Back Translation for Quality Control of Informed Consent Forms

By David Grunwald and Norman M. Goldfarb

FDA regulations and ICH guidelines both require that “the information that is given to the subject or the representative shall be in language understandable to the subject or the representative.” 1,2 Obviously, if an Informed Consent Form (ICF) is written in a language that the subject does not understand, it must be translated into a language the subject does understand.

ICFs are highly technical documents, so careful translation by certified medical translators is essential. Translation errors can change the meaning of important content, causing potential subjects to receive inaccurate information. They can also confuse meaning, so the ICF is more difficult to understand.

Many professional translation companies and independent translators are well-qualified to translate ICFs. However, even with certified medical translators, errors can occur because:

- Translation is more of an art than a science.
- Translators are unlikely to specialize in the specific medical condition under study.
- Time and money are usually limited.

In a normal translation process, the translator translates the document; an editor then reviews the translation and makes corrections. A more robust process includes “back-translation”, whereby a second translator translates the foreign language ICF back into the original language. The back translator should have excellent command of both languages, and perform a more literal translation than normal. The original and back-translated versions of the ICF can be compared side-by-side by the original authors of the document or the IRB. Back-translation addresses the first two causes of error cited above, but at the cost of the third – time and money.

Table 1 presents three paragraphs from a fictional English-language ICF along with two unedited and one edited translation into Spanish. Table 2 presents the respective translations back into English.

Comparing the unedited back translations to the original text reveals:

- As indicated by the highlighted words, both translations include substantive changes. Some of these changes, such as deleting the word “experimental” or adding the word “suffering”, change the meaning in important ways. Others, such as changing “hair growth” to “capillary growth” are medically incorrect. Others, such as “experimental blood”, make no sense.
- Spanish and English have different grammatical structures, so the numerous changes in wording and phrasing may or may not reflect changes in readability.
- The error rate suggests that quality control is essential.
- The translations have entirely different errors. The errors in a specific translation are thus unpredictable.

The edited translation (2a) makes numerous phrasing changes, but corrects none of the substantive changes. Table 3 describes the substantive changes. It demonstrates that back-translations are not definitive, but can be used to identify possible problems for review.
Even this small amount of data illustrates three different reasons why back translations may differ from the original text:

- Translator changed the meaning in the forward-translation.
- Translator changed the meaning in the back-translation.
- Literal back-translation of correct forward-translation appears to be error

The amount of data in this experiment is far too small to reach any definitive conclusions. It does, however, suggest that:

- Back-translations are valuable tools, but cannot replace editors.
- It may be essential for ICF authors to read the back-translations.
- A larger, more definitive, experiment would be worthwhile.

Back-translation increases the cost of translation by about 80%. A typical $800 ICF translation charge would thus increase to about $1,400. In addition, it takes time to make the necessary comparisons and correct errors. However, given the importance of accurate translations, the additional investment is more than justified.

Some Institutional Review Boards (IRBs) require back-translation of ICFs. For example:

"The Principal Investigator must translate the consent form if subjects expected to be enrolled are not fluent in written English. A completely translated copy of the informed consent and a complete back-translation done by two qualified translators must be submitted to the IRB before the translated ICF is approved." 3

(The ambiguity in this text reinforces the message that writing errors are easy to make. Does one translator do the forward-translation and another the back-translation, or do the two translators work together as a team on both translations?)

Because quality control personnel at translation companies are unlikely to speak every language their company translates, back-translation can also play an important role in identifying qualified translators.

<table>
<thead>
<tr>
<th>Table 1. Translations to Spanish</th>
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<tr>
<td><strong>Original</strong></td>
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<tr>
<td>You are being asked to participate in this study because you have been diagnosed with alopecia (hair loss) of the scalp. The purpose of this study is to determine if an experimental “study drug,” a patch containing capsaicin, is safe and effective when given to people with your condition. An experimental drug is one that has not received approval by the U.S. Food and</td>
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<td>Drug Administration (FDA).</td>
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Capsaicin is a man-made peppery substance found in chili peppers. Low-concentration capsaicin creams and patches are available without prescription for controlling pain from arthritis (swelling of the joints), back pain and painful muscle soreness. However, it is unknown if the experimental patches containing 10 to 20 times higher concentrations of capsaicin will be helpful in reversing alopecia. It is also unknown if any hair growth that results from treatment will be temporary or permanent.

If you qualify for the study, you will come in for two visits. At the first visit, we will measure your vital signs (blood pressure, heart rate, breathing rate and temperature), perform a physical exam, photograph your scalp, and take your medical history. We will collect a blood sample to measure the level of harontin in your blood. Harontin is a natural hormone associated with hair growth. We will collect approximately 2

| Si califica para el estudio, vendrá a dos consultas. En la primera consulta se tomarán sus constantes vitales (presión arterial, frecuencia cardíaca, frecuencia respiratoria y temperatura), se le hará un examen médico, se tomará una fotografía de su cuero cabelludo y se obtendrá su historia clínica. Obtendremos una muestra de su sangre para determinar el nivel de harontin. El harontin es una hormona natural asociada con el crecimiento capilar que resulte del tratamiento serán útiles para revertir la alopecia. Sin embargo, se desconoce si el crecimiento de cabello que pueda producirse a raíz del tratamiento será temporal o permanente. |
| La capsaicina es una versión sintética de una sustancia picosa que se encuentra en los chiles. Existen cremas y parches con bajas concentraciones de capsaicina, de venta sin receta, para el control del dolor causado por la artritis (inflamación de las articulaciones), dolor de espalda y fuerte dolor muscular. Sin embargo, no se sabe si los parches experimentales que contienen 10 a 20 veces la concentración de capsaicina serán útiles para revertir la alopecia. Tampoco se sabe si el crecimiento de cabello que pueda producirse a raíz del tratamiento será temporal o permanente. |
| En el caso de que usted califique para participar en el estudio, deberá presentarse a dos visitas médicas. En la primera visita, mediremos sus señales vitales (presión arterial, ritmo cardíaco, ritmo respiratorio y temperatura), realizaremos un examen físico, tomaremos una fotografía de su cuero cabelludo y hareemos una historia clínica. Haremos una extracción de sangre para medir el nivel de la harontinina en su sangre. La harontinina es una hormona natural que se encuentra en su sangre. La extracción de sangre será una parte importante del estudio y se realizará de manera que no cause dolor. En el caso de que usted califique para participar en el estudio, deberá presentarse a dos visitas médicas. En la primera visita, mediremos sus señales vitales (presión arterial, ritmo cardíaco, ritmo respiratorio y temperatura), realizaremos un examen físico, tomaremos una fotografía de su cuero cabelludo y hareemos una historia clínica. Haremos una extracción de sangre para medir el nivel de la harontinina en su sangre. La extracción de sangre será una parte importante del estudio y se realizará de manera que no cause dolor. |

Capsaicin is a man-made version of a peppery substance found in chili peppers. Low-concentration capsaicin creams and patches are available without prescription for controlling pain from arthritis (swelling of the joints), back pain and painful muscle soreness. However, it is unknown if the experimental patches containing 10 to 20 times higher concentrations of capsaicin will be helpful in reversing alopecia. It is also unknown if any hair growth that results from treatment will be temporary or permanent.

If you qualify for the study, you will come in for two visits. At the first visit, we will measure your vital signs (blood pressure, heart rate, breathing rate and temperature), perform a physical exam, photograph your scalp, and take your medical history. We will collect a blood sample to measure the level of harontin in your blood. Harontin is a natural hormone associated with hair growth. We will collect approximately 2
You are being asked to participate in this study because you have been diagnosed with alopecia (hair loss) of the scalp. The purpose of this study is to determine if an experimental "study drug," a patch containing capsaicin, is safe and effective when given to people with your condition. An experimental drug is one that has not received approval by the U.S. Food and Drug Administration (FDA).

Capsaicin is a man-made version of a peppery substance found in chili peppers. Low-concentration capsaicin creams and patches are available without prescription for controlling pain from arthritis (swelling of the joints), back pain and painful muscle soreness. However, it

You have been asked to participate in the study because you have been diagnosed with alopecia (hair loss) on the scalp. The purpose of this study is to determine whether the "experimental blood" of the study, a patch which contains capsaicin, is safe and efficacious when administered to persons suffering from your condition. An experimental drug is one which has not been approved by the United States Food and Drug Administration (FDA).

Capsaicin is a synthetic version of a spicy substance which is found in hot peppers. There are creams and patches with low concentrations of capsaicin, which are sold without a prescription, for the control of pain caused by arthritis (joint inflammation),

You are invited to participate in this study because you have been diagnosed with alopecia (hair loss) of the scalp. The purpose of this study is to determine if the "medication under study", a capsaicin patch, is safe and effective when provided to persons with your condition. An experimental medication is one that has not received the approval of the Food and Drug Administration of the United States.

Capsaicin is a manmade version of a spicy substance found in hot peppers.Creams and patches with a low concentration of capsaicin can be purchased without a medical prescription, for arthritis (swelling of the joints), back pain and muscle pain. However, it is unknown
is unknown if the experimental patches containing 10 to 20 times higher concentrations of capsaicin will be helpful in reversing alopecia. It is also unknown if any hair growth that results from treatment will be temporary or permanent.

shoulder pain and severe muscular pain. However, it is not known whether the experimental patches, which contain 10 to 20 times the concentration of capsaicin, will be useful for reversing alopecia. Nor is it known whether the hair growth which may be produced as a result of the treatment will be temporary or permanent.

if experimental patches with capsaicin concentrations 10 to 20 times stronger will serve to reverse alopecia. It is also unknown if the capillary growth resulting from treatment will be temporary or permanent.

However, it is not known if the experimental patches, which contain concentrations 10 and 20 times higher of capsaicin, will help to reverse alopecia. Neither is it known if the capillary growth resulting from treatment will be temporary or permanent.

If you qualify for the study, you will come in for two visits. At the first visit, we will measure your vital signs (blood pressure, heart rate, breathing rate and temperature), perform a physical exam, photograph your scalp, and take your medical history. We will collect a blood sample to measure the level of harontin in your blood. Harontin is a natural hormone associated with hair growth. We will collect approximately 2 tablespoons of blood. You will be asked to rate any discomfort or pain you have before, during and after the study patch application.

If you qualify for the study, you will come to two consultations. At the first consultation, your vital signs will be taken (blood pressure, heart rate, respiration rate and temperature), you will be subjected to a medical examination, a photograph of your scalp will be taken and your clinical history will be recorded. We will take a sample of your blood in order to determine the level of harontin. Harontin is a natural hormone associated with hair growth. We will take approximately 2 spoonfuls of blood. We will ask you to tell us the level of pain you experience during and after the application of the study patch.

If you qualify to participate in the study, you shall come for two medical visits. At the first visit, we will measure your vital signs (blood pressure, heart rate, respiratory rate and temperature), perform a physical examination, take a photograph of your scalp and complete a medical history. We will take a blood sample to measure the level of harontonina in your blood. Harontonina is a natural hormone associated with capillary growth. We will take approximately 2 tablespoons of blood. You will be asked to assess the level of discomfort of pain that you feel before, during and after applying the patch under study.

In the event that you meet the criteria for participating in this study, you shall go to two medical appointments. In the first appointment, we will measure your vital signs (blood pressure, heart rate, respiratory rate and temperature), perform a physical exam, take a photograph of your scalp and prepare your medical history. We will take a blood sample to measure the level of harontonina in your blood. Harontonina is a natural hormone associated with capillary growth. We will take approximately 2 tablespoons of blood. You will be asked to assess the level of discomfort of pain that you feel before, during and after applying the patch under study.

Table 3: Translation 2a Substantive Changes

<table>
<thead>
<tr>
<th>Change</th>
<th>Comments</th>
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<tbody>
<tr>
<td>Changed &quot;experimental 'study drug'&quot; to &quot;medication under study&quot;.</td>
<td>&quot;Medication under study” does not fully communicate the concept of “experimental drug”. The change was made in the forward-translation.</td>
</tr>
</tbody>
</table>
Changed “hair” to “capillary.”

“Capillary” in English means “a very small blood vessel.” In Spanish, “capilar” has that meaning and also “related to the hair.” The forward-translation was correct.

Changed “visits” to “medical appointments”.

Most clinical research is not “medical care”. The subject may, for example, receive a placebo. Calling visits “medical appointments” may increase the subjects’ therapeutic misconception. The change was made in the forward-translation.

Changed the term “harontin” to “harontina”.

The change was made in the forward-translation. The invented term “harontin” is not in the dictionary, so the translator took the liberty of giving it a Spanish flavor.

Changed “discomfort or pain” to “discomfort of pain”

The concept is lost that pain may be so minor as to be classified as mere discomfort. The forward-translation was correct; the change was made in the back-translation.

References

1. 45 CFR 46.116
2. ICH Subpart B Section 50.20

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