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CLINICAL TRIALS

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Evaluation of the readability of information sheets for healthy volunteers in phase-I trials

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Abstract *Objective*: The aim of the present study was to assess whether information sheets/consent forms submitted to the healthy volunteers of the Clinical Pharmacology Unit (C.P.U.) panel at Glaxo-Wellcome (Verona, Italy) could be considered understandable and to verify the readability and comprehensibility of these documents. Since a volunteer bases his/her decision to take part in a study on the information sheet provided, it is of paramount ethical importance to know whether the sheet conveys all relevant information. In addition, a thorough awareness by the volunteer of the reasons and procedures of the study would increase compliance.
Methods: Four indices were used: Flesh-Vacca, Kincaid, Gunning's Fog and Gulpease. All indices rate the degree of difficulty of a text, in the light of the level of schooling of the target population. The documents evaluated were information sheets presented to volunteers. The level of schooling of the population that participated in at least one study was determined: 61.7% of volunteers finished high school and 22.6% had a University degree or diploma; the remaining 15.7% did not finish high school or the datum was not available.
Results: The results showed that, when the present study began, all information sheets were ''readable'' by all volunteers who had at least finished high school. After these preliminary results, some additional linguistic and graphic refinements were adopted in drawing up information sheets. Readability improved to such a degree that all information sheets could be understood by virtually all volunteers.
Conclusion: A number of suggestions were identified, which are set out in this paper to assist in the preparation of improved information sheets and a recommendation to value the readability of consent sheets before giving them to the volunteers. The suggestions were split into three categories: communications to the volunteer, text format and text organisation.

Key words Phase-I trials · Readability · Volunteers

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Introduction

Experimentation with healthy volunteers is a vital part of the development of a new drug. There are several reasons why healthy volunteers are preferable to patients; they include the need not to influence pharmacological response due to a pathologic state and the possible interaction of the experimental drug with other drugs taken by the patient in the course of treatment of the pathology [1]. Undoubtedly, the ethical problems arising in this phase of experimentation are singular and need to be looked at closely. One of these problems is that the decision to take part in an experiment should be the expression of a free consent.

This study specifically addresses the question of the information provided to healthy volunteers whose co-operation in the phase-1[1] [2] experimentation of various molecules is so important. One of the requirements for recruitment is that the volunteer gives his/her informed consent to the procedures and the aims of the research. Information is provided by means of information sheets

[1] Phase 1 is defined as ''first trials of a new active ingredient in man, often healthy volunteers. The purpose is to establish a preliminary evaluation of safety and a first outline of the pharmacokinetic/pharmacodynamic profile on the active ingredient in humans''

signed by the volunteer indicating his/her willingness to take part and the fact that he/she has understood the terms of the co-operation. Some authors [3] have shown that the way the information sheet is written and its contents in terms of "information" may influence the volunteer's decision to take part or not to take part in the study.

Evaluating how easy a certain text is to understand is a difficult task. Ease or difficulty in understanding a text depends on certain unvarying, objective factors – related entirely to the text – and on other variable, subjective factors – related to the reader. It is practically impossible to analyse all subjective factors. For this reason, research has concentrated for many years on the text rather than the reader.

Study objectives

At the Glaxo-Wellcome Clinical Pharmacology Unit (C.P.U.) in Verona, research has been carried out for a number of years with healthy volunteers, to the most rigorous scientific and ethical standards. Fully aware of the complexity of the information contained in these sheets, however, no objective evaluation of readability and easy of understanding has been carried out beyond the opinions of C.P.U. staff and the opinion of the ethics committee. This is the reason behind this study, which had two aims:

1. To evaluate the complexity and ease of understanding of information sheets produced by the C.P.U. at Glaxo Wellcome and used to obtain volunteer's informed consent.
2. To propose methods for creating information sheets that are increasingly easy to read and understand.

Methods

Study phases

The first part consisted of (1) establishing the level of education of healthy volunteers enrolled at the C.P.U. who had taken part in at least one clinical study; (2) the choice of parameters of readability, their description and features; and (3) interpretation of criteria for readability relative to the educational background of volunteers. The second part included (4) an analysis of documents using the readability criteria; (5) a comparison between readability and educational background; and (6) operational proposals based on the types of writing problems highlighted by the software programme and on the currently available literature on how to improve the readability of texts.

First part

The average level of education of healthy volunteers in the C.P.U. panel was receival of a high school diploma, the equivalent of 13 years of schooling; many of the volunteers, however, despite their "last qualification" being the high school diploma, had further educational backgrounds, consisting of some period of university studies. The indices used were the Flesh-Vacca Index [4], Kincaid Index [5], Gunning's Fog Index and Gulpease Index [6]. The four indices were used to analyse the same text from different perspectives (e.g. sentence construction, length of paragraphs, etc.). They were only partially superimposable: convergent results confirm the reliability of the indices themselves. According to the international literature, they are always used together.

There are some limits to the instruments and methods used. Readability measured with mathematical formula of this kind is a rather simplistic approach. The criteria used are objective and quantitative and, as mentioned above, do not take subjective variables into account, such as the overall organisation of the text, the continuity of thought, the complexity of the concepts expressed, the individual style of the writer, the reader's motivations, his/her age, memory, and so on. Despite these limits, the above-mentioned formulae are used by almost all studies into readability and the ease of understanding a text. As far as we know, no study of readability or the ease of understanding of information sheets used to obtain volunteers' informed consent for phase-1 studies has previously been carried out.

The expected average values for the indices analysing readability and the easy of understanding of information sheets are as shown in Table 1.

Second part

We assessed, at the beginning of the study, the latest 16 documents issued by the C.P.U. and submitted to the volunteers. We informed the authors of the results and gave them the suggestions for improving readability. The evaluation of the following three information sheets showed a sensible increase in the indices' values. After 1 year, we randomly chose three more documents among those written in the previous year, and the results showed that the recommendations given were permanently acknowledged.

Each sheet was analysed according to the following procedure:

- *Whole text*: analysis of the entire text
- *Procedures*: a part of the text that is considered particularly important, and which varies from study to study, containing the explanation of procedures, side effects, obligations and restrictions

The following documents were also analysed:

- "Consent" to take part in the panel of volunteers, handed in once only, at the moment of volunteers' applications
- "Study consent" (the same for all protocols): the version used until beginning of the present study and the current version

The vocabulary of these texts was compared with the vocabulary of the most commonly used words in the Italian language. The average number of words in each sentence was also calculated.

Results

A comparison was made between readability and the volunteers' school level. The average readability of the documents was close to the expected value. Some protocols had widely different values according to the

Table 1 Expected value for the indices of readability (according to the school level)

Flesh-Vacca Index	Values of or above	50
	Critical frequency	40–49
Gunning's Fog Index	Values between	9–13
	Critical frequency	> 14
Kincaid Index	Values between	10–15
	Critical frequency	> 15
Gulpease Index	Values above	49
	Critical frequency	35–49

index used and some had considerable differences of readability within the protocol itself. This can be seen by comparing the values for the "procedures" section with the values for the text as a whole. The quantitative measurement of readability and the easy of understanding of the documents shows the "acceptability" of these documents, above all in relation to the average educational background of volunteers, although there is still room for improvement.

Figure 1 shows readability values according to the Flesh-Vacca Index over the period under investigation. The improvement is evident, beginning from the date readability was tested experimentally. This improvement raises readability to well above the acceptable level in the light of the average educational background of volunteers.

Observations about the qualitative analysis of protocols

In addition to the quantitative analysis, the software used allowed some "qualitative" elements to be assessed, relating to the style of the text, thus producing a semi-qualitative analysis of the documents. The prefix "semi-" is necessary because the analysis does not refer to the contents of the text, but to the repetition of certain errors, spoken rather than written linguistic forms, "*consecutio temporum*", punctuation and/or typing. The qualitative analysis of the protocols showed a number of problems relating to vocabulary and grammar. From the linguistic point of view, the use of technical words and expressions can be expected to be higher than in the language as a whole. From the stylistic point of view, numerous passive constructions were used, which make the text more difficult to read and to understand. It was also noticeable that documents with good readability scores had few words per sentence, on average.

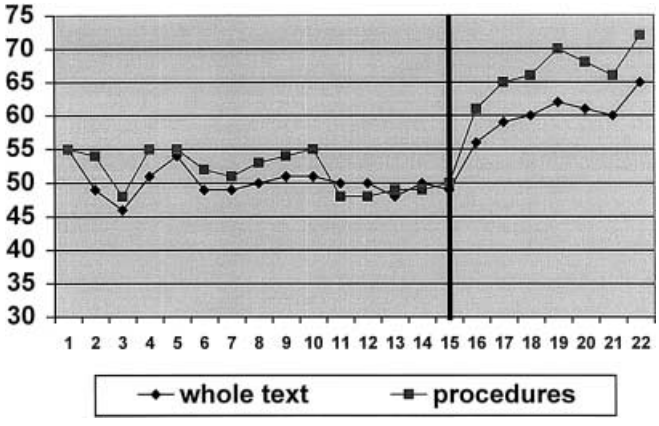

Fig. 1 Values according to the Flesh-Vacca Index

Discussion and conclusions

We improved the readability by operating on the objective factors related to the text only; we could not operate on the subjective variables related to the individual. The recommendations assemble what already mentioned in the literature with what resulted from our analysis. The suggestions were split into three categories, as already done by Freeman [7], distinguishing between the format of the text, elements making communications between the volunteer and the research team easier, and the presentation of the text. Rivera [8] suggests, in addition, that automatic readability and ease of understanding indices be used systematically, in order to have an idea of their complexity as they are being written.

In the light of the above and a study of international literature on the subject of the ease of understanding written texts, it is possible to make some concrete recommendations about how to draw up future texts.

Table 2 summarises some concrete recommendations on how to improve the readability of texts. "Guided

Table 2 Practical suggestions for making information sheets easier to understand

Communications to the volunteer	**Text format**	**Text organisation**
Bear in mind the target reader (age, educational background, previous experiences, etc.)	Highlight the most important words or key words in the text	Give the aim of the study in the first part of the text
Identify the most relevant information to include	Keep the right balance between white space and printed text	Divide the information sheet into sections and paragraphs
Define study procedures clearly and specifically	Use a legible character	Present the paragraphs in a logical order
Explain difficult or technical words	Use size 12–14 for the text and size 16–18 for the headings	Organise the sections in such a way that it is easy to remember
Avoid the use of ambiguous terms		Communicate one piece of information per paragraph
Use instruments to test the text		Write in an informal style
Express concepts in a concise fashion		Avoid using passive constructions
Assess the readability of the text		Avoid long words
Be willing to change the text		Avoid trying to simplify the text by using simpler but less commonly used expressions
Give a verbal presentation and explanation of the text		Keep sentences short
		Use personal rather than impersonal pronouns

reading'' may be an excellent technique for improving readability. This technique consists of carrying out a number of actions to optimise the understanding of the aims of the study, its procedures, the obligations arising from taking part, the contraindications and any dangers, for the purpose of obtaining consent which is thoroughly informed. ''Guided reading'' procedures can be summarised as follows:

- Individual presentation of the document by doctor and, if required, by all other research team members
- Willingness to answer questions immediately and/or on the telephone
- At the group level, reading of the document immediately after the presentation of the document by the doctor in charge of research
- Willingness to give explanations at all times, before, during and after the study

Undoubtedly, in addition to the work of the ethics committee, the real guarantee of protection for volunteers recruited to studies is related to the ethical commitments and habits of researchers who, in a variety of ways discussed above, are able to ensure that consent is thoroughly informed. New guidelines for ethics committees, passed into law by Italian Ministerial Decree on 18 March 1998, now specifically require ethics committees to ''examine how consent was obtained before approving the study''. Nonetheless, ''since informed consent represents an imperfect safeguard of the volunteer'' – the decree continues – ''obtaining the informed consent of the volunteer is not a sufficient guarantee of the ethical status of the study and hence the ethics committee must evaluate the experimental study in all its aspects.''

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