

Signant Health and University Hospital Basel collaborate to create electronic version of the

**NEUROSTATUS-EXPANDED
DISABILITY STATUS
SCALE (EDSS)**



INTRODUCTION

Signant Health is the leading electronic Clinical Outcome Assessment (eCOA) provider for collecting multiple sclerosis (MS) data in clinical trials.

Signant Health and a clinical research group at the University Hospital Basel (UHB), led by Professor Ludwig Kappos, collaborated to develop an electronic Neurostatus-Expanded Disability Status Scale (EDSS) instrument for capturing clinical trial data on an electronic device. The Neurostatus-EDSS has been adopted as standard in more than 160 phase II and III clinical trials in MS and Neuromyelitis optica (NMO) in the last 20 years, and has been implemented in most of the pivotal trials that have led to the approval of current MS treatments. The electronic Neurostatus-EDSS presents a new option for study teams looking to enhance their data collection in MS clinical trials.

In this case study, we'll examine how the electronic Neurostatus-EDSS replaces the way data is captured in the traditional assessment that requires EDSS raters to complete paper forms that suffer from all the typical issues with inter- and intra-rater reliability (slow review process, limited interactivity, etc.). We'll also review how the electronic version streamlines data collection to not only facilitate the capture of higher quality data, but reduce burden on sites and patients by significantly speeding up the process.

Finally, we'll examine three (3) clinical trials that are currently leveraging the electronic Neurostatus-EDSS assessment by Signant Health. The following stakeholders are key players in all three (3) studies:

- **SPONSORS:** Pharmaceutical companies that are hosting the clinical trials to evaluate the effects of their MS drug
- **SUBJECTS:** Individuals providing information about their condition and health status
- **EDSS rater:** On-site trained and certified clinician that performs the electronic Neurostatus-EDSS assessment; this includes a standardized clinical examination and questions about their condition
- **UNIVERSITY HOSPITAL BASEL (UHB)/EXPERT REVIEWER:** Team of clinical neurologists that provide various training modalities for EDSS raters, supervise the programming of the electronic Neurostatus-EDSS, review inconsistent assessments detected by the algorithm and provide guidance to the raters
- **STUDY COORDINATOR:** Study team member that creates the subject in SmartSignals™ eCOA, activates the subject's visit, activates or removes an attack assessment, activates or removes an unscheduled visit, deactivates the subject from the web diary, and creates and tracks DCFs
- **PRINCIPAL INVESTIGATOR:** Reviews completed electronic Neurostatus-EDSS assessment data (applies to one sponsor in this case study)



THE CHALLENGE

The Neurostatus-EDSS requires EDSS raters to determine:

-  Seven Functional System Scores (FSS), referring to the assessment of each respective Functional System (Visual, Brainstem, Pyramidal, Cerebellar, Sensory, Bowel and Bladder, and Cerebral)
-  The Ambulation Independence Score (AIS), referring to the assessment of the walking capacity (distance possible and use of assistance)
-  The appropriate EDSS step as summarized in the Neurostatus-EDSS calculation table

One of the biggest hurdles to overcome in the electronic Neurostatus-EDSS is identifying potential inconsistencies between these scores. It is important that study teams using the electronic version quickly recognize and reconcile potential errors in the assessment data. With up to 120 different signs and symptoms that need to be assessed and recorded, it's very important that the information be documented carefully.

Furthermore, it is imperative that the scores, based on the complexity of the scale, be checked in real-time for inconsistencies. If the inconsistencies cannot be resolved, an individual review process is implemented. Paper can't do this for study teams, and even if a review process was set up, it could never be done as quickly as an electronic version with real-time feedback.

Other challenges include:

- Enhancing the interactive loop between the EDSS rater and EDSS expert reviewer (UHB) for faster turnaround time
- Producing higher quality data by improving consistency and thus reducing measurement noise
- Providing easy navigation for accurate assessment performance



Paper and pencil is a silent method. There's no feedback, and it's not interactive. By not reviewing the data or getting feedback, it's very likely that errors might occur due to the complexity of the assessment rules. Similarly, without having an interactive instrument with real-time feedback, the communication between EDSS raters and the expert team from the UHB would be greatly reduced and delayed, which is the opposite of what we were trying to do.

Dr. Marcus D'Souza

Neurologist & Head of Neurostatus, University Hospital Basel



STUDY DESIGN

Study 1



1 language



150 subjects



28 countries

Study 2



1 language



1311 subjects



34 countries

Study 3



1 language



1323 subjects



36 countries

COLLECT OUTCOMES ASSESSMENT DATA

Assessments are completed using Signant's eCOA system solution



VIEW & MANAGE DATA

Data is reported on and analyzed using Signant's management utility solution



THE SOLUTION

The electronic Neurostatus-EDSS assessment follows the process outlined below. From start to finish, these steps are crucial for achieving high quality data:

01

Based on a full standardized neurological examination including some standard questions about specific symptoms, an EDSS rater performs a standardized EDSS assessment according to the Neurostatus definitions.

02

After completing and documenting the assessment, the EDSS rater can receive immediate, automated feedback (based on an algorithm created by the University Hospital Basel) on any potential inconsistencies in the scores (this automatic real-time feedback can be utilized up to 4 times).

03

The EDSS rater can reconsider her/his decision if inconsistencies are detected After 4 rounds of feedback, or if the EDSS rater does not change her/his values despite inconsistencies, the assessment will be sent to and reviewed by an EDSS expert from the UHB who provides comments/suggestions in a timely manner to speed up the data collection and submission process. The final decision remains with the EDSS rater.

04

If the assessment is finalized with no inconsistencies, the form is marked complete.

05

The data is then sent onto Signant's eCOA system for reporting and analysis by the Principal Investigator.

Several usability features were implemented in the electronic Neurostatus-EDSS to make it easy for study teams to use:

INCONSISTENCY TRACKING WITH DATA SCORING ALGORITHM

There are numerous possible outcomes that can be presented as a result of the many different scenarios that EDSS raters report from subject evaluations, so the ability to get feedback on the EDSS rater scores is very beneficial. The EDSS rater simply clicks a button and an algorithm works behind the scenes to identify any inaccuracies with data scoring. They also have the option to send the data onto an expert reviewer at the University Hospital Basel if the data is marked with inconsistencies but EDSS raters still feel the data is correct.

EXPERT PROVIDES DATA ACCURACY

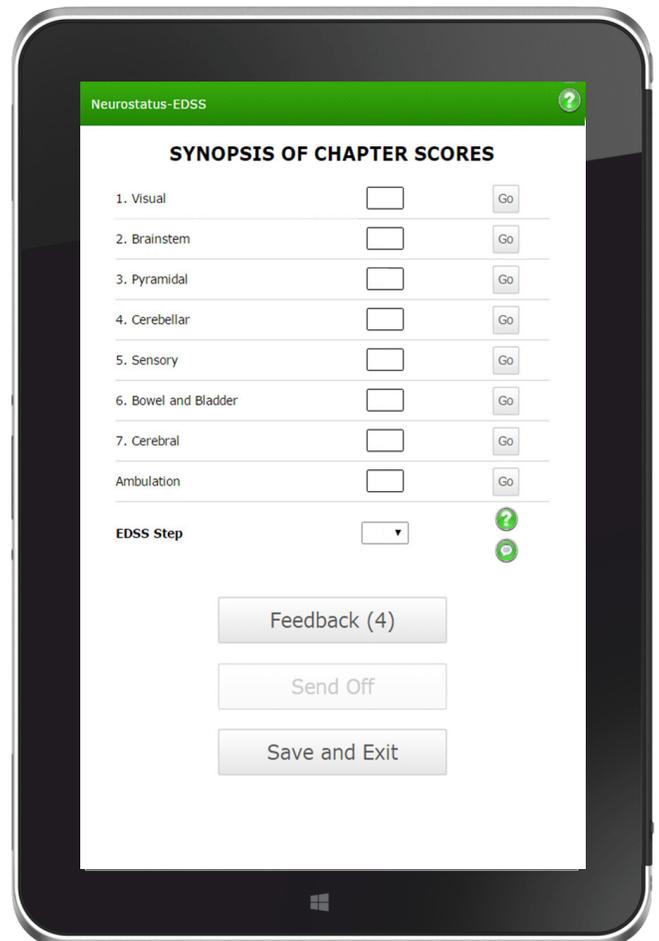
Because the data is so closely reviewed for inconsistencies, study teams have confidence that they are working with verified data. Data is pre-checked by not one but two systems: an automated algorithm and an expert, leaving little room for the data to be anything but consistent and accurate.

ACCESSIBLE “HELP” ICONS

The electronic Neurostatus-EDSS form was created with built-in icons that assist EDSS raters when they have questions or want to obtain more information. For example, if they want more information about how to score based on an observation, they can click the “?” icon to see detailed information about the question. Traditionally, site investigators need to refer to a lengthy guidance document for this type of specific information. Therefore, icons help investigators quickly find what they need.

WIRELESS DATA TRANSMISSION

Easy transfer of data from Signant’s eCOA system to its management utility solution provides the experts at the University Hospital Basel with data that needs to be actioned in real-time. Without this feature, data would be reviewed days, weeks, or even months after being submitted to the experts. Getting data quickly allows the experts to prioritize forms and respond in a timely manner.

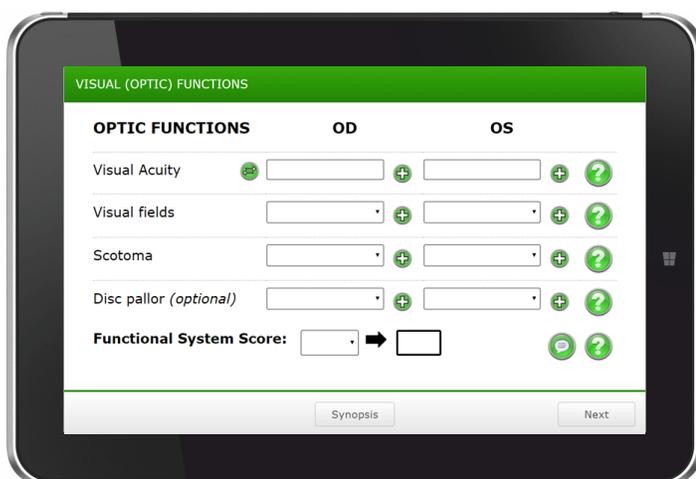


The above screenshot depicts one of the first screens that EDSS raters see when they begin assessing a subject. They simply select an area in which to begin, such as “Visual,” document the scores, and so on, until all sections are completed.

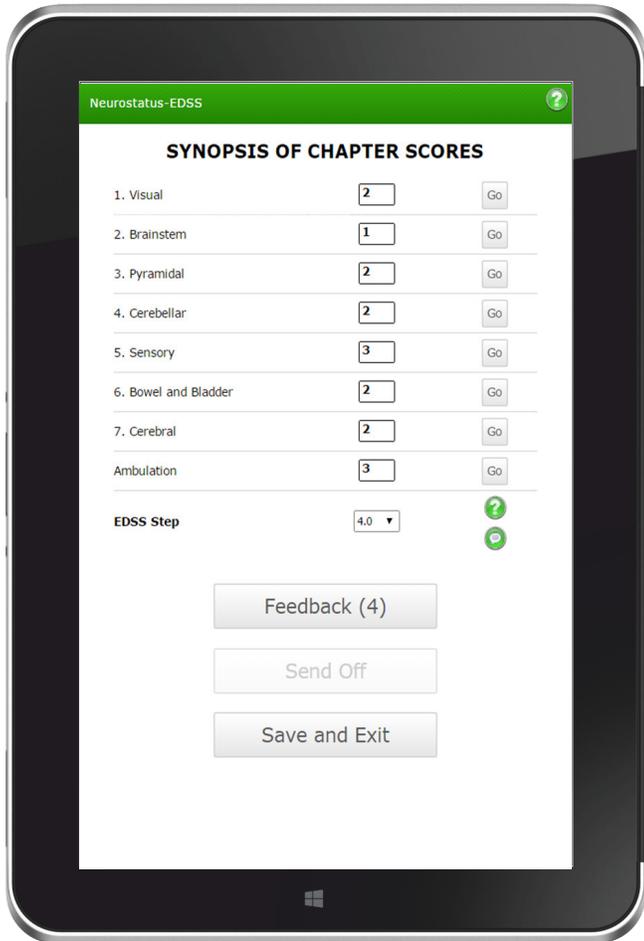
QUICKER REVIEW PROCESS

The electronic Neurostatus-EDSS checks a lot of data on the backend and provides clues about inconsistencies of their entries to the EDSS raters once they complete the Neurostatus-EDSS assessment. This is much faster than paper, which is slow because paper forms need to be manually sent to reviewers. The electronic data is immediately available to the EDSS raters and, if inconsistencies are detected, they can instantly either amend these on site or, in case of disagreement, send the Neurostatus-EDSS data to the experts at the University Hospital Basel for review. Alternatively, if the data is accurate with no inconsistencies, it is marked complete.

(Left) This screen requests information from the EDSS rater about specific function of the subject being examined.



EDSS raters have 4 opportunities to request feedback from the form to ensure accuracy with the data. If any data is missing, it is noted in red under the area missing information. Once all 4 feedback reviews are used, or once the EDSS rater is confident in the scores presented, they simply select "Send Off" to transfer the data.

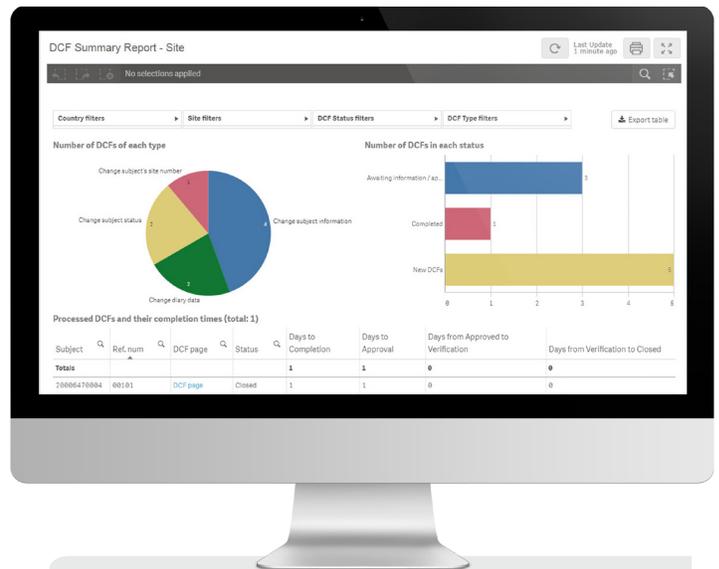


REPORTING FOR EASY DATA ANALYSIS

Several reporting tools are available to study teams using the SmartSignals eCOA platform. Reports include a summary of: Neurostatus-EDSS assessments awaiting review, initiated DCFs, last visit data and current visit data, and attack or unscheduled visits. Reports provide the study teams with access to real-time data, oversight of study data, and monitoring support.

INVESTIGATOR VIEW IN MANAGEMENT UTILITY

The Principal Investigator for these studies does not want to see data until it is finalized. Using eCOA for the Neurostatus-EDSS makes this easy by allowing access rights to be tailored so that the investigator is sure they are only reviewing finalized data.



The above report provides an overview of the DCFs completed or awaiting action as well as other pertinent information needed to understand the status for all DCFs.

STUDY RESULTS

→ **311,808** potential data points collected (during the combined three studies)

The electronic Neurostatus-EDSS streamlines the data collection process during clinical trials, enhancing studies with higher quality data and reduced burden on sites and subjects.

“Future clinical trials that use the electronic Neurostatus-EDSS will have a positive experience with improved consistency of the assessment data and reduced measurement noise. Further, all the information that study teams need is right there, at their fingertips and ready for evaluation,” said Dr. Marcus D’Souza, adding, “I see a bright future for the electronic Neurostatus-EDSS, where EDSS raters are more comfortable and confident in what they’re doing thanks to the technology.”

Signant Health has a wealth of knowledge in neurological studies and is happy to report that our technology was recently responsible for capturing the primary endpoint for trials in both relapsing and primary progressive forms of multiple sclerosis. Based on results of these studies, this is the first and only medicine for primary progressive MS that was approved by the FDA. “It was our initial collaboration and positive experience on these studies that we decided to work with Signant Health again to implement the electronic Neurostatus-EDSS in these ongoing trials,” commented Dr. D’Souza.



ABOUT SIGNANT HEALTH

Signant Health, the leader in clinical evidence generation, focuses on leveraging industry-leading software, deep therapeutic and scientific knowledge, and operational expertise to consistently generate quality evidence for clinical studies across traditional, virtual, and hybrid trial models.

For more than 20 years, over 400 sponsors and CROs of all sizes – including all of Top 20 pharma – have trusted Signant Health solutions for remote and site-based eCOA, eConsent, RTSM, supply chain management, and data quality analytics.

For more information, please visit www.signanthealth.com
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