WHY NOT MAKE IT SIMPLE? WRITTEN MESSAGES IN DRUGS WORLDWIDE

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ABSTRACT

This research addresses the problem of the worldwide high percentage of therapeutic failures caused by misinterpretation of written instruction in medicines.

This participatory study involved designers, pharmacists and patients. It examined the existing written information and warnings used in medicines worldwide to complement prescription communications, with the aim of exploring ways to make those instructions more readable and effective, thus allowing: i) the integrations of vulnerable audiences (people undergoing multiple treatments at the same time, people with lower intellectual abilities); ii) an improvement of autonomy in health practices of the ageing population; iii) ameliorating communication for social and cultural global movements (foreigners, tourists, migrants).

To achieve those goals, our challenge is to bridge knowledge from these two disciplinary areas, design and pharmacy, by designing a set of cross-cultural short messages easier to read, quicker to consult and intelligible to all.

INTRODUCTION

Medicines allow us to make diagnoses, treat or prevent diseases. But often, at the moment of administration, diverse obstacles can prevent full benefits to be obtained. We all know that medicines, if they are mismanaged, not correctly used or interrupted, can be very dangerous. Taking them as prescribed is, first of all, understanding posology correctly. The written instructions (prescriptions, leaflets and labels) may be not hard to follow. However, thousands of people misinterpret them every day.

A multitude of different analogical and digital tools continue to be developed to complement patient's information leaflets (PILs), to highlight specific warnings regarding the medicine and addressing five main areas of information:

(1) place of application, (2) how it should be taken, (3) storage and handling recommendations, (4) potential side effects, (5) drug frequencies.

In spite of those efforts, our research shows that the information relating to prescriptions addressed to patients, given at different moments and in different supports, is often contradictory, confused, redundant, wordy, thus contributing to reinforce defective communication. The interdisciplinary research team integrated the participatory contribution of designers, pharmacists, linguists and patients. Our ambition was to improve written instructions not only in terms of graphical representation but also of the often-neglected written captions/instructions, in order to develop a new ordered set of messages aligned for international labelling practices. This involves to attempt linguistic standardization of the most important messages and to associate them with therapeutic graphic symbols capable of being understood by people all over the world. This set of messages should be suitable to be used in different supports, including the new digital tools, not only by patients but also by health

professionals. More readable and effective medicines labels instructions will promote:

i. integration of vulnerable audiences (people undergoing multiple treatments at the same time, people with reading difficulties, lower intellectual abilities, lack of memory);
ii. improvement of autonomy in health practices of the ageing population;
iii. better and reinforced communication for social and cultural global movements (foreigners, tourists, migrants).

Our main objectives are to combat medication errors, to encourage uninterrupted adherence to medication, to avoid overdosing, and, more broadly, to improve health literacy, patient education and self-management in treatments adherence and outcomes, by contributing to differentiate language information for patients from information for doctors, pharmacists and nurses.

CONTEXT

There is a growing international concern in the area of health and medicinal drugs regarding forms of communication and transmission of knowledge, namely with reference to the associated risks inherent in the use and handling of medicines and the interpretation of treatments. Since the 1970s the need for better information about drugs has been recognised (Linkewich, 1974; Merrett, 1977). And at the 37th World Health Assembly, held in 1984, the World Health Organization (WHO) recognized the need for information about drugs, and encouraged countries to give their support to the preparation and dissemination of objective and comprehensive pharmacological messages. In 2003, WHO quoted a statement by Haynes et al saying that '*increasing the effectiveness of adherence interventions may have a far greater impact on the health of the population than any improvement in specific medical treatments.*' (WHO, 2003). And in 2011 they stressed that some researchers estimated that 50% of citizens do not take medicines properly (WHO, 2011). Finally, in March 2017, WHO launched a global effort to reduce by half avoidable medication-related errors over the next 5 years (WHO, 2017).

'*We all expect to be helped, not harmed, when we take medication," said Dr Margaret Chan, WHO Director-General. "Apart from the human cost, medication errors place an enormous and unnecessary strain on health budgets. Preventing errors saves money and saves lives.*' (WHO 2017).

In the last four decades, more than 60 international authors have been working on information problems in prescription and PILs related to usage, misinterpretation and understanding of instructions, overdosage, nonadherence to and remembering treatment, handling of medicines and side effects - aspects which involve not only Actions but Handling and Effects. Some of the big issues embrace (without specific order):

- the high rates of therapeutic failure (Linkewich 1974);
- support tools to medicines instructions (Merrett 1977, Morrell 1990)
- distinctive programs to target patients (Ngoh 1997, Knapp 2005);
- problems of cultural contexts (Camacho 2011);
- people-centred health care (WHO 2003, 2011, 2017);
- information design about warnings, coloured print, legibility and readability (Clark 2006; Wogalter 2006;);
- analysis of comprehension and recalling (Sojourner 1998);
- treatments with different iconic degrees drawings Morrow 1996, Mansoor 2003, Morrow 1996); Camacho 2013; Ayres 2006);
- lack of readability of leaflets (Camacho 2008, Koo 2003, van Beusekom 2016, Wolf MS 2007, Hoffmann 2004, Grime 2007).

The amount of mandatory information on medicines is growing, it is heavily regulated and PILs are therefore increasingly dense and extensive. In the USA, the Food and Drug Administration (FDA) determines the requirements for patient information leaflets (PILs), and drugs packages, at least since 1970. In Australia, the Department of Health and Ageing, division of Therapeutic Good Administration (TGA), has too their own appliances regulating therapeutic goods, Product Information (PI) and Consumer Medicine Information (CMI). In Europe, even though countries have their own legislation, the European Medicines Agency (EMA) is responsible for the scientific evaluation and supervision of medicines. In parallel to this effort of regulation, pharmacists highlight short messages regarding instructions and warnings in PILs and underline prescription directions in an attempt to avoid error. Warning labels proliferate, but readability and/or graphic legibility have not improved, and there appears to be no international coordination or guidelines showing awareness of real users 'needs (EC 2009).

DATA, METHODS, EVALUATION, INITIAL RESULTS

WRITTEN MESSAGES COLLECTION (1ST RESULT)

As far as we know, there is no compilation of therapeutic short messages (on actions, handling and effects), international guidelines or a list of mandatory captions. Our 1st result was the collection of over a thousand, the first huge step, within a one year period. Research showed that communication in drug dispensing uses different channels - oral, written and pictorial. It was crucial that our participatory study could include designers, pharmacists, linguistics and patients. The posology messages were initially collected through an international literature web search, which included messages developed by Faculties of Medicine

and Pharmacy, international pharmaceutical institutions, agencies regulating medicines, pharmacopoeias, pharmaceutical associations, pharmaceutical industry, catalogues of pharmaceutical products, hospitals, medical institutes, standardization institutes, private companies, design agencies and some developed by unknown authors. To these were added 50 Portuguese PILs; verbal and written messages discussed with 100 professional pharmacists from all districts of Portugal, and patients' suggestions.

For this research, we originally considered written messages in 8 languages (English, French, Spanish, Portuguese, German, Korean, Chinese and Japanese), from more than 20 countries and the EU (Australia, Austria, Brazil, Canada, Denmark, Estonia, Finland, France, Germany, Iceland, India, Italy, Japan, Norway, Portugal, Romania, Slovenia, South Africa, Spain, Switzerland, UK and USA), covering the last 45 years. In order to study the quantitative and qualitative diversity of the written posology messages, more than 1000 short sentences were: (1st) collected, (2nd) analysed, (3rd) grouped (4th) compared, (5th) final set selected, and (6th) set result in three languages - English, Portuguese and French.

The decisions made by the interdisciplinary team were based on contributions coming from different types and levels of experience and of expertise. Discussion was open, dynamic, not confined to the scientific areas or pre-structured: the contribution of all participants was essential to the result.

SESSIONS FOR DATA ANALYSIS (2ND RESULT)
Considering the extensive data and assuming that it could take various forms, the organization of the messages for analysis was subject to participatory discussions. The captions/instructions collected from written, drawn and verbal sources were first grouped into 3 categories, prohibition, information and dangers, in order to subsequently carry out a participatory survey with pharmacists and patients, in order to define and choose vocabulary and phrasal construction.

Keywords were defined in a brainstorm session around four main topics: human body, objects, food, abstract concepts. The extensive universe of more than 1000 written messages was then grouped and organized. Our 2nd result was 47 tables, within 58 pages, created and assembled in 5 main groups: Place of application, Handling, Effects, Frequency and doses, The medicine (figures 1 to 5). Each table comprised groups of messages related to the topic, for example, table 1, Eyes: 'Do not apply to the eyes', 'Eye drops', 'Eye ointment' (messages 1, 32, 34, fig.12).

The main purpose of the 47 tables created (that can be seen in Camacho 2013, pp 200-258) was to organize, select and reorder the messages according to the needs and the importance that were being ascertained during the dynamic process of discussion and survey (figure 10).

01. Eyes.
02. Noise.
03. Ears.
04. Rectal and vaginal.
05. Skin.
06. Oral.
07. Specific areas of treatment.

Figure 1: Seven tables under 'PLACE OF APPLICATION' [1 to 7].

08. Wash hands.
09. Specific opening.
10. Drops and injectable.
11. To dissolve.
12. Shake.
13. Do not crush.
14. With water.

Figure 2: Seven tables under 'HANDLING' [8 to 14].

15. Medications combination.
16. Attention and allergies.
17. Alcohol interactions.
18. Interactions with specific products.
19. Dairy products.
20. Vehicles and machinery.
21. Sleepiness.
22. Dizziness.
23. Sun exposure.
24. Infants and babies.
25. Pregnancy.
26. Breast-feeding.

Figure 3: Twelve tables under 'EFFECTS' [15 to 26].

27. Pick up medicine.
28. Capsule and tablet.
29. Once a day, morning / on waking.
30. 1 time a day, noon / afternoon.
31. 1 time per day, night / bedtime.
32. 2 times a day.
33. 3 times a day.
34. 4 times a day.
35. Lunch dinner.
36. Breakfast / Brunch.
37. With food.
38. Before meals.
39. After meals.
40. Empty stomach.
41. Duration;
42. Overdose.

Figure 4: Sixteen tables under 'FREQUENCIES AND DOSES' [27 to 42].

43. Humidity and sunlight expose
44. Refrigerate.
45. Sharing and validity;
46. information leaflet;
47. emergencies.

Figure 5: Five tables under 'THE MEDICINE' [43 to 47].

SESSIONS FOR LINGUISTIC EVALUATION (3ᴿᴰ RESULT)

Although using a simple vocabulary, fewer and less technical words than the PILs, the therapeutic messages found on captions and instructions showed a great linguistic diversity for the same message, and redundancy, regardless of the language(s) used. Extensive written communication analysis was focused in how noticeable, comprehensible, readable, graphically intelligible, easy to learn and memorize, attention catching and motivating the message was. Language diversity, lexical density, syntactic complexity, were subject to critical analysis and several shortcomings were detected:

- Cultural abbreviations;
- Cultural word meanings;
- Too long and dense sentences;
- Complex sentences combining different warnings;
- Variety vocabulary in the same warning;
- Countless words for one single caption;
- Mixing negative and affirmative sentences for the same warning;
- Confusing modalities (affirmative, exclamatory, indicatory, suggestions or prohibitions);
- Puzzling typographic fonts and sizes on the same label;
- Ambiguous parenthesis, upper and lowercase;
- Unclear bold, underlined, italic and outlined type;
- Confusing meaning in coding, colours, type and background;
- Deficient graphic legibility, contrast and size;
- Indistinctive labelling format;
- Poor print readability;
- No association with equal international warnings out of medicinal context.

Research showed that the most common posology message is the warning about driving, associated with drowsiness or dizziness caused by the medicine. Also frequent are messages associated with the correct therapy, such as: 'Do not drink alcohol while taking this medicine', 'Take on an empty stomach', 'Take with meals', 'Take until gone', 'Shake well before using', 'Keep out of reach of children', 'Not to give to children and babies' or 'Do not take if pregnant or breast-feeding'.
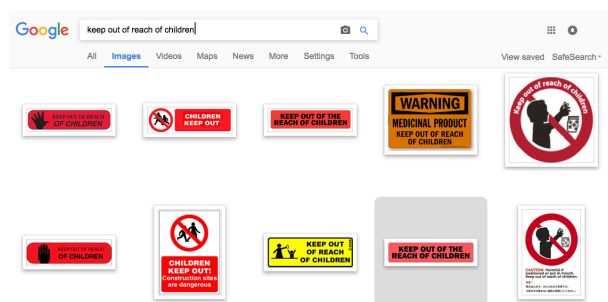

Figure 6: Examples on Google search for the message 'Keep out of reach of children' (Google 2017).
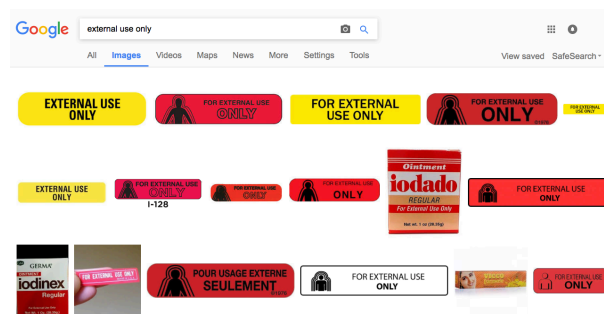

Figure 7: Examples on Google search for the message 'External use only' (Google 2017).

Some of the written messages found showed consensus on phrases in labels, not only in medicines, but in toxic products as well, e.g. 'Keep out of reach of children' [table 24] (figure 6) and 'External use' [table 5] (figure 7). Particular non-consensual examples, showing great variety of words and numbers, are common, and sometimes used also in other contexts - different products and foods, public spaces and buildings signage. Temperature awareness is a good example. Related to 'Keep away from heat' [table 43], 'Store in the refrigerator' and 'Do not freeze' [table 44], references are often shown on thermometer numbered scales, but they are confusing. Professional pharmacists encourage instead the use of three distinct uniform scales, '11°- 25°', '1°- 8°' and '+5°', respectively. Another confusing example, suggesting cultural differences, is related with 'Taking with food' [table 37] where very different are used for food, such as 'milk', 'toasts', 'rice', 'chicken', 'banana', 'fish' and 'hotdog'.

Regarding language diversity and cultural obstacles, several abbreviations were registered: AM for 'before midday', PM for 'after midday', HS (*hora somni*) for 'before sleep' but also for 'highly sensitive', PRN (*pro re nata)* for 'as needed' and finally 'RX' (meaning recipe) for 'prescription take' as the most used [table 12, 15, 27, 43, 44, 45 and 46].

Negative and affirmative sentences used for the same warning are often found, although they are strongly discouraged by professional pharmacists. In their opinion, negatives should be avoided whenever possible, because they amplify communicational problems. Some examples highlighted by the participatory team:

- use only 'Store in the refrigerator' and eliminate 'Do not store in the refrigerator', because this last sentence can actually mean 'Store in a dry and cool place' or 'Store away from heat and direct sunlight (11°- 25°)';
- use only 'Take by mouth' and eliminate 'Do not take by mouth' and 'Do not ingest' [table 6], as they actually mean 'External use only' [table 5], an injunction commonly used out of medicines labels;

- use only 'Shake well before use' and eliminate 'Do not Shake' [table 12];
- use only 'Take on empty stomach' and eliminate 'Do not take with meals' [table 40] that can be easily confused with 'Take with meals'.

As for the warning concerning the danger of handling vehicles and machines, linked with drowsiness, dizziness and sleepiness, the research revealed that for the same basic warning 'Do not drive' (figure 8) there were 23 different redundant captions, varying from 1 to 20 words.

DANGER
WARNING
CAUTION
Be careful
Do not drive
Be very careful
Driving: see prospectus
Attention, danger. Do not drive
Drowsiness and impair to ability to drive
If this medicine makes you dizzy, do not drive
Do not drive if this medicine makes you sleepy
May reduce the ability to drive or operate machines
Medical products contraindicated to vehicle drivers
Do not drive for the resumption of driving for the doctor's advice
Products which may reduce the ability to drive or operate machines
Be very careful. Do not drive without washing a health professional
May cause drowsiness
Be careful when driving a car or using machinery
Medical products which may reduce
the ability to drive or operate machines
Attention danger: do not drive
For driving resumption ask the doctor for advice
Medical products which significantly reduce
the ability to drive or operate machines
CAUTION THIS DRUG ALONE OR WITH ALCOHOL
MAY IMPAIR YOUR ABILITY TO DRIVE
May cause drowsiness. Alcohol may intensify this effect
Be careful when operating a car or using machinery
This drug may impair the ability to drive or operate machinery
Use care until you became familiar with its effects

Figure 8: Example of linguistic diversity in the same message 'Do not drive'. 23 different messages, from 1 word to 20 words.

Further examples with too many words, and extra-long sentences with more than 3 different warnings, were collected. The longest caption found concerned Storage instructions, with 39 words (figure 9).

KEEP THIS MEDICICINES IN A SAFE, DRY AND COOL PLACE THAT IS AWAY FROM HEAT AND DIRECT SUNLIGHT. DO NOT STORE THEM IN A BATHROOM OR NEAR A SINK, OR LEAVE THEM IN THE CAR OR ON A WINDOWSILL

Figure 9: The longest caption reaches 39 words, for the message 'Do not store near heat or in sunlight'.

SESSIONS FOR GRAPHIC DESIGN EVALUATION (4TH RESULT)

The posology written messages analysed were over 1000. Concerning graphic legibility, several peculiar examples were found, more graphically creative than informative in terms of typographies and calligraphy, combination of sizes, colours, uppercase and lowercase, bolds, underlines and outline types (figure 6 and 7).

Researchers also concluded that important graphic and linguistic relations link medicines messages to other areas of international warnings and instructions: road code signs; tourist pictograms; signage project symbols; symbols of labels, leaflets, products, vehicles and machines. In these areas, massive steps have been taken to improve international communication for social and cultural global movements, and for groups of people such as foreigners, tourists and migrants. This reinforces how important and urgent it is to develop international guidelines and a standardized system of medicines labels and instructions.

SURVEY AND PROCEDURES (5TH RESULT)

A questionnaire was applied to 100 Portuguese professional pharmacists and patients, within a three-month period, with the aim of (1) evaluating the level of importance of each warning, (2) collecting recommendations and suggestions to complement the linguistic content analysis, in order to (3) determine the final group of worldwide written messages for medicines.

The choice of a questionnaire appeared to us to be the most accurate to cover a large and geographically diverse number of professionals and patients involving urban and rural environments. Contacts were made by phone, personal letter delivered by hand and, in very few cases, by mail. Later, again, by phone. A 6 pages' questionnaire was sent by mail, where 75 messages were considered, linked to general categories of 'prohibitions', 'precautions' and 'information' (figure 10).
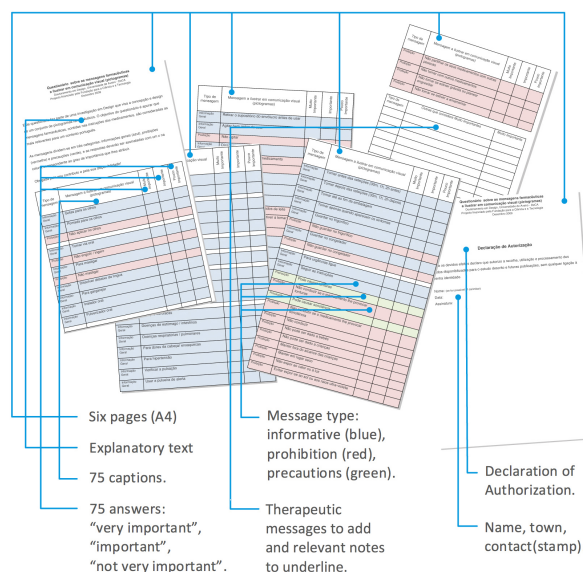

Six pages (A4)
Explanatory text
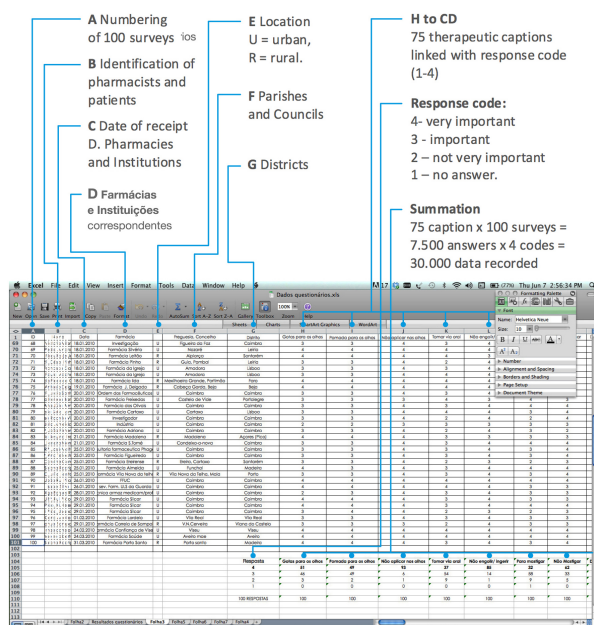75 captions.
75 answers:
"very important",
"important",
"not very important".

Message type:
informative (blue),
prohibition (red),
precautions (green).

Therapeutic
messages to add
and relevant notes
to underline.

Declaration of
Authorization.

Name, town,
contact(stamp).

Figure 10: Survey procedures

A Numbering
of 100 surveys ios

B Identification of
pharmacists and
patients

C Date of receipt
D. Pharmacies
and Institutions

D Farmácias
e Instituições
correspondentes

E Location
U = urban,
R = rural.

F Parishes
and Councils

G Districts

H to CD
75 therapeutic captions
linked with response code
(1-4)

Response code:
4- very important
3 - important
2 – not very important
1 – no answer.

Summation
75 caption x 100 surveys =
7.500 answers x 4 codes =
30.000 data recorded

Figure 11: Survey data collected – Microsoft Excel (2010)

Extraordinarily, adhesion was 100%, involving 74% respondents in urban areas and 26% in rural areas. 7.500 responses and 30.000 data were collected (figure 11).

FINAL RESULT AND DISCUSSION

The interdisciplinary study synthesis, and the survey, resulted in an original, and unique, set of 75 basic written therapeutic messages (figure 12), for three languages – English, Portuguese and French. Although the number of messages is the same – 75 – the messages are not the same. But this is a dynamic set, that may evolve and change as our research continues and the links with symbol messages in other areas is further exploited. For example, the message 'Do not ingest' was replaced by 'External use only', because professionals considered that negative messages should be avoided, the survey respondents considered that one eliminated the other and because 'External use only' is already internationally recognised. But this decision may need further testing, reflection and discussion.

Additionally, in the impossibility of standardize and implement all the messages at the same time, the Survey respondents ordered the messages according to their importance and the research team highlighted some messages as the more urgent group to standardize:

- 'Do not apply to the Eyes',
- 'Do not drink Alcohol while taking the medicine',
- 'Store in the refrigerator (1°-8°)',
- 'Keep out of reach of children',
- 'Do not drive or operate machines',
- 'Take with meals',
- 'Finish all this medicine',
- 'Do not take if you are Pregnant or if you think you are pregnant'.

1. Do not apply to the Eyes.
2. Do not drink Alcohol while taking the medicine.
3. Store in Refrigerator (1°- 8°).
4. Do not take with milk or Dairy products.
5. External use only.
6. Do not take if you are Pregnant or if you think you are pregnant.
7. Do not take if Breast-feeding.
8. Do not give this medicine to Children 3-12 years old.
9. Do not give this medicine to Babies 0-3 years old.
10. Keep out of reach of Children.
11. Do not take with Caffeine.
12. Do not Drive or operate machines.
13. Do not Break or Crush the tablets.
14. Do not take at Bedtime /
15. Do not Open the capsules.
16. Finish all this medicine.
17. Do not Drive if the medicine makes you sleepy.
18. Take on Empty stomach.
19. Shake well before use.
20. Take before Meals.
21. Do not Chew.
22. Do not take other Medicines with this medicine.
23. Take after Meals.
24. Store away from Heat and direct Sunlight (11°-25°).
25. Store in a Dry and Cool place (11°-25°).
26. Dissolve under the Tongue.
27. Avoid too much Sun or use of sunlamp.
28. Dissolve in Water.
29. Take with Meals.
30. Do not Share your medicines with others.
31. Injection use only.
32. Eye Drops.
33. Ear Drops.
34. Eye Ointment.
35. May cause Drowsiness.
36. Nose drops.
37. Ear use only.
38. For Rectal use only.
39. For emergencies Help call: ----------------.
40. Oral Inhaler.
41. Taken in the Morning, at wake up.
42. Taking at night, Bedtime.
43. Oral use only.
44. Take in the afternoon.
45. Take 1 time a day, 24 in 24 hours.
46. Nasal Spray.
47. Take with plenty of Water.
48. Take 4 times a day, 6 in 6 hours.
49. Take 3 times a day, 8 in 8 hours.
50. Use this medicine as a Gargle.
51. For Heart problems.
52. Take 2 times a day, 12 in 12 hours.
53. Apply to Skin only.
54. To Chew.
55. For Hypertension /high blood pressure..

56. For Lung / respiratory problems.
57. For Stomach / intestinal disorders.
58. May cause Dizziness.
59. Wash hands before and after.
60. Take only if Symptoms appear.
61. Wear medical alert.
62. For Headaches.
63. Check pulse and record before administration.
64. Remove foil before use.
65. Read the Label.
66. Patient allergic to: -----------.
67. Do not Smoke.
68. Bone fracture.
69. For Arthritis.
70. Days of Treatment: -------------.
71. For continual use.
72. Take as needed.
73. Limited dosage.
74. Dosage strength.
75. Limited validity after opening (6M, 9M, 12M, 36 M).

Figure 12: Result of Survey: 75 set messages ordered by respondents - English version

The most important caption, 'Do not apply to the Eyes', has no significant expression in the worldwide collection. This warning appears only twice in more than 1000 warnings in 20 countries researched. The warnings 'Keep out of reach of children' and 'Do not take if you are Pregnant or if you think you are pregnant' are already mandatory by legislation in PILs, nevertheless they are often difficult to notice in the dense texts, typical of PILs. The message 'Do not drive or operate machines' is one that, for the EU, most needs to be widely understood. Yet, it is the message that more shortcomings revealed (figure 8).

CONCLUSIONS AND FURTHERMORE
The final 75 messages in three languages allow particular items in the present long posology leaflets addressed to patients to be emphasized, providing a coherent and solid communication of relevant instructions and warnings, following a uniform logical linguistic and visual system (Zwaga 1984). We believe that sharing evidence-based information on medicines will open research to the world standardization of captions and labels and their graphic legibility. Furthermore, research on pharmaceutical pictograms across cultures is underway and captions can be displayed together with those pictograms.

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