.5	28.6	94



## Results of the Wilcoxon test to identify significant differences between package leaflet versions with short text.

Compared Package leaflets		Significance between leaflet versions		
		Correct answers	Wrong answers	Not found answers
UK-Model-temp.	UK-QRD-temp.-7.3.1	p ≤ 0.001	p ≤ 0.001	n.s
UK-Model-temp.	UK-QRD-temp.-8			
UK-QRD-temp.-7.3.1	UK-QRD-temp.-8			
DE-Model-temp.	DE-QRD-temp.-7.3.1	p ≤ 0.001	p ≤ 0.001	p = 0.006
DE-Model-temp.	DE-QRD-temp.-8	p = 0.026		n.s
DE-QRD-temp-7.3.1	DE-QRD-temp.-8	p = 0.002		



## Results of the Wilcoxon test to identify significant differences between package leaflet versions with BfArM text

Compared Package leaflets		Significance between leaflet versions		
		Correct answers	Wrong answers	Not found answers
DE-Model-temp.	DE-QRD-temp.-7.3.1	p = 0.001	p = 0.001	p ≤ 0.001
DE-Model-temp.	DE-QRD-temp.-8	n.s		
DE-QRD-temp-7.3.1	DE-QRD-temp.-8	p ≤ 0.001		n.s



## Question

**"Can you take this medicine if you are allergic to lactose?"**

	Model template	QRD template 7.3.1	QRD template 8
Heading	No subheading Lactose only listed in section 6 in the list of excipients	<b>Important information about some of the ingredients of Enal</b> + warning Excipients Guideline	<b>Enal contains lactose</b>  + warning Excipients Guideline



**Percentages of correct, wrong and not found answers for each package leaflet for question “Can you take this medicine if you are allergic to lactose?”**

Package leaflet	Average (%)			n
	Can you take this medicine if you are allergic to lactose? (contraindication question)			
	Correct answers	Wrong answers	Not found answers	
UK-Model-temp.-short	41.8	10.4	47.8	67
UK-QRD-temp.-7.3.1-short	33.8	60.0	6.2	65
UK-QRD-temp.-8-short	20.0	75.4	4.6	65
DE-Model-temp.-short	38.7	20.0	41.3	75
DE-QRD-temp.-7.3.1-short	29.2	61.1	9.7	72
DE-QRD-temp.-8-short	30.1	68.5	1.4	73
DE-Model-temp.-BfArM	35.5	20.4	44.1	93
DE-QRD-temp.-7.3.1-BfArM	36.6	50.5	12.9	93
DE-QRD-template-8-BfArM	37.2	57.4	5.3	94



## What should you do if you need a dental operation while taking Enal? (warnings/precautions question)

	<b>Model template</b>	<b>QRD template 7.3.1</b>	<b>QRD template 8</b>
<b>Subheading in section 2</b>	<b>Consult your doctor in the case of</b>	<b>Take special care with Enal:</b>	<b>Warning and precautions</b> Talk to your doctor, pharmacist or nurse before taking Enal in the case of:



## What should you do if you need a dental operation while taking Enal?

Package leaflet	Average (%)			n
	What should you do if you need a dental operation while taking Enal?			
	Correct answers	Wrong answers	Not found answers	
UK-Model-temp.-short	91.0	0	9.0	67
UK-QRD-temp.-7.3.1-short	12.3	70.8	16.9	65
UK-QRD-temp.-8-short	72.3	0	27.7	65
DE-Model-temp.-short	97.3	1.3	1.3	75
DE-QRD-temp.-7.3.1-short	48.6	40.3	11.1	72
DE-QRD-temp.-8-short	89.0	2.7	8.2	73
DE-Model-temp.-BfArM	88.2	1.1	10.8	93
DE-QRD-temp.-7.3.1-BfArM	80.6	3.2	16.1	93
DE-QRD-template-8-BfArM	81.9	2.1	16.0	94





# How many people are affected by a side effect if it is “rare”?

	<b>Model template</b>	<b>QRD template 7.3.1</b>	<b>QRD template 8</b>
<b>Method of presenting frequencies of side effects</b>	<b>Frequencies described as part of side effect list</b>	<b>Table at start of section 4</b>	<b>Frequencies described as part of side effect list</b>
<b>Method of description of side effects</b>	<b>Rare, affects 1 to 10 per 10,000 people</b>	<b>Rare: less than 1 in 1000, but more than 1 in 10,000 patients</b>	<b>Rare: may affect up to 1 in 1,000 people</b>

## How many people are affected by a side effect if it is “rare”?

Package leaflet	Average (%)			n
	How many people are affected by a side effect if it is “rare”?			
	Correct answers	Wrong answers	Not found answers	
UK-Model-temp.-short	100	0	0	67
UK-QRD-temp.-7.3.1-short	95.4	1.5	3.1	65
UK-QRD-temp.-8-short	100	0	0	65
DE-Model-temp.-short	96.0	4.0	0	75
DE-QRD-temp.-7.3.1-short	90.3	5.6	4.2	72
DE-QRD-temp.-8-short	98.6	1.4	0	73
DE-Model-temp.-BfArM	93.5	2.2	4.3	93
DE-QRD-temp.-7.3.1-BfArM	90.3	7.5	2.2	93
DE-QRD-temp.-8-BfArM	92.6	6.4	1.1	94



**Answers to the question:  
 “How many people are affected by a side-effect if it is rare?”  
 (Grey shading shows the method of frequency  
 description used for each template version)**

Description of frequency	Subjects (%)					
	QRD-template 7.3.1		QRD-template 8		Model template	
	DE	UK	DE	UK	DE	UK
1 – 10 people from 10,000	1.9	3.2	0	0	90.2	97.0
Less than 1 in 1000 but more than 1 in 10,000	64.3	82.3	0	1.5	0	0
1 in 1000*	23.0	12.9	97.5	98.5	1.8	0
1 in 10*	0	0	0.6	0	1.2	0
1 in 10,000	6.4	1.6	0.6	0	1.8	1.5
Other	4.4	0	1.2	0	5	1.5
Number of participants who provided frequencies in numbers	157	62	163	65	163	67

\* An asterisk indicates overestimation of the frequency



# What should you do if you notice the side effect runny nose?

	<b>Model template</b>	<b>QRD template 7.3.1</b>	<b>QRD template 8</b>
<b>Statement in section 4</b>	Always inform your doctor or pharmacist if you notice side effects.	If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.	If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet.



# What should you do if you notice the side effect runny nose?

Package leaflet	Average (%)			n
	What should you do if you notice the side effect runny nose?			
	Correct answers	Wrong answers	Not found answers	
UK-Model-temp.-short	82.1	3.0	14.9	67
UK-QRD-temp.-7.3.1-short	26.2	47.7	26.2	65
UK-QRD-temp.-8-short	95.4	1.5	3.1	65
DE-Model-temp.-short	78.7	6.7	14.7	75
DE-QRD-temp.-7.3.1-short	69.4	15.3	15.3	72
DE-QRD-temp.-8-short	83.6	1.4	15.1	73
DE-Model-temp.-BfArM	50.5	6.5	43.0	93
DE-QRD-temp.-7.3.1-BfArM	55.9	20.4	23.7	93
DE-QRD-temp.-8-BfArM	69.1	8.5	22.3	94



## Are the information box or certain repetitions necessary in the PIL?

**Information contain in the information box: “Is this medicine available with or without prescription by a doctor?”**

<b>Model template</b>	<b>QRD template 7.3.1</b>	<b>QRD template 8</b>
No information box. In section 5: Enal is prescribed only for you.	Information box at start of leaflet: This medicine has been prescribed for you.	Information box at start of leaflet: This medicine has been prescribed for you.

**“Name the active substance in Enal“**

<b>Model template</b>	<b>QRD template 7.3.1</b>	<b>QRD template 8</b>
Listed once: <ul style="list-style-type: none"> <li>• In section 6 under “Composition”</li> </ul>	Listed twice: <ul style="list-style-type: none"> <li>• At start of leaflet under medicine name</li> <li>• In section 6: What Enal contains</li> </ul>	Listed three times: <ul style="list-style-type: none"> <li>• At start of leaflet under medicine name</li> <li>• In section 1: Enal contains enalapril.</li> <li>• In section 6: What Enal contains</li> </ul>

## Are certain PIL elements or repetitions necessary?

Package leaflet	Average (%)						n
	Is this medicine available with or without prescription by a doctor?			Name the active substance in Enal.			
	Correct answers	Wrong answers	Not found answers	Correct answers	Wrong answers	Not found answers	
UK-Model-temp.-short	80.6	1.5	17.9	100	0	0	67
UK-QRD-temp.-7.3.1-short	87.7	1.5	10.8	100	0	0	65
UK-QRD-temp.-8-short	87.7	4.6	7.7	98.5	0	1.5	65
DE-Model-temp.-short	65.3	1.3	33.3	92.0	1.3	6.7	75
DE-QRD-temp.-7.3.1-short	80.6	5.6	13.9	95.8	1.4	2.8	72
DE-QRD-temp.-8-short	76.7	4.1	19.2	98.6	0	1.4	73
DE-Model-temp.-BfArM	79.6	1.1	19.4	78.5	14.0	7.5	93
DE-QRD-temp.-7.3.1-BfArM	82.8	5.4	11.8	75.3	23.7	1.1	93
DE-QRD-temp.-8-BfArM	83.0	3.2	13.8	81.9	12.8	5.3	94



## Which elements are required in the QRD template for the package leaflet?

- **Contents list** – study showed an index is not essential
- **Extra sections for pregnancy and breast feeding** – not present in the model template which was not inferior to the QRD template PILs
- **Prescription status** – element on outer packaging
- **List of MAH representatives**
- **Information box** – most of the information is contained elsewhere in the package leaflet
- **Repetition of active ingredient**





## 3. Summary

- QRD template 8 has shown a number of improvements when compared to its predecessor e.g. new subheading "Warnings and precautions"
- Reducing the number of template words with a shorter model template did not reduce readability
- Description of side effect frequencies should be reconsidered as those provided in QRD template 8 had a significantly lower rate of comprehensibility
- Deletion of the information box, contents list, all repetitions such as active ingredient and the list of 29 MAHs should be considered



## 4. Conclusions

- It is possible to improve the QRD template
- Keeping the QRD template as concise as possible should be a major priority in the future
- MAHs should be encouraged to exclude all non-mandatory information in the template
- New versions of the template should be user tested before publication



Thank you for your attention