

Standard Operating Procedure

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This SOP describes the use of the TRICALS Eligibility – Risk Profile Calculator, which can be found at <https://tricals.shinyapps.io/risk-profile/>. The TRICALS Risk Profile is a prognostic summary value of seven patient characteristics and is used for patient selection in clinical trials; its validation and calculation is described elsewhere.^{1, 2} The Risk Profile Calculator estimates the TRICALS Risk Profile, evaluates patient eligibility and generates a downloadable report that can be stored in the patient's Case Report Form (CRF).

The following patient information is required:

1. Study subject ID
2. Date of screening
3. Date of birth
4. Date of diagnosis
5. Date of symptom onset
6. El Escorial Definite classification
7. Site of symptom onset
8. Presence of frontotemporal dementia
9. ALSFRS-R total score at screening
10. Vital capacity at screening

IMPORTANT: The calculator does not save any patient information; all information is erased when the browser is closed. The source code of the calculator is available on request.

Definitions

- Definitions of **date of diagnosis**, **date of symptom onset** and **site of symptom onset** can be found at: <https://www.encals.eu/wp-content/uploads/2016/09/2015-01-14-ALS-Core-clinical-dataset.pdf>.
- **EI Escorial Definite classification** is defined as the presence of upper and lower motor signs in 3 or more regions.³
- For rating the **ALSFRS-R total score** we refer to the latest ALSFRS-R SOP version at: <https://www.encals.eu/outcome-measures/>.
 - The ALSFRS-R questionnaire can be found at: <https://www.encals.eu/outcome-measures/> (available in different languages).
 - **The ALSFRS-R needs to be scored at the day of screening**
- **Vital capacity** can be either Slow Vital Capacity (SVC) or Forced Vital Capacity (FVC) and is provided in percentages relative to the reference standard. The required reference standard is the GLI-2012.⁴ If the GLI-2012 is not available in the spirometer, the GLI-2012 tool at <http://reactive.tricals.org> can be used to obtain the correct percentage.
 - The latest SVC/FVC SOP can be found at <https://www.encals.eu/outcome-measures/>.
 - **The Vital Capacity needs to be scored at the day of screening**

Using the Calculator (1)

Step 1: Proving information

The calculator is programmed based on reactive software, meaning that information will be seamlessly analyzed after every new input. In order to generate a report, please ensure that a **Subject ID** is provided and a **Trial Acronym** selected (orange arrows).

The screenshot displays the TRICALS calculator interface with the following fields and values:

- Subject ID:** Enter Subject ID (indicated by an orange arrow)
- Date of screening:** 2020-12-18
- Diagnosis:**
 - El Escorial: Other (dropdown)
 - Onset: Other (dropdown)
 - ALS-FTD: Absent (dropdown)
- Dates:**
 - Date of birth: 1955-12-18
 - Date of onset: 2019-06-19
 - Date of diagnosis: 2020-06-21
- Clinical measures at screening:**
 - ALSFRS-R: 40 (spinner)
 - %Predicted FVC: 100 (spinner)
- Select trial:** (indicated by an orange arrow)
 - MAGNET
 - Lighthouse II
 - MetFlex

Using the Calculator (2)

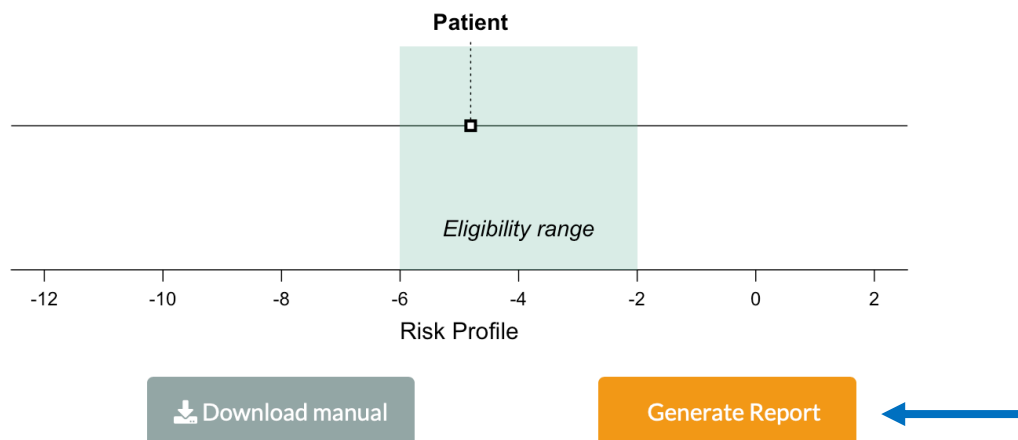
Step 2: Assessing Eligibility

The grey panel summarizes the input information. The exact risk profile can be found under “Risk Profile” (*orange arrow*). Based on this score, and the selected eligibility window (*green shaded area in figure*), a patient is either eligible or not eligible. **The eligibility window could depend on the selected trial.**

Note: No further information is given about the interpretation of the risk profile. If the patient wishes to learn more about his or her prognosis, we refer to the original ENCALs survival prediction model (<http://encalssurvivalmodel.org>).

Summary of patient characteristics			
Age at screening (yrs):	65.0	DeltaFRS:	-0.45
Diagnostic delay (mths):	12.1	Risk Profile:	-4.81
Symptom duration (mths):	18.0	Result:	Included

Include patient



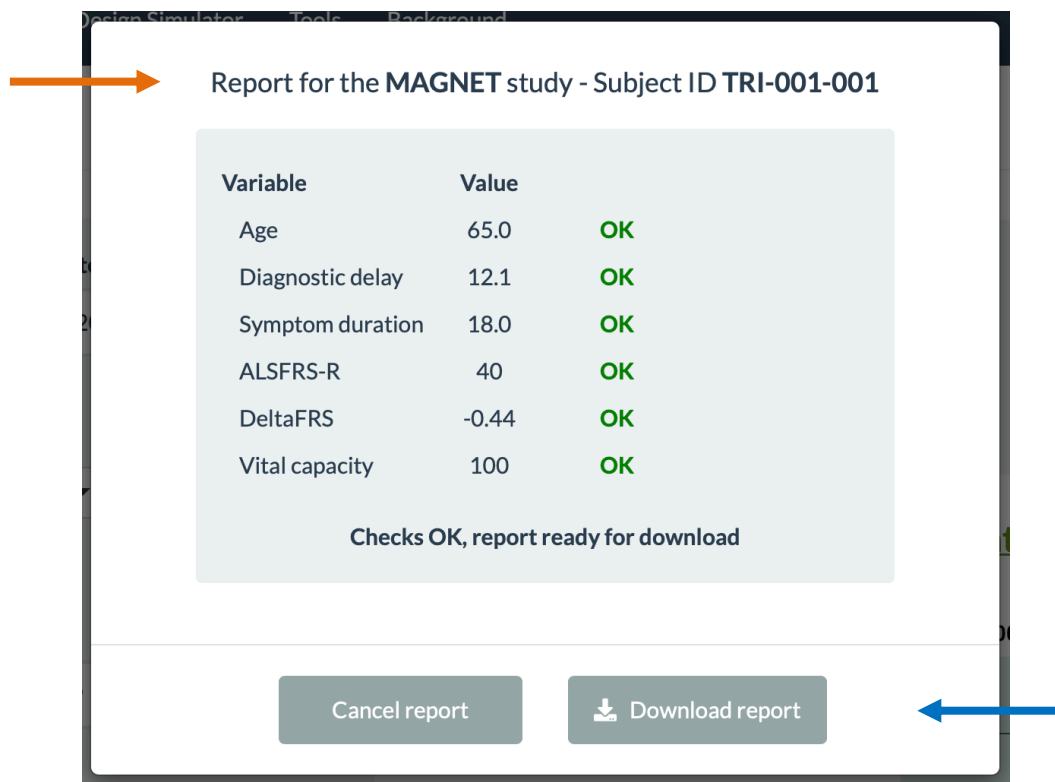
To generate a report, click “**Generate Report**” (*blue arrow*). Please ensure that a **Subject ID** is provided and a **Trial Acronym** selected (see Step 1).

Using the Calculator (3)

Step 3: Generating the report

After clicking “**Generate Report**” (Step 2), a pop-up window appears. Please ensure the selected Study Acronym and Subject ID are correct (*orange arrow*); these will be used in the final Eligibility Report.

Automated checks will be performed on the provided data to screen for potential errors. If all data is considered OK, a download button appears below to create a .docx file (*blue arrow*).




Using the Calculator (4)

Step 4: The Eligibility Report

After clicking “**Download report**” (Step 3), a .docx word file is generated. Please ensure that the file is saved in the CRF (either printed or electronically).

Eligibility Report



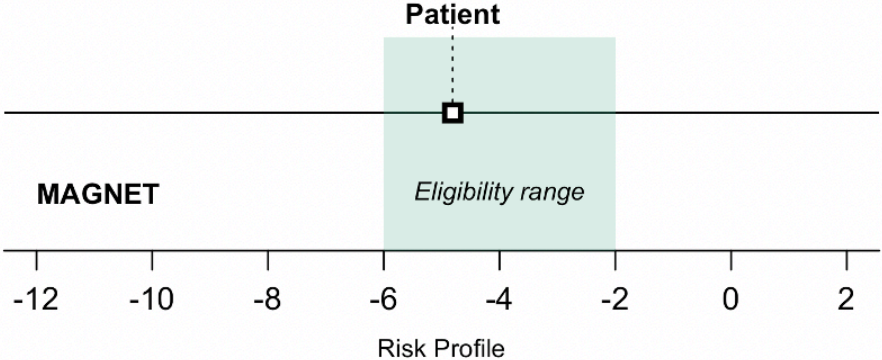
Subject TRI-001-001

To whom it may concern,

Patient TRI-001-001 was screened for eligibility for the **MAGNET** study on 2020-10-28 and was found **ELIGIBLE** for the TRICALS Risk Profile. Please find below a summary of the findings.

Year of birth:	1955	Age at onset:	63.5
Date of diagnosis:	2020-05-01	Diagnostic delay:	12.1
Date of onset:	2019-04-29	Symptom duration:	18
Site of onset:	Other	ALSFRS-R:	40
EI Escorial:	Not definite	DeltaFRS:	-0.44
ALS-FTD:	Absent	%Predicted VC:	100

The TRICALS Risk Profile is: **-4.81 (ELIGIBLE)**



Patient

-12 -10 -8 -6 -4 -2 0 2

Risk Profile

MAGNET Eligibility range

Using the Calculator (5)

Trouble-shooting 1

In step 3, automatic data checks will be performed. Variables have to fall within certain ranges to be valid (e.g. ALSFRS-R score falls within the range 0 - 48). If by accident invalid information is provided, an error message will be raised (*orange arrow*). Please review the flagged variable accordingly to resolve the error by clicking on “**Cancel Report**”.

Report for the **MAGNET** study - Subject ID TRI-001-001

Variable	Value	Status
Age	165.0	ERROR: INVALID
Diagnostic delay	12.1	OK
Symptom duration	18.0	OK
ALSFRS-R	40	OK
DeltaFRS	-0.44	OK
Vital capacity	100	OK

Invalid data, please resolve error(s)

Cancel report

Note: An orange arrow points to the 'ERROR: INVALID' status for the 'Age' variable.

Using the Calculator (6)

Trouble-shooting 2

Sometimes data may be valid, but could be unlikely to observe. This may potentially be an input error and a warning message will be generated (*orange arrow*). Please review the information carefully, if this is not an error, please click "**Proceed**" (*blue arrow*) to download the report.

Report for the **MAGNET** study - Subject ID TRI-001-001

Variable	Value	Status
Age	15.0	WARNING: RARE
Diagnostic delay	12.1	OK
Symptom duration	18.0	OK
ALSFRS-R	40	OK
DeltaFRS	-0.44	OK
Vital capacity	100	OK

Possible error(s), please click [Proceed](#) to overrule

Cancel report Proceed

References

1. van Eijk RPA, Westeneng HJ, Nikolakopoulos S, et al. Refining eligibility criteria for amyotrophic lateral sclerosis clinical trials. *Neurology* 2019.
2. Westeneng HJ, Debray TPA, Visser AE, et al. Prognosis for patients with amyotrophic lateral sclerosis: development and validation of a personalised prediction model. *Lancet Neurol* 2018;17:423-433.
3. Brooks BR, Miller RG, Swash M, Munsat TL, World Federation of Neurology Research Group on Motor Neuron D. El Escorial revisited: revised criteria for the diagnosis of amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Other Motor Neuron Disord* 2000;1:293-299.
4. van Eijk RPA, Bakers JNE, van Es MA, Eijkemans MJC, van den Berg LH. Implications of spirometric reference values for amyotrophic lateral sclerosis. *Amyotroph Lateral Scler Frontotemporal Degener* 2019;20:473-480.