Item 10. Who generated the allocation sequence, who enrolled participants, and who assigned participants to interventions

Examples—“Determination of whether a patient would be treated by streptomycin and bed-rest (S case) or by bed-rest alone (C case) was made by reference to a statistical series based on random sampling numbers drawn up for each sex at each centre by Professor Bradford Hill; the details of the series were unknown to any of the investigators or to the co-ordinator … After acceptance of a patient by the panel, and before admission to the streptomycin centre, the appropriate numbered envelope was opened at the central office; the card inside told if the patient was to be an S or a C case, and this information was then given to the medical officer of the centre.”

“Details of the allocated group were given on coloured cards contained in sequentially numbered, opaque, sealed envelopes. These were prepared at the NPEU and kept in an agreed location on each ward. Randomisation took place at the end of the 2nd stage of labour when the midwife considered a vaginal birth was imminent. To enter a women into the study, the midwife opened the next consecutively numbered envelope.”154 “Block randomisation was by a computer generated random number list prepared by an investigator with no clinical involvement in the trial. We stratified by admission for an oncology related procedure. After the research nurse had obtained the patient’s consent, she telephoned a contact who was independent of the recruitment process for allocation consignment.”

Explanation—As noted in item 9, concealment of the allo‑ cated intervention at the time of enrolment is especially important. Thus, in addition to knowing the methods used, it is also important to understand how the random sequence was implemented—specifically, who generated the alloca‑ tion sequence, who enrolled participants, and who assigned participants to trial groups. The process of randomising participants into a trial has three different steps: sequence generation, allocation con‑ cealment, and implementation (see box 3). Although the same people may carry out more than one process under each heading, investigators should strive for complete sepa‑ ration of the people involved with generation and allocation concealment from the people involved in the implementation of assignments. Thus, if someone is involved in the sequence generation or allocation concealment steps, ideally they should not be involved in the implementation step. Even with flawless sequence generation and allocation concealment, failure to separate creation and concealment of the allocation sequence from assignment to study group may introduce bias. For example, the person who generated an allocation sequence could retain a copy and consult it when interviewing potential participants for a trial. Thus, that person could bias the enrolment or assignment proc‑ ess, regardless of the unpredictability of the assignment sequence. Investigators must then ensure that the assign‑ ment schedule is unpredictable and locked away (such as in a safe deposit box in a building rather inaccessible to the enrolment location) from even the person who generated it. The report of the trial should specify where the investigators stored the allocation list.