QOL Office Checklist of instructions for the administration of Patient Reported Outcome Measures

The QOL Office recommends that this this checklist is used in conjunction with the SPIRIT-PRO and PRO CoMiDa Form

Preamble

Patient-Reported Outcome measures (PROMs) should be administered in a standardised manner to maximise PRO completion rates and reduce the potential for response bias - which may be caused when patients are given different information or instructions about the PRO study.

The Quality of Life Office has developed this checklist for PROM administration for people who work on trials led by the national Cancer Clinical Trials Group (CCTG), e.g. clinical research associates, trial managers, study coordinators, site coordinators, and research nurses. CCTGs may use this checklist to develop PRO aspects of site manuals, standardised operating procedures etc. for trial staff.

The checklist includes examples of how to address each checklist item in a study coordinator's manual. These examples are not exhaustive and are illustrative only. CCTGs may adapt the text to suit specific trials.

This document was prepared by Rebecca Mercieca-Bebber on behalf of the QOL Office, drawing on published literature, existing guidance from international trials groups (South West Oncology Group (SWOG) Training Module, presented by Dr Lisa Hansen; and the EORTC Clinical Trial Guidelines); interviews with Australian site coordinators, and the QOL Office's experience with PRO administration. We acknowledge early feedback on required content at the 2013 Inter-group QOL Management and Planning Meeting by representatives from the Cancer Clinical Trials Groups (CCTGs), specifically Dianne Lindsay, Corinna Beckmore (ANZBCTG), Janey Stone (ALLG), Elizabeth Paton (ANZMTG), Dagmara Poprawski (ANZUP), Haryana Dhillon (ANZUP, ALLG, PoCoG), Rasha Cosman (COGNO) and Melissa Crain (TROG), as well as feedback provided on the final draft at the2015 Inter-group QOL Management and Planning Meeting by CCTG representatives: Howard Chan (AGITG/ANZUP), Megan Sanders (ALLG), Natasha Roberts (ALTG),: Peey-Sei Kok (ANZGOG/ALTG), Ashleigh Qama (PC4), Joan Torony (TROG), Margaret-Ann Tait (QOL Office), Corrina Beckmore (ANZBCTG), Janelle Jones (ANZCHOG), Linda Cowan (ASSG), Renee Swanson, Merryn Hall (COGNO).

Acronyms

CCTGs	Cancer Clinical Trials Groups
CoMiDa Form	The PRO Completion and Missing Data Form Available at: http://www.pocog.org.au/docview.aspx?id=211
PRO	Patient-Reported Outcomes (including QOL)
PROM	Patient-Reported Outcomes Measure (questionnaire)
QOL	Quality of life
SPIRIT-PRO	Standard Protocol Items for Randomised Intervention Trials – Patient-Reported Outcome extension

PRO administration

Section	Checklist item	Hardcopy (H) PRO	Electronic (E) PRO	Elaboration	Example
Delegation log/responsible person/s	1. Name the staff member/s responsible for PRO administration	✓	✓	**H/E:** Ensure staff are aware of their responsibility to administer PROs. PRO administration may also be recorded as a task in the Trial Delegation Log.	**Responsible person** **H/E:** Jane Smith, Site coordinator, is responsible for administration of PROs and associated follow-up in the ABC123 trial at Site X.
Informed consent process	2. Procedures for providing information about the PRO study	✓	✓	**H/E:** Ensure patients are adequately informed about the PRO study (purpose, assessment schedule, who will see the data, when and how PRO data will be used).	**Informed consent process** **H/E:** Site staff should have a process in place for informing patients about the PRO study such as detailed informed consent process (i.e. verbal explanation as well as a patient information sheet).
	3. Aspects of PRO study to discuss with patient	✓	✓	**H/E:** Consider how and where consent will be obtained. E.g. face-to-face in the clinic or online. If obtaining consent electronically, ensure patients have access to clear information about the PRO study & contact details of an authorized member of the team with whom to discuss queries.	**H/E:** Patients usually are overwhelmed with clinical information at the consent stage, however the site coordinator should discuss the following aspects of PRO assessment & ensure the patient understands (in addition to Patient Information Sheet): • **H/E:** why PROs are being assessed (e.g. to determine whether and how long surgery has an impact on the patient's daily functioning & specific symptoms). • **H/E:** schedule of PRO assessments (e.g. baseline, hospital discharge, 3 months post- surgery, 1 year). • **H/E:** responses should be honest and the patient's own. • **H/E:** only the central research team will view their PRO responses. • **H/E:** De-identified data will be analysed in one year and at the end of the study (in approx. 3 years). • **H/E:** PRO data will not be used to inform their care. Health concerns should be

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					raised with their clinician. • **H/E:** PRO questionnaires and data will be securely stored. • **H/E:** More information on the PRO study is included in the Information Statement or they can contact the site coordinator. • **E:** Patients must have access to a computer, smart phone or tablet to take part. • **E:** All assessments will be completed online – from anywhere that has an internet connection. Patients will receive an email to complete PRO assessments and a reminder. • **E:** Patients will be issued a log-in and password which they need to use for the duration of the study. • **E:** Patients can contact the site coordinator for technical assistance.
Patient details	4. Specify what contact information is required.	✓	✓	**H/E:** The patient's contact details may be required for follow-up assessments (e.g. e-mail address, home address or phone number).	**Patient contact details** • **H:** For longitudinal research the patient's preferred contact details (e.g. e-mail/home address and phone number) may be required for follow-up PRO assessments. • **E:** e-mail address or mobile phone number may be required.
	5. Procedures for maintaining up-to-date patient records	✓	✓	**H/E:** Keep details and treatment records up-to-date. (particularly death dates).	**H/E:** Update patient records regularly by checking patient details at clinic visits, or contacting patient GPs
Patient eligibility/ Registration/ randomisation	6. PRO-specific eligibility criteria	✓	✓	**H/E:** Specify any PRO study-specific eligibility criteria (language/s of questionnaire availability, physical ability to	**Eligibility** • **H/E:** Patient must be able to read/write in English to take part in the PRO study; • **E:** Patient must have access to a personal

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				complete questionnaires).	computer and a personal e-mail address (for sending the survey link and reminders). It is not acceptable for patients to use a family member's or friends email address; • **E:** Patient must understand how to use email/computer.
	7. PRO-specific registration/ randomisation requirements	✓	✓	**H/E:** Specify any PRO study registration requirements (baseline PRO completion, additional consent – if required). Baseline PRO assessment is crucial for analysis and interpretation of PRO data, and it is commonly a trial inclusion criterion.	**Registration/randomisation requirements.** • **H/E:** Baseline PRO assessment must be complete prior to trial randomisation; • **H/E:** Patients are automatically registered onto the PRO study as part of the trial registration. If patient is ineligible for the PRO study, please complete XX form. • **E:** On the ADMINISTRATION page: The site coordinator should register the patient to the PRO study database using the participant's trial registration ID as log-in and participant's own chosen password. • **E:** Return to the landing page so the participant can enter their log-in information. • **E:** Once logged in, participants should click the assessment due (in RED text). • **E:** If patient is ineligible for the PRO study, please complete XX form in REDCap.
	8. Procedures for registering participants to the PRO study (if separate from main study)	✓	✓		
Preparation	9. Instructions for preparing PRO assessment	✓	✗	**H:** Specify how PRO measures should be prepared (e.g. insertion of participant ID numbers, etc).	**Preparation:** • **H:** Insert the patient's trial registration number and date onto the cover and each subsequent page of the questionnaire booklet with black or blue ink. • **H:** Participants should complete the questionnaire in back or blue ink.

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Information about accessing PRO questionnaires electronically	10. Provide a link to questionnaire (if online) or access to a PRO app.	✗	✓	**E:** Provide details of the steps involved in administering questionnaire online. <u>*Note:*</u> Site staff will require training in how to use the device and how to trouble shoot basic technical issues that patients might face in navigating and completing questionnaires.	**The Questionnaire database** • **E:** The PRO assessment database is available at <<insert web link>>
	11. Provide instructions for navigating and completing the electronic questionnaire.	✗	✓		<u>Issues for site staff</u> • **E:** The LANDING page includes the participant information sheet, an administration link and log-in/password fields. • **E:** The site coordinator should click the ADMINISTRATION link to issue the participants with a database log-in (trial registration ID).Ask the patient to choose their own password (6-10 characters). • **E:** The site coordinator will need to keep track of when assessments are due in order to send reminders to patients. <u>Instructions for patients</u> • **E:** Participants log-in to the assessment on the landing page. • **E:** Once logged in, participants will see a list of all PRO assessments scheduled for the trial. The assessment due will be in RED text. Completed assessments will be in GREEN. Future assessments are in grey font. • **E:** Participants will only be able to access surveys during the active PRO assessment time windows*. • **E:** Participants should click on the assessment hyperlink to access the survey. • **E:** Instructions for the patient are included in the email text. Staff will send reminder

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					emails to participants prior to each upcoming assessment.
	12. Details of contact person for technical support.	✗	✓		• **E:** Contact ___ for technical support via <email> and <phone> • **E:** A hardcopy of the questions is included as an appendix in the relevant trial documentation
PRO administration	13. Verbal instructions for the patient (at first PRO assessment and subsequent assessments if necessary).	✓	✓	**H/E:** If patients are unaware of the purpose and importance of PRO data, they may miss questions or fail to complete questionnaires, thus this should be explained to patients at their first assessment, and at subsequent assessments, if required.	Instructions for the patient (at first PRO assessment and subsequent assessments, if necessary) • **H/E:** Explain the purpose of PRO assessment and read questionnaire instructions to the patient and ensure they understand. The following script may assist: *"We are interested in learning about how this treatment impacts your daily life throughout treatment and into your recovery. This questionnaire lists some issues that you may or may not be experiencing. Each question has four response options: "not at all, a little, quite a bit, very much".* *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 and wont impact the treatment that you receive. It's really important that you answer all of the questions as best you can, and that you are honest – as this information will be very useful for future patients.* *If you have any questions or if the questionnaire raises any concerns for you, please let me know. "* • **E:** Explain that the patient will need to use their login to access this and all future surveys.

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	14. Specify time of PRO completion.	✓	✓		**Timing and place of completion** • **H/E:** Patients should complete questionnaires prior to seeing their clinician. • **H/E:** Patients should complete questionnaires independently, in a quiet/private location. • **H:** Discourage patients from taking questionnaires home.
	15. Specify place of PRO completion.	✓	✓		
	16. Procedures for contacting patients for PRO assessments	✓	✓		**PRO administration** • **E:** Email the survey link & patient's username to the patient on the day the assessment is scheduled as per protocol; or at the beginning of the allowable assessment period if a time window* is specified in the protocol. Instructions for how the participants can access and complete the questionnaire should be included in the email text. • **H:** If PRO assessment does not coincide with clinic visit, email or post a paper version with instructions for how to complete and return the questionnaire.
	17. Who patients can contact if they require technical assistance	✗	✓		• **E:** The email should include who the patient can contact for technical assistance, including lost passwords, access problems or other technical faults.
Assessment reminders (if permitted)	18. Specify PRO assessment reminder schedule.	✓	✓	**H/E:** Specify whether/when reminders by e-mail, phone or post are permitted. Include email/letter templates and telephone scripts.	**Assessment reminders:** • **H/E:** Use the email/letter templates provided for all correspondence. • **H/E:** Contact the patient (by text message, phone call, e-mail) to complete their assessment on Day X (or within the allowable assessment period if a time window* is specified in the protocol).
	19. Specify PRO assessment reminder procedures.	✓	✓		

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					• **H/E:** For protocols that specify a time window*, if the patient has not completed the questionnaire by the middle of the time-window*, send an email reminder or text message according to the following reminder schedule: ○ Contact 1: sent Day 1 of time window* ○ Reminder 1: mid-time window* ○ Reminder 2: day before time window* ends **H/E:** If no response is received by the time of the second reminder, you may call the patient to alert them of the assessment.
Patients in need of assistance	20. Nature of assistance allowed from coordinators	✓	✓	**H/E:** Some patients may need assistance completing hardcopy or online questionnaires. Not providing assistance when required may lead to missing data. It is important that assistance is provided in an objective manner and that the nature of assistance is documented.	**Allowable levels of patient assistance** • **H/E:** A trained site coordinator can read questions to the participant and/or record participant's responses on the questionnaire if the patient ○ **H/E:** left reading glasses at home or is visually impaired ○ **H/E:** has severe arthritis preventing them from being able to write or type • **E:** if patient cannot get access to the internet during the study window, responses may be collected via telephone. • **H/E:** The assisting staff member should: ○ only read questions and record patient's responses. ○ always allow the participant to choose responses. ○ maintain an objective voice tone, without making any comments on the patient's responses. ○ avoid rephrasing and interpreting the

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					questions if patient asks for clarification. ○ document the level of assistance required on the CoMiDa form. • **H/E:** Generally, patient's family/friend should not provide assistance due to potential for unconscious bias either by patient or family/friend.
	21. Instructions for non-English speaking patients (if permitted by the protocol)	✓	✓	**H/E:** If validated questionnaire translations are available, participants may choose to complete questionnaires in their preferred language. Assistance may be required for informed consent. English questionnaires should not be translated by staff, family members or hospital translators as this may introduce bias.	**Non-English-speaking participants** • **H/E:** Patients may choose to complete the questionnaire in any of the following languages, for which validated language translations are available : Afrikaans, Arabic, Cantonese, Dutch, English, French, German, Russian….etc • **H/E:** A translator should NOT be used to assist study participants complete questionnaires as they can introduce bias. • **H/E:** If a validated questionnaire translation is not available for a certain language, the participant may need to be excluded from the PRO study. Contact the central trial office for advice.
Proxy assessment (if protocol allows). A proxy is a person (typically a family care-giver or health professional) who reports an outcome on behalf of a patient, as if he or she was the patient him or herself.	22. Conditions proxy assessment is allowed	✓	✓	**H/E:** Proxy assessment may be permitted for these patients, if permitted by the protocol. This involves a third party completing a questionnaire about the health status of the patient.	**Proxy assessments** • **H/E:** Proxy assessment may be permitted for patients who are unable to self-report due to cognitive impairment. This involves a third party completing a questionnaire about the health status of the patient.

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	23. Suitable proxies	✓	✓	**H/E:** Ideally a proxy is able to accurately and reliably report on the patient's health status as if they were the patient. Suitable proxies must therefore be sufficiently familiar with the patient's health status, level of functioning and symptom experience.	• **H/E:** If proxies must be used, try to ensure each patient uses the same proxy to complete all assessments (i.e. always the mother of Patient X, always the daughter of patient Y, always the husband of Patient Z). This will improve reliability of responses for each patient. • **H/E:** A close family member or friend may act as the proxy. • **H/E:** In certain situations a nurse who has consistently provided care for the patient may be a suitable proxy.
	24. Special/additional instructions for proxy assessment.	✓	✓		• **H/E:** Document the relationship of the proxy to the patient on the CoMiDa Form.
Common problems	25. Procedures (as per protocol) for assessing PROs in patients who come off the trial early.	✓	✓	**H/E:** When participants are taken off trial for toxicity or progression, the decision of whether to continue administering PROs depends on the trial. Please consult the trial protocol. Some trials specify that PRO assessment ceases when the patient comes off the treatment they were initially allocated to, while other trials continue to administer PROs indefinitely, until patient is too sick to complete.	**Patients who withdraw/deviate from treatment protocol** • **H/E:** All patients, regardless of treatment status, should be assessed at all scheduled PRO assessment time points (final assessment two-years post treatment commencement). • Once a patient's cancer has progressed while on allocated treatment, a final exit PRO questionnaire should be completed.
	26. Procedures (as per protocol) for patients who withdraw from the PRO study.	✓	✓		• **H/E:** If a patient wishes to withdraw from the PRO study, do not administer further PRO assessments. Complete the PRO withdrawal form in REDCap.

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	27. Assessment schedules for when patients' treatment schedule differs from the treatment protocol.	✓	✓	If the participant's treatment schedule differs from the treatment protocol, refer to the protocol – does it specify whether to adjust the patient's PRO assessment schedule.	• **H/E:** If a patient's treatment schedule is altered during the trial, only PRO assessments scheduled during treatment (Cycle 2 and Cycle 4) should be adjusted to take place on the first day of each treatment cycle. Subsequent assessments (6, 12, 18, 24 months post-treatment commencement) should not be altered (i.e. they should be calculated using Day 1 of treatment as the reference point).
	28. Who to contact in the event of technical problems.	✗	✓	Provide guidance for handling common technical problems and who to contact in the event of a technical problem.	**Technical issues** • **E:** Contact <support person> for technical support via <email> and <phone> • **E:** If the patient is having trouble completing the assessment online at home, try to offer guidance over the phone. If not possible, you may use a hardcopy of the questionnaire (see appendix) and read the questions to the patient over the phone. Record their answers on a paper copy or directly into the study database. • **E:** Record the assistance provided on the CoMiDa Form.
Completed PRO assessments	29. Procedures for checking questionnaires and resolving incompleteness	✓	✗	**H:** Implement strategies for assessing completeness of the current questionnaire. Staff should check for any missing data (e.g. missed items or pages) and resolve with patients immediately, before they leave the clinic.	**Completed PRO assessments** While the patient is still in the clinic, staff should: • **H:** Review questionnaires for completeness while the patient is present, focussing on completeness of responses only; ○ **H:** Site staff should remain neutral when checking questionnaires. Don't express opinion about responses. • **H:** Missed question? Politely inform the patient they have missed the question and ask if they would like to answer it. If not, note that the patient declined to complete the question on

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					the CoMiDa form. • **H:** Missed page? Pages may be stuck together or only one side of a double-sided questionnaire completed. Politely inform the patient they have missed some of the questionnaire and ask if they would like to complete the remainder. If necessary, ask if they would like some assistance. If the patient does not wish to complete the questionnaire, include a note accordingly on the PRO CoMiDa Form.
	30. Procedures for addressing common problems with hardcopy questionnaires	✓	✗	**H:** Staff should check for any other completion problems (e.g. multiple responses to a single question) and resolve with patients immediately, before they leave the clinic.	How to address common problems: • **H:** Two responses for one question? Ask patient to check & choose the response that best describes their health status.
	31. Procedures for enhancing patient engagement with completion of future questionnaires	✓	✓	**H/E:** Implement strategies for enhancing patient engagement with completion of future questionnaires e.g. staff showing appreciation when completed questionnaires are submitted will reinforce the importance of PRO data to patients.	Strategies for enhancing patient engagement: • **H/E:** show appreciation when questionnaires are completed. • **H/E:** ask the patient if they have any concerns.
Missed PRO assessments	32. Specify procedures for following up missed PRO assessments (e.g. alternative mode of administration).	✓	✓	**H/E:** Every effort should be made to obtain the required PRO data within the assessment time window* – to avoid missing data. This may be due to a missed clinic appointment or running out of time when the patient is in the clinic. In such cases, the questionnaire can be administered by an alternative mode. A recent systematic review confirmed that changing the mode of questionnaire administration does not lead to bias.	**Missed PRO assessments** **H/E:** Every effort should be made to obtain the required PRO data within the assessment time window*. This may involve: • **H/E:** rescheduling appointments so that data may be collected in the clinic. • **H/E:** administering the questionnaire by phone soon after the missed clinic visit. • **H/E:** texting patient with a reminder to complete the questionnaire by the end of the time window*.

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					• **H/E:** document the mode of completion on the CoMiDa Form. If the questionnaire is not completed within the time window*, document the reason for non-completion on the CoMiDa Form.
E-mail bounces	33. Specify procedure for email bounces.	✗	✓	**E:** Patient email contact details may change.	**Email bounces** • **E:** If emails bounce, attempt to contact the patient by phone to update the email address.
Recording reasons for missing data	34. Complete the PRO CoMiDa form	✓	✓	**H/E:** The PRO CoMiDa Form is a data management tool, designed to provide standardised documentation of the completion or reasons for non-completion of PRO assessments by patients in a clinical trial/study. Such documentation is crucial for quality assurance since missing data are the greatest threat to the generalisability and interpretability of PRO data.	**Complete the PRO CoMiDa Form** **H/E:** Complete the PRO CoMiDa Form – for each patient, for each scheduled assessment (upon completion, or by the end of assessment time window* if PROs not completed)
Concerning PRO data	35. Procedures if patient reports concerning symptoms/health status	✓	✓	**H/E:** High levels of symptoms or health status problems may be indicated by a patient's PRO responses. Refer to the protocol to determine whether or not PRO data will be monitored during the study to inform the clinical care of participants and if so how this will be managed in a standardized way.	**Concerning PRO data may be dealt with in different ways by different trial teams as these two contrasting examples indicate:** • **H/E:** As specified in the protocol, if a research nurse or site staff member identifies a high level symptom or health status problem when reviewing questionnaire responses, the site coordinator should alert the treating clinician immediately. The clinician will decide whether to refer the patient to other health services. • **H/E:** As specified in the protocol and patient information sheet, questionnaire responses will not be viewed by a member of the patient's treatment team. Suggest to report any concerns directly to the treatment team.

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				Patients may also become distressed by the process of answering a PRO questionnaire. Refer to the participant information sheet and consent form for referral process for these patients. Procedures should be implemented consistently to avoid introducing bias.	**H/E:** Some people may become distressed by the process of completing a PRO questionnaire. As specified in the protocol and patient information sheet, patients who become upset or distressed as a result of participation in this research may contact the study doctor or be referred to counselling services, e.g. Cancer Council Helpline (13 11 20) or Lifeline (13 11 40) or staff trained to work with distressed callers. • **H/E:** Keep a record of any referrals the patient receives.
Forwarding PRO data to central office	36. Procedures for returning completed questionnaires to central office / data entry	✓	✗		**Forwarding PRO data to** central **office** • **H:** The site coordinator should enter PRO data into REDCap within two weeks of completion. • **H:** Stored completed questionnaires at the site.
Data storage	37. Data storage requirements	✓	✓	Data storage requirements should be in line with GCP data protection guidelines, as for all trial CRFs.	**Data storage** **H/E:** Completed PRO questionnaires should be stored securely in an online database, at the site or in an approved archive centre for 15 years. After this period, contact the central office for instructions.

***Time window: a predefined time frame before and after the protocol-specified PRO assessment time point whereby the result would still be deemed to be clinically relevant[1].

[1] Fayers PM, Hopwood P, Harvey A, Girling DJ, Machin D, Stephens R; MRC Cancer Trials Office. Quality of life assessment in clinical trials—guidelines and a checklist for protocol writers: the UK Medical Research Council experience. Eur J Cancer. 1997;33(1):20-28.