



Software for randomisation in clinical trials

What is ALEA?

ALEA is a software package to support online patient registration and randomisation in healthcare research. It was developed to meet the needs of four of the largest Data Centres for cancer trials in Europe and the current software draws on extensive operational experience amassed over the last decade. The current version is suitable for virtually any trial in health care. ALEA has been built as a series of components, in order to support interoperability and customized extensions. The components make use of a common standard representation of data and metadata: the Operational Data Model of CDISC. Within ALEA, the components share a database for storing and retrieving information about the trial, and a separate database for storing and retrieving patient data. The components of ALEA are described below.

Study Definition module

The *Study Definition Module* is a web application to define and modify randomisation forms, link notifications to forms, manage the participation of sites in trials, and manage information about the status of the trials. It allows the user to define a variety of questions (including advanced calculations), to define eligible answer ranges, and to set questions to be used as stratification factors in the randomisation. The user defines treatment groups for the trial and specifies the method to be used to generate the sequence for allocating participants to these groups. ALEA supports the use of different ratios for the number of participants in the groups, allowing researchers to choose, for example, to put twice as many people in the active treatment group compared to the control group. The Study Definition Module holds a 'white list' for each trial containing the centres and investigators involved in the trial. This Module is also used to select and design the notifications that can be sent after a participant has been randomised. In order to facilitate the exchange of study metadata, the Study Definition module supports the import and export of CDISC Operational Data Model (ODM) files (www.cdisc.org).

Online randomisation module

The *Online Randomisation Module* is a web browser application that supports online randomisation of patients into healthcare trials. It requires initial login with a username and password, and then prompts the user to provide identification, eligibility, and stratification information on the person to be randomised. After completion of this randomisation form, a treatment is allocated. In this way, the allocation is kept secure and concealed until the patient information has been entered and the person requesting the randomisation has confirmed that they wish to proceed with entry into the trial. The Online Randomisation Module contains tools to help people monitor and manage the trial. These include comprehensive reporting tools, audit tools, and tools for monitoring operational system components such as print, fax and email queues.

Interactive Voice Recognition (IVR) Module

The *Interactive Voice Response (IVR) Module* supports randomisation using a touch tone telephone. The IVR system reads the questions to the caller, and allows the caller to respond using the digits on the telephone. ALEA contains a language support system, which allows the form to be defined in different languages. The person requesting a randomisation can then choose a preferred language for their interaction with the IVR system.

SOAP Randomisation Service

Researchers may have access to one of the many different data entry packages available and so, if they do not wish to use ALEA's Online Randomisation Module to enter the patient information, they can use custom Remote Data Entry tools through ALEA'S SOAP (Simple Object Access Protocol) based XML Web Service. This service accepts calls in the CDISC ODM format and returns the treatment allocation and patient number to the caller. Hence, ALEA customers can use any data entry front-end to complete

the ALEA randomisation form, and then invoke online randomisation using SOAP. This also allows randomisations to be obtained using regular telephones, through the IVR Module.

Notifications Service Module

The *Notifications Service Module* is responsible for the distribution of notifications after randomisation. These may be sent by email or fax, or printed directly on a printer attached to the randomisation server network. Most notifications are triggered by the randomisation of a patient into the trial and such notifications may be sent to, for example, the responsible clinician, a study monitor at the sponsoring organisation (eg a pharmaceutical company), or a pharmacist who will prepare the study medication. As well as notifications sent after randomisation, the Notifications Service Module can distribute periodic status reports on the trial, or generate reports after specific events within the trial.

Address Book module

The *Address Book Module* provides tools to manage a comprehensive database of people and organisations involved in the trial, including clinicians, departments, institutes and user accounts. In order to prevent duplication of data, this information is stored in a relational database. The Address Book Module comes with advanced export facilities to provide connectivity to flat structures such as LDAP and X.500 directory services. Information needed to deliver notifications, as well as all user access privileges, are retrieved from the Address Book Module.

ALEA randomisation methods

ALEA supports the following methods of randomisation for healthcare trials. It supports trials with any number of treatment groups, and randomisation ratios other than 1:1.

Minimisation: The randomised groups are balanced on the basis of the characteristics of each participant. Each new participant is allocated to the group that has the fewest number of people like him or her at that time. The default setting is that the allocation uses simple randomisation only if there is no difference between the groups when the new participant is being entered into the trial.

Adapted minimisation: Adapted minimisation is like minimisation, but simple randomisation is used whenever the imbalance between the strata totals in each treatment group is less than or equal to the number of stratification factors. This reduces the predictability of allocations, especially if the trial only has one stratification factor.

Efron biased coin: This technique biases the random allocation in favor of the under-represented treatment group when the imbalance between the groups passes some threshold. This method can be used to help ensure balanced patient characteristics within each group.

Block randomisation: Participants are allocated to the treatment group that is next in a block of allocations. Within each block, each treatment group occurs the same number of times. The user selects the block size for their trial as a whole or for specific parts of their trial.

Random block randomisation: To make it less likely that the next allocation can be predicted, this method varies the size of each block. ALEA chooses the size of each block by multiplying the number of treatments groups by a whole number between 1 and a minimum block size set by the user.

Simple randomisation: Each participant has an equal chance of being allocated to any of the treatment groups, regardless of any imbalances that have already built up within the trial.

Blinding

If participants in the trial are not to know which treatment they will receive, ALEA can convert the treatment allocated into a box number or code, and returns this rather than the treatment. ALEA helps the user to prepare these numbers or codes, so that the trial material can be prepared in advance.



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For more information

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