EORTC
European Organisation for Research and Treatment of Cancer
*The future of cancer therapy*

# GUIDANCE ON THE IMPLEMENTATION AND MANAGEMENT OF EORTC QUALITY OF LIFE INSTRUMENTS IN ELECTRONIC APPLICATIONS

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on behalf of the EORTC Quality of Life Group

# Contents

# 1. Introduction

## 1.1. The European Organisation for Research and Treatment of Cancer (EORTC)

The European Organisation for Research and Treatment of Cancer (EORTC) exists to develop, conduct, coordinate and stimulate translational and clinical research in Europe to advance the management of cancer and related problems through increased survival and improved quality of life (QOL). Multinational and multidisciplinary in nature, the EORTC network comprises over 300 hospitals and cancer centres in over 30 countries that include some 2,500 collaborators from all disciplines involved in cancer treatment and research.

In response to an identified need within the EORTC for a coherent policy on QOL research, a dedicated Quality of Life Group (QLG) was formed in 1981 to advise on the design, implementation and analysis of QOL studies within selected phase III clinical trials. Comprising a broad range of professionals (including oncologists, radiotherapists, surgeons, palliative care specialists, psychologists, social workers and research methodologists) the QLG has undertaken to develop a scientifically rigorous, standardised approach to the assessment of QOL across a spectrum of different cancers.

## 1.2. EORTC questionnaires

The EORTC QLG is best known for being responsible for the development of the Quality of Life Core Questionnaire (QLQ-C30). Having undergone several revisions since the original QLQ-C36 introduced in 1987 by Aaronson et al. (Aaronson 1993), the QLQ-C30 is designed to assess generic aspects of QOL in cancer. Additionally, in order to address aspects specific to particular tumour sites, treatment modalities or symptoms, a modular approach was adopted with further cancer-specific items included alongside the 30 core items. A highly standardised approach has been adopted for the development of these modules to ensure uniformly high quality.

The EORTC maintains the copyright on the QLQ-C30 and the modules which have been translated and validated in a variety of languages for use in studies worldwide. Funds generated through the copyright arrangement are used to support ongoing research of the QLG on the development and refinement of quality of life instruments.

### 1.2.1. CHES platform

To facilitate the integration of the EORTC QOL measures into research projects and daily clinical practice, the EORTC Quality of Life Group has partnered with Evaluation Software Development (www.ches.pro) to run a dedicated web platform, the CHES platform, which is currently accessible through the EORTC QOL website (https://eortc.ches.pro/).

## 1.3. Electronic patient-reported outcomes (ePRO)

Electronic patient-reported outcomes measures (ePROs) have increasingly been adopted by industry sponsors looking to benefit from the significant advantages associated with their use. Improvements in data integrity, a reduction in missing data and the accelerated availability of data (with the possibility of real-time monitoring) help ensure that the maximum value is realized from data collection during clinical trials. Whilst some instruments are developed initially in an electronic format, the majority of measures including those developed by the EORTC originate as pen-and-paper measures. Although research increasingly suggests that suitably migrated electronic versions perform similarly to their traditional counterparts, it is essential that assumptions are not made concerning the validity of such instruments and the extent to which they are equivalent to traditional pen-and-paper questionnaires. Sponsors may be required to provide evidence that supports comparability or measurement equivalence between electronic and traditional measures, and this can entail additional work on the part of sponsors to ensure that this is successfully achieved.

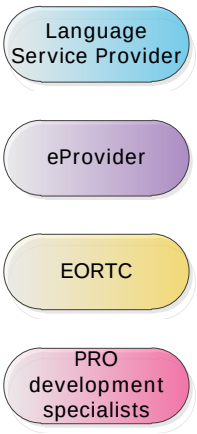
## 1.4. EORTC Guidance on the implementation and management of instruments

The EORTC has developed this guidance document to assist parties interested in using any of the available EORTC instruments in an electronic format. The intent of this document is to provide a framework for the implementation of these instruments in a consistent and controlled fashion. The EORTC is keen to promote consideration of QOL for people with cancer and understand that this is best served through ensuring good practice in the use of its instruments.

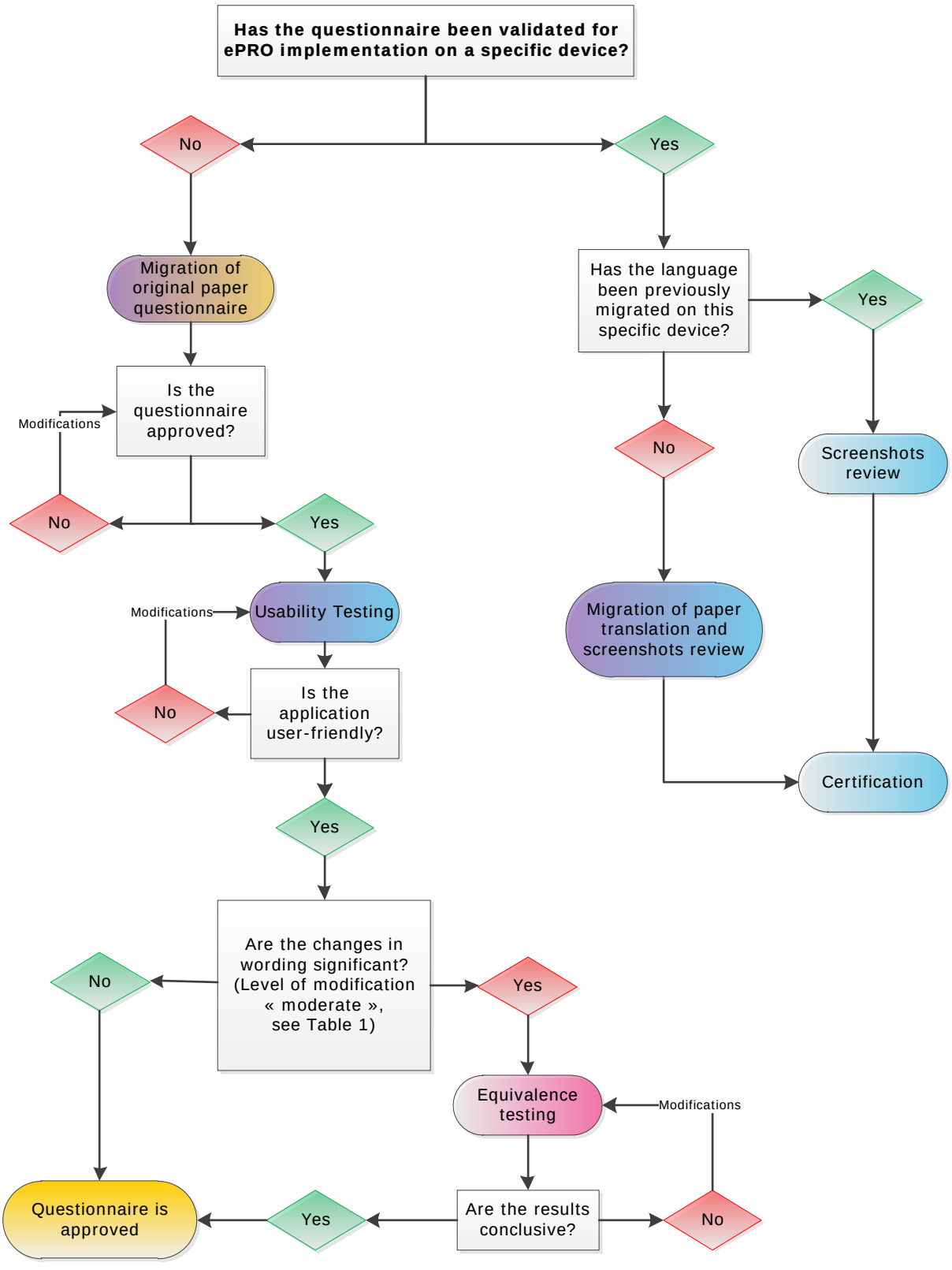
# 2. ePRO development and certification process

The flowchart on the following page shows the ePRO development and certification process and the relevant parties involved at each step.

The colour code is to be read as follows:




When several parties are involved they both appear in the “step cell”: 


Has the questionnaire been validated for ePRO implementation on a specific device?
No
Yes
Migration of original paper questionnaire
Is the questionnaire approved?
Modifications
No
Yes
Usability Testing
Modifications
No
Is the application user-friendly?
Yes
Are the changes in wording significant? (Level of modification « moderate », see Table 1)
No
Yes
Equivalence testing
Modifications
Questionnaire is approved
Yes
Are the results conclusive?
No
Has the language been previously migrated on this specific device?
Yes
No
Screenshots review
Migration of paper translation and screenshots review
Certification

# 3. Definitions

## 3.1. Migration of EORTC questionnaires to electronic formats

In order to migrate traditional pen-and-paper questionnaires to an electronic format it is essential that steps are taken to ensure that the method of administration does not introduce any unwanted influence on participant responses. Changes in presentation format may encourage participants to respond differently either intentionally or unintentionally. Ensuring that electronic versions of a questionnaire perform in the intended fashion is essential to be confident that the differences between administration methods do not lead to systematic differences in the data obtained and so results can be interpreted in the same way.

A substantial amount of research has been undertaken in order to establish the equivalence of properly adapted instruments and this has culminated in the publishing of various guidance documents on the topic. The EORTC recognizes that the recommendations (Coons 2009) produced by the ISPOR ePRO Good Research Practices Task Force represent a widely accepted and practical framework for consideration of questionnaire migration. The approach advocated by the ISPOR ePRO Task Force is to establish the equivalence of electronic and traditional measures through assessing the magnitude of modifications made in the migration process. Based on the magnitude of modification, evidence for measurement equivalence can be generated through a combination of different methodologies, namely cognitive debriefing/testing, usability testing or equivalence testing. Where the extent of modifications exceeds what could be deemed reasonable in preserving the integrity of the measure, full psychometric testing may be necessary.

## 3.2. Design specifications for EORTC instruments

See section 4.2.

## 3.3. Testing

Once the platform is developed and agreed upon by the EORTC and the eProvider, it will go through various levels of testing.

### 3.3.1. Usability testing

The purpose of the Usability Testing is to test the user-friendliness of the electronic version of each instrument with the targeted population through interviews. In this context, the goal of the interviews is not to evaluate the understanding of the questionnaire itself; rather, the usability testing covers the functional aspects of using electronic versions of the questionnaire. The cognitive component of the usability testing ensures instructions for completion are correctly understood by the target population. Major issues of concern in usability testing typically include aspects such as device complexity, navigation and response selection. This test is performed after the beta testing in order to avoid any technical problems during the administration of the ePRO in the target population. It is completed in the language and country in which the original instrument was developed, generally US English or UK English, by a trained interviewer.

### 3.3.2. Equivalence studies

Equivalence studies are typically deemed necessary when more substantial changes have been made in the instrument migration process, such as significant changes in wording, presentation format or the use of different cognitive processes (visual presentation to aural, for example). Equivalence testing typically involves either parallel or crossover administration of the different instrument versions and the use of statistical methods to compare the results. This is significantly more burdensome than the typical cognitive debriefing process commonly used and should be accompanied by substantial usability testing. In most instances, it is unlikely that equivalence testing will be required for appropriately migrated EORTC instruments as per the licensing agreement with the EORTC, which states that no major changes in wording are allowed and that any minor changes in wording will require the consent of the EORTC. Where equivalence testing is required as specified in the guidance (see section 4.1), developers will be required to notify the EORTC of their desire to undertake work sufficient to satisfy requirements.

## 3.4. Migration and certification of translations

A highly standardized ePRO translation certification process effectively ensures that the high level of requirement applied to various language versions of paper PROs will also be applied to ePRO versions of the EORTC instruments.

The ePRO translation certification process aims to:

(1) Update the translated version of the PRO so that it is in line with the ePRO source language version (English) of the instrument. This only focuses on updating the instructions for electronic completion (e.g., changing “circle” into “select”), adding/correcting any necessary formatting tags to reflect bolding, segmentation of items, etc.;

(2) Once the ePRO target language version is ready, have native-speaking linguists check the content and format as seen by the user in the application, backed up by standard quality control processes.

Failure to follow these critical steps may lead to less accurate translation of the user interface or instructions, errors in layout ranging from repeating items, missing an item altogether or mixing up response options, and ergonomic problems such as the translated text being too long or large and not fitting completely into the designed space.

# 4. EORTC requirements

## 4.1. ISPOR compliant

Recommendations of the ISPOR ePRO Task Force (Coons 2009)

**Table 1.** PRO to ePRO measurement equivalence: instrument modification and supporting evidence

| Level of modification | Rationale | Examples | Level of evidence required |
|---|---|---|---|
| **Minor** | The modification can be justified on the basis of logic and/or existing literature. No change in content or meaning. | 1) Nonsubstantive changes in instructions (e.g., from circling the response to touching the response on a screen).<br>2) Minor changes in format (e.g., one item per screen rather than multiple items on a page). | Usability testing and cognitive debriefing |
| **Moderate** | Based on the current empirical literature, the modification cannot be justified as minor. May change content or meaning. | 1) Changes in item wording or more significant changes in presentation that might alter interpretability.<br>2) Change in mode of administration involving different cognitive processes (e.g., paper [visual] to IVR [aural]). | Equivalence testing<br>Usability testing |

| | | | |
|---|---|---|---|
| **Substantial** | There is no existing empirical support for the equivalence of the modification and the modification clearly changes content or meaning. | 1) Substantial changes in item response options<br>2) Substantial changes in item wording | Full psychometric testing<br>Usability testing |

At all times, the methodology applied in the EORTC process will follow the ISPOR requirements.

## 4.2. EORTC recommendations for migration

With this document, the EORTC presents guidance that aims at ensuring comparability of its instruments migrated onto different devices. eProviders are encouraged to perform "faithful migrations" by minimizing the amount of modification to the content and format of the original paper version and by considering the recommendations in this document.

### 4.2.1. General considerations

- Given the general context of use of EORTC instruments, considerable attention should be paid to issues related to accessibility (e.g. sensory impairment or motor problems). Developers will be required to undertake and document usability testing of electronic versions and appropriate consideration of these issues early in the development process will help minimize the likelihood of problems occurring.
- There are no requirements for developers to use any specific font, colour or layout in displaying the EORTC instrument but they are encouraged to try and retain the simple and clear appearance of the pen-and-paper version.
- There are no explicit requirements regarding the number of items allowed per screen. A sensible layout will be agreed upon by the EORTC and the eProvider that should adhere as closely as possible to the original EORTC instrument whilst maintaining usability.

### 4.2.2. Instrument identification

- The instrument name, version number and the EORTC logo should be displayed prior to the items appearing on screen. The copyright details should be displayed at the end of each questionnaire (if the QLQ-C30 is being used with a module, the copyright of the QLQ-C30 should be displayed with the last question of the QLQ-C30, and the copyright of the module with the last question of the module).

### 4.2.3. Navigation

- The user is not required to provide a response to an item before they can continue with the next question.
- If the EORTC instrument has a skip pattern, the electronic version may show only the items that the subject needs to complete.
- The user should be permitted to revisit items and to change responses as necessary, and in such cases, the most recent response should be recorded. This should be possible at any point during completion until the final confirmation step.

- The user should not be required to make use of scrolling at any point during completion of the EORTC measures. An alternate presentation format should be employed if the items cannot be accommodated (one item or section per screen, for example).

### 4.2.4. Instructions

- The instructions provided at the start of the instrument should remain as consistent as possible with those presented in the pen-and-paper version of the instrument. It is suggested that the following instruction text is presented for the QLQ-C30:

  "We are interested in some things about you and your health. Please answer all of the questions yourself by selecting the number that best applies to you. There are no "right" or "wrong" answers. The information that you provide will remain strictly confidential."

  Individual modules have varying instructions and should be revised similarly. For example:

  "Patients sometimes report that they have the following symptoms or problems. Please indicate the extent to which you have experienced these symptoms or problems during the past week. Please answer by selecting the number that best applies to you."

- Where items are presented in a format which deviates from the original (such as one item per page), all appropriate instructions relevant to completion of that item should be included on the same screen (e.g. shortened item stem including the recall period).
- Additional sections with their own distinct instructions should employ similar wording revisions to address changes in method of completion. Any changes should first be discussed and approved by the EORTC.

### 4.2.5. ID, birthdate and completion date

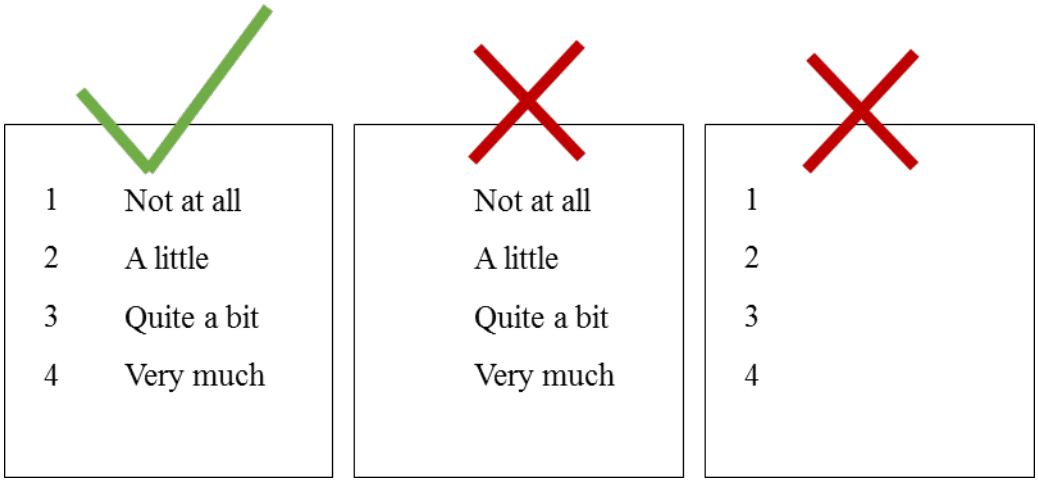
These fields may be automatically generated by the system. Where this does not occur, the following should apply:

- The birthdate field should use the appropriate regional date format and display text clearly to aid user completion (e.g. DD/MM/YYYY (**UK**), MM/DD/YYYY (**US**)). This can be modified as per local legislation requirements.
- If used, the completion date field should use the appropriate regional date format and display text clearly to aid user completion (e.g. DD/MM/YYYY (**UK**), MM/DD/YYYY (**US**)).

Where necessary this can be modified/deleted to accommodate national/regional legal and ethical standards.

### 4.2.6. Item response

- All response options available for an individual item should be displayed along with the item itself.
- No response options should be selected by default.
- All information relating to response options should be presented, i.e. the numerical responses with their associated text.




It is insufficient to present the numerical response options without the category descriptions.

- Any response which has been selected should be clearly visible to the user. This may take the form of highlighting, enclosing, marking or any other method which clearly indicates that the response option is selected. This method should not obscure or grey out other response options which could be subsequently selected if the user changes their mind.

### 4.2.7. Completion

- Respondents should be provided with an opportunity to confirm that they are satisfied with their responses prior to ending the item completion process.
- The name of the EORTC instrument and the associated copyright information should be present at some point during the completion process.

## 4.3. EORTC requirements for testing

### 4.3.1. Usability testing

Usability testing should be conducted each time a questionnaire is newly implemented on a device or operating system (e.g. iOS, Android).

#### *4.3.1.1 Usability testing methodology*

For the UT to be conducted, the ePRO (screenshots) must have been previously approved by the EORTC according to the requirements listed above (section 4.2.) and the UAT completed.

The interviews should be conducted face-to-face with eight respondents, who are native speakers of UK English, and should be audio-recorded. The recruitment criteria will be determined by the impact the disease has on the respondents when considering the electronic questionnaire completion as defined in the recruitment criteria table. The sample should be diverse in terms of age, gender, occupation, level of education (low to medium), handedness (left- or right-handed) and familiarity with technology.

The interviews will be conducted by experienced interviewers trained in UT interviewing and maintaining respondent confidentiality. Prior to the interviews, interviewers will be briefed to ensure they understand the study objectives and to ensure interviews are conducted consistently. The interviewer will take notes during the interviews regarding verbal and non-verbal participant reactions. Interviews will be non-interventional and will not influence the treatment and care a patient receives.

The interviews will be divided into two steps. First, respondents will complete the ePRO without any external help while the interviewer observes the respondent's reaction. Once the ePRO has been completed by the respondent, the interviewer asks them a set of questions to obtain feedback on the electronic platform, ease of use, navigation, comprehension of instructions, potential improvements, comparability with paper completion, etc. Once all interviews are complete, the interviewer reports all positive or negative feedback based on the respondents' answers to the questions, and the verbal and non-verbal participant reactions (boredom, sighs, irritation, etc.) during completion.

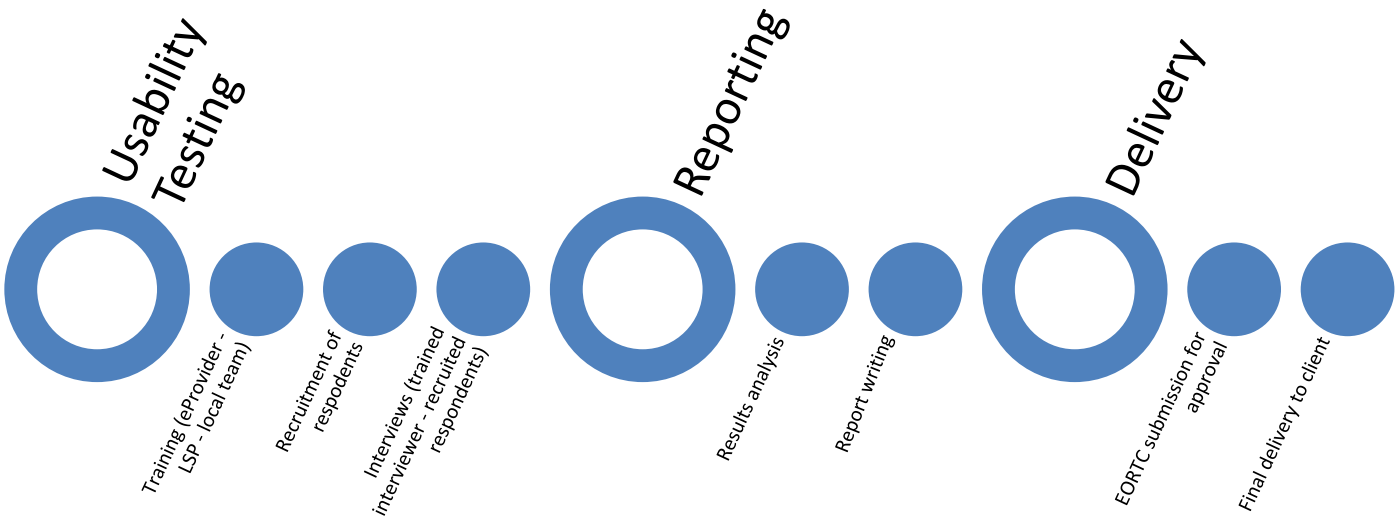
These results are then analysed and compiled in a report. If the results of the usability testing meet the following requirements, the questionnaire is considered ready to be used:

- The subject being tested proceeds quickly and without oral guidance through the questionnaire.
- The subject has no difficulty in understanding instructions.
- Text display is accurate (size, typography).

- No major improvements are recommended by the subject.

The report is then submitted for validation to the EORTC. Should there be any need for major modification or major improvement further to the interviews, a new UT is conducted with a new sample of respondents following the same process.

**Diagram 1.** UT workflow.




The diagram below shows a visualization of the UT workflow.

- Training: the eProvider trains the LSP and/or fieldworker on how to use the device.
- Recruitment of the respondents who will be testing the ePRO on the device as per agreed criteria.
- Interviews: conducted by trained interviewer, face to face, audio recorded.
- Results analysis: analysis of the respondents' reactions to the ePRO and their answers to the defined questions.
- Report writing: writing of a report summarizing respondent profiles, respondent feedback and recommendations.
- Delivery: report to be sent to the EORTC for approval, discussion, and if needed, clarifications. If the report is rejected, a new round of usability testing is needed.

#### *4.3.1.2 Usability testing validity*

The Usability Testing validation expires:

- When the device is changed (i.e. smartphone vs tablet, etc.), leading to major difference in screen size, change to a different operating system, and so on. This applies to device-based ePRO;
- When the operating system has undergone major upgrades such as design or performance (app-based ePRO) improvements. This can be assessed during screenshot review through a comparison.

Furthermore, UT validity is eProvider-dependent.

### 4.3.2. Equivalence studies

The necessity for equivalence testing is established by the extent of modification required in order to migrate the instrument according to the recommendations of the ISPOR ePRO Task Force (see table 1, section 4.1). It is unlikely that equivalence testing will be required in most circumstances but could be necessary for efforts involving changes in the method of administration which might require other cognitive processes (e.g. moving from pen-and-paper to an IVRS system). If developers identify the potential need for equivalence testing then they should notify the EORTC.

Equivalence studies undertaken using EORTC instruments should follow the guidelines specified in Coons et al. (2009). Where practical, it is recommended that a randomized crossover design is employed and that weighted kappa, ICC and/or mean score comparison statistics are reported at a minimum. A brief report should be prepared which documents the methodology employed, the results obtained, and which provides detailed information on the instrument migration. Where developers are unfamiliar with the design and conduct of such studies, it is highly recommended that they seek appropriate support. The EORTC can provide assistance in identifying potential partners for such efforts.

Note: Where the level of modification reaches the “substantial” threshold as indicated in table 1 (see section 4.1), the extent of changes indicates that the instrument deviates significantly from the format of the original pen-and-paper EORTC measure. Such deviations constitute a departure from the original instrument and need to be discussed directly with the EORTC before additional work is undertaken to ensure that appropriate research and copyright issues are addressed.

## 4.4. EORTC requirements for migrating and certifying translations

### 4.4.1. Migration of translations from paper to electronic format

The migration of target language PROs can be initiated once the English electronic version of a PRO:

- Has been approved by the EORTC (screenshots).
- Has gone through the various levels of testing.
- Has been certified as being in line with the paper PRO and suitable for use.

The purpose of this step is to migrate existing PRO instruments previously validated through a complete linguistic validation process into electronic versions for electronic devices (smartphones, tablets, etc.). Based on the English resource template provided by the eProvider, native speakers of the target language populate the resource file (.txt, .xls, .xml, .js, .Json, etc) with the existing paper PRO and update completion instructions to match electronic administration of the instrument (changing “circle” into “select”, for example). The wording which requires updates is identified and approved by the EORTC prior to the migration step. Once proofread, the file is sent to the eProvider for the creation of screenshots.

### 4.4.2. Checking and certification of screenshots

After the eProvider generates screenshots for the target language, these are sent to the in-country reviewer together with the corresponding screen report template. The screen report may include screen numbers, the English screens and target language screens, a column for comments, etc. The in-country reviewer then compares:

- The target language screenshots with the paper translations to ensure accurate retrieval of the validated wording.
- The English source screenshots with the target language screenshots, focusing on wording, layout, spelling, grammar, bolding, capitalization, title bars, etc.

Should corrections be needed, the in-country reviewer will report them in order for the eProvider to implement them. This process is followed until the target language screenshots are error-free.

Target language ePROs can be certified once they have been confirmed as being in line with the corresponding existing paper version in terms of wording and with the original English electronic version in terms of layout, and provided they remain free of any display, spelling or grammar issues.

# 5. Expiration date of the guidance

This document is the first edition of the ePRO Guidance. It is valid for two years from the date of its publication (January 2018). It will be revised and republished before January 2020.

# 6. References

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