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Clinical Research Progress Notes

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When writing a progress note, many investigators use the same format whether it's for a clinical practice patient or a clinical research subject. However, while the progress note for a patient visit should focus on the diagnosis, treatment and status of a medical condition, the progress note for a study visit should provide a broader perspective on the changes (or lack thereof) since the last visit. The study coordinator needs comprehensive notes for case report form entry and various reports. The site monitor and, possibly, auditor or FDA investigator need them for source document verification and confirmation that the investigator has properly overseen the subject's safety.

Based on the standard SOAP (Subjective, Objective, Assessment, Plan) format for progress note writing, the following are the key elements of a progress note for a clinical research study visit or other interaction:

Subjective

Identify the study subject with his or her subject number and initials. Identify the study with its number and/or abbreviated name. Identify the study visit and date or that it is an unscheduled visit. For example:

> Subject 001/JPD presents for the Cardio-M 2015 study 1-month visit on January 1, 2016…
>
> Subject 001/JPD presents for an unscheduled visit for the Cardio-M 2015 study on January 1, 2016…

Objective

Despite protocol-specific training, investigators might not report adverse events and other observations that are normally expected in clinical practice but significant to a clinical research study. For example, in heart-valve surgery, post-operative arrhythmia is a common finding. In clinical practice, it is monitored and treated as a matter of course. However, in clinical research, it most likely is an adverse event per the study protocol, since it is a change from baseline or medical history. When the biostatisticians analyze the study data for subject safety, they might be led astray by an apparent lack of arrhythmias.

Itemize and discuss *all* new medical events and all medications, covering changes, treatments and tests that have occurred since the prior study visit. Include adverse events (AEs) that were ongoing at the prior study visit. For example:

> The following interim events have been identified through discussion with the subject: vertigo, right wrist pain. Previously noted conduction disturbances, LBBB & 1st AV, remain ongoing. None of these events appear to be related to the device. Current medications: Metoprolol, aspirin, simvastatin; Coumadin discontinued, 1-year prophylaxis completed; no other med changes.

Study subjects often forget adverse events, medication changes, etc., especially if visits are months apart. Therefore, the study coordinator should review the subject's medical records,

if available, prior to the visit, and inform the investigator of anything that might be relevant to his or her review and assessment in the progress note. For example:

> Study coordinator reviewed the electronic records and found that the subject had several ED visits for epistaxis that were not mentioned by subject – Confirmed as AE.

Discuss any instances in which the study visit was not conducted per protocol. Doing so will assist the site in identifying protocol deviation trends that might require notification of the IRB. Note any corrective actions. For example:

> Subject's blood pressure was taken in a sitting position, instead of the prone position required by the protocol. Reminded study coordinator of the proper procedure.

Include the investigator's findings for the exams specified in the protocol, which might be different than the investigator's normal clinical practice. Note whether any findings are clinically significant.

For example, a cardiovascular study might require coagulopathy labs, such as plasma-free hemoglobin, LDH, and haptoglobin, which are not routinely ordered for a clinic visit. The lab reports for these tests should be reviewed by the investigator for clinical significance and their review either documented on the lab report itself or on the visit progress note. Annotate EKG, CT reports, etc., to confirm review by the investigator in accordance with hospital/clinic policy. In the case of an abnormal coagulopathy lab, a statement like "plasma free Hgb: elevated – 45.1 – NCS, no evidence PVL" would document the PI's review of the result.

In cases where the investigator disagrees with the documentation of an event, so indicate, preferably with an explanation. For example, for a cardiovascular study:

> Review of the electronic records by the study coordinator found that the subject had an EKG performed at his primary care provider that indicated bradycardia, a one-time finding, not an AE, not considered significant.

In the event of an FDA audit, the investigator will need to explain the omission of events that otherwise meet the protocol specifications.

Follow hospital/clinic policy for annotating lab, EKG, CT, etc., reports to confirm review by the investigator.

Assessment

Based on the clinical examination, including a review of lab and other test results, comment on clinical significance and whether any events meet the AE reporting requirements of the protocol. For example:

> The following interim events have been confirmed as new AEs: vertigo and thrombocytopenia.

An event has clinical significance if it is a new or existing condition that requires additional active management, e.g., new medication, change of dose, discontinuation of a medication, close observation, more frequent follow-up assessments, or further diagnostic investigation. Always consult the AE reporting section of the protocol. However, in most cases, an AE should be documented when a clinically significant finding is confirmed by the investigator.

State whether any newly identified AE appears to be related to the study drug or device. For example:

> The following events appear related to the study drug/device: …

Provide full documentation of the investigator's causality assessment in an AE Log or an AE source document worksheet.

State the disposition of AEs that were documented in previous progress notes. For example:

> All previously observed AEs have resolved, except: …"
>
> The following prior events have resolved: … and the following are ongoing: .

Comment on any reason(s) for medication changes, so it is always clear why a medication has changed. For example:

> Subject has completed his required course of anticoagulant therapy (Coumadin). No further treatment required.

State the subject's study drug (and possibly device) adherence, so any untoward trends can be identified and addressed. For example:

> Since the last visit, subject missed two study drug doses, due to a change in work schedule. Advised subject to discuss the situation with his work supervisor, should his schedule change again.

State whether the subject continues to meet study eligibility requirements and has reconfirmed consent. For example:

> The subject remains eligible and is committed to actively continue in this study.

Plan

Comment on the next scheduled study visit and/or any planned unscheduled visits. For example:

> Subject 001/JPD continues to do well. He remains eligible and committed to actively continue in this study and will be seen at his next scheduled visit in July 2016. He will contact us if any problems occur or he has any questions.
>
> Subject 001/JPD will need to return in two weeks for a follow-up exam of his wound infection.

Comment on any follow-up exams or treatments required for adverse events. For example:

> I have notified his cardiologist of the results of this visit should the subject's low platelet level not improve.

If all parts of the study visit were not completed, indicate the timeline for their completion. For example:

> Schedule a treadmill test for the subject within one week.

Sign and date progress notes so they can be considered adequate documentation per FDA ALCOA standards must meet regulatory requirements for record keeping. (*FDA Guidance on Computerized Systems Used in Clinical Investigations (Apr. 1999))

Progress Note Example 1: Device Study

February 1, 2016

Subject 001/JPD, a 65-year-old white male, status post mitral valve replacement in January 2015 presents for the Cardio-M 2015 Study One Year visit. Since his last visit, he states he is doing well, able to walk longer distances and exercise more. However, he did have

several bouts of vertigo in September 2015, which have not occurred since; they may have been due to the heat.

Vitals: BP 127/82; R 18; HR 82; Weight 86kg

Current medications: Metoprolol, aspirin, simvastatin; required course of Coumadin prophylaxis completed; no other med changes.

EKG: LBBB, 1st AV block not changed from prior visits.

Echo: Valve functioning correctly with no stenosis or insufficiency noted.

Labs: WBC 5.1, RBC 3.46, Hgb 11.1, Hct 34.7, Platelets significant at 125, otherwise unremarkable. Note: chemistry lab not done due to lab staff error; staff counseled to follow printed orders.

The following interim events have been confirmed as new AEs: vertigo, thrombocytopenia. Previously noted conduction disturbances, LBBB & 1st AV, remain ongoing. None of these events appear to be related to the device.

Subject continues to do well and remains eligible & committed to actively continue in this study and will be seen at his next scheduled visit in July 2016. He will contact us in the meantime if any problems occur or he has any questions. I have notified his cardiologist of the results of this visit should the subject's platelet level not improve.

Doctor Mentright, February 1, 2016

Progress Note Example 1a (Follow Up)

July 5, 2016

Subject 001/JPD, a 65-year-old white male, status post mitral valve replacement in January 2015 presents for the Cardio-M 2015 Study 18-Month visit. Mr. C's endurance continues to improve, so he is now playing one round of golf each day, walking the entire distance. He has lost a few pounds in the process.

Vitals: BP 122/79; R 19; HR 78; Weight 83kg

Current medications: Metoprolol, aspirin, simvastatin; no med changes.

EKG: LBBB, 1st AV block not changed from prior visits.

Echo: Valve functioning correctly with no stenosis or insufficiency noted.

Labs: WBC 5.1, RBC 3.46, Hgb 11.1, Hct 34.7, Platelets 178, creatinine 0.99

No new AEs, platelet levels stabilized. Previously noted conduction disturbances, LBBB & 1st AV, remain ongoing, not related to the device.

Subject continues to do well and remains eligible & committed to actively continue in this study and will be seen at his next scheduled visit in November 2016. He will contact us in the meantime if any problems occur or he has any questions.

Doctor Mentright, July 5, 2016

Progress Note Example 2: Drug Study

February 1, 2016

Subject 001/JPD, a 65-year-old white male, presents for the XYZ Hypertension Study# 073 One Year visit. Since his last visit, he was hospitalized for heart failure in September 2015

and has just recently recovered to do basic tasks. Otherwise, he states there have been no new medical problems.

Vitals: BP 137/82; R 18; HR 82; Weight 86kg

Current medications: Metoprolol, aspirin, simvastatin, multivitamin, calcium; no med changes.

Labs: WBC 5.1, RBC 3.46, Hgb 11.1, Hct 34.7, Platelets 225

Due to his hospitalization, he missed several doses of study drug, which accounts for 84% overall adherence. Reminded subject to always notify medical staff of his participation in a clinical research study.

The following interim event has been confirmed as a new AE: heart failure. Previously noted UTI and left leg ache AEs have resolved. He continues to have intermittent headaches. None of these events appear to be related to the study drug. Note: review of records indicate he was also seen at the local ED for a hearing problem, but no action was taken — not an AE, not considered significant.

Subject continues to do well and, despite the adherence issue, remains eligible & committed to actively continue in this study and will be seen at his next scheduled visit in July 2016. He will contact us in the meantime if any problems occur or has any questions.

Doctor Mentright, February 1, 2016

Conclusion

Because research study documentation requirements are more extensive than those for a clinical practice patient, investigators should pay attention to the requirements of clinical research study protocols when writing progress notes. Consistent documentation of adverse events and treatments will enable the study coordinator to complete case report forms in a timely manner, minimize deliberation on adverse events, and speed up monitor visits.

References

"Documenting Clinically Significant Lab Values," S. Eric Ceh, Journal of Clinical Research Best Practices, Vol. 5, No. 1, January 2009.

"Adverse Event Reporting: During the Study," S. Eric Ceh, Journal of Clinical Research Best Practices, Vol. 5, No. 8, August 2009.

For the principal recordkeeping requirements for clinical investigators and sponsors developing drugs and biologics, see 21 CFR 312.50, 312.58, 312.62, and 312.68. For medical devices, see 21 CFR 812.140 and 812.145.

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