1. \*What is the current diagnosis? (choose only one)

[ ]  RIS (Radiologically Isolated Syndrome)

[ ]  CIS (Clinically Isolated Syndrome)

[ ]  MS (Multiple Sclerosis) (Go to question 2 to specify clinical course, then skip to question 6)

[ ]  NMO (Neuromyelitis Optica) spectrum disorder (Go to question 3 to specify clinical course, then skip to question 7)

[ ]  ADEM (Acute Disseminated Encephalomyelitis) (Go to question 4 to specify clinical course, then skip to question 7)

[ ]  Other CNS demyelinating disorder (Go to question 5 to specify clinical course, then skip to question 7)

1. Clinical course – MS
2. \*Onset Course: [ ]  Relapsing [ ]  Progressive
3. \*Current Disease Course[[1]](#footnote-1):

[ ]  Relapsing remitting (RRMS)

[ ]  Secondary progressive (SPMS)

[ ]  Primary progressive (PPMS)

[ ]  Clinically Isolated Syndrome (CIS)

[ ]  Uncertain

1. If RRMS, indicate if active or not active[[2]](#footnote-2):

[ ]  Active

[ ]  Not active

1. If SPMS or PPMS, indicate if:

[ ]  Active and with progression

[ ]  Active but without progression

[ ]  Not active but with progression

[ ]  Not active and without progression (stable disease)

1. Clinical course – NMO Spectrum Disorder[[3]](#footnote-3):
2. Type:

[ ]  Monophasic

[ ]  Relapsing

[ ]  Other, specify:

1. If Relapsing:

[ ]  Recurrent optic neuritis

[ ]  Recurrent transverse myelitis

[ ]  Combination

1. If one of the NMO spectrum disorder types above, choose all that apply:

[ ]  Optic neuritis, specify laterality:

[ ]  Right [ ]  Left [ ]  Bilateral [ ]  Unknown

[ ]  Acute myelitis, specify involvement of which segments (choose all that apply):

[ ]  Cervical (C) [ ]  Thoracic (T) [ ]  Lumbar (L)

[ ]  Contiguous spinal cord lesion on MRI >3 vertebral segments[[4]](#footnote-4)

[ ]  Brain MRI not meeting diagnostic criteria for MS

[ ]  NMO-IgG seropositive

[ ]  NMO-IgG seronegative

[ ]  NMO-IgG sero status unknown

[ ]  MOG-IgG seropositive

[ ]  MOG-IgG seronegative

1. Time between onset of first optic neuritis and first myelitis: (please specify) months or [ ]  N/A
2. Clinical course – ADEM:
3. Type:

[ ]  Monophasic

[ ]  Recurrent

[ ]  Multiphasic

[ ]  Unknown

[ ]  Other, specify:

1. Signs/Characteristics experienced (choose all that apply):

**[ ]**  Presence of encephalopathy (behavioral change or alteration in consciousness)

**[ ]**  Improvement by clinical exam, MRI or both after acute event

**[ ]**  Multifocal lesions predominantly involving white matter

**[ ]**  New event of ADEM, 3 or more months after the initial event with recurrence of the initial symptoms and signs (recurrent ADEM)\*

**[ ]**  ADEM followed by a new clinical event also meeting criteria for ADEM, but involving different anatomic areas of the CNS\*

\* see IPMSSG definitions [[5]](#footnote-5)

1. Clinical course – Other CNS demyelinating disorder:
2. Specify disorder:
3. Type:

[ ]  Monophasic [ ]  Recurrent [ ]  Unknown [ ]  Other, specify:

1. (For MS patients ONLY) Indicate which diagnostic criteria the patient fulfills: (choose only one)

RRMS\*:

**[ ]**  ≥ 2 attacks; objective clinical evidence of ≥ 2 lesions or objective clinical evidence of 1 lesion with reasonable historical evidence of a prior attack

**[ ]**  ≥ 2 attacks; objective clinical evidence of 1 lesion

Dissemination in space, demonstrated by

* ≥ 1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical/cortical, infratentorial, or spinal cord); or

**[ ]**  1 attack; objective clinical evidence of ≥ 2 lesions

Dissemination in time, demonstrated by:

* Simultaneous presence of symptomatic or asymptomatic gadolinium-enhancing and non-enhancing lesions at any time; or
* A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or
* CSF-specific oligoclonal bands

**[ ]** 1 attack; objective clinical evidence of 1 lesion (clinically isolated syndrome)

Dissemination in space and time, demonstrated by:

For DIS:

* Additional attack implicating different CNS site
* ≥ 1 T2 lesion in at least 2 of 4 MS-typical regions of the CNS (periventricular, juxtacortical/cortical, infratentorial, or spinal cord); and

For DIT:

* Simultaneous presence of symptomatic or asymptomatic gadolinium-enhancing and non-enhancing lesions at any time; or
* A new T2 and/or gadolinium-enhancing lesion(s) on follow-up MRI, irrespective of its timing with reference to a baseline scan; or
* CSF-specific oligoclonal bands

PPMS3:

**[ ]**  1 year of disease progression (retrospectively or prospectively determined) plus 2 of 3 of the following:

Evidence for DIS in the brain based on ≥ 1 T2 symptomatic or asymptomatic lesions in the MS-characteristic (periventricular, juxtacortical/cortical, or infratentorial) regions

Evidence for DIS in the spinal cord based on ≥ 2 T2 lesions in the cord

Positive CSF (isoelectric focusing evidence of oligoclonal bands and/or elevated IgG index)

SPMS4:

[ ]  Initial RR disease course followed by progression with or without occasional relapses, minor remissions, and plateaus

see Thompson 2017 for additional details[[6]](#footnote-6)

see Lublin-Reingold 2014 for additional details[[7]](#footnote-7)

1. Onset History
2. Year of first diagnosis\*: yyyy
3. Did occurrence of onset clinical event occur:

[ ]  Within 1-month post-infection? [ ]  Within 1-month post-vaccination? [ ]  Neither

1. Indicate first onset was (choose only one): [ ]  Unifocal [ ]  Multifocal
2. Did the patient receive treatment for clinical event? [ ]  Yes [ ]  No [ ]  Unknown
	1. If Yes, indicate treatment (choose all that apply): [ ]  Steroids [ ]  Plasmapheresis [ ]  IVig
3. Was the patient fully recovered from this relapse within a year?[ ]  Yes [ ]  No [ ]  Unknown
4. \*Month/Year of first symptoms: / mm/yyyy
5. Initial symptoms:
6. Vision: [ ]  Yes [ ]  No [ ]  Unknown
	1. If Yes, specify (choose all that apply): [ ]  Bilateral [ ]  Right [ ]  Left [ ]  Unknown
7. Motor: [ ]  Yes [ ]  No [ ]  Unknown
	1. If Yes, specify (choose all that apply): [ ]  Bilateral [ ]  Right [ ]  Left [ ]  Unknown
8. Sensory: [ ]  Yes [ ]  No [ ]  Unknown
	1. If Yes, specify (choose all that apply): [ ]  Bilateral [ ]  Right [ ]  Left [ ]  Unknown
9. Coordination: [ ]  Yes [ ]  No [ ]  Unknown
	1. If Yes, specify (choose all that apply): [ ]  Bilateral [ ]  Right [ ]  Left [ ]  Unknown
10. Bowel/Bladder: [ ]  Yes [ ]  No [ ]  Unknown
11. Fatigue: [ ]  Yes [ ]  No [ ]  Unknown
12. Cognitive: [ ]  Yes [ ]  No [ ]  Unknown
13. Encephalopathy: [ ]  Yes [ ]  No [ ]  Unknown
14. Other, specify:
15. Localization of clinical event:
16. Optic nerve: [ ]  Yes [ ]  No [ ]  Unknown
17. If Yes, specify observation method (choose all that apply):

[ ]  Exam [ ]  MRI [ ]  History [ ]  Unknown

1. Cerebrum: [ ]  Yes [ ]  No [ ]  Unknown
2. If Yes, specify observation method (choose all that apply):

[ ]  Exam [ ]  MRI [ ]  History [ ]  Unknown

1. Brainstem/Cerebellar: [ ]  Yes [ ]  No [ ]  Unknown
2. If Yes, specify observation method (choose all that apply):

[ ]  Exam [ ]  MRI [ ]  History [ ]  Unknown

1. Spinal cord: [ ]  Yes [ ]  No [ ]  Unknown
2. If Yes, specify observation method (choose all that apply):

[ ]  Exam [ ]  MRI [ ]  History [ ]  Unknown

1. \*Do you have a family history of MS? [ ]  Yes [ ]  No [ ]  Unknown

## General Instructions

This module contains questions related to the diagnosis and disease course of major demyelinating diseases, which may be important in some studies depending on their focus. Core items have been defined below which are specific to MS-focused studies. References to recent diagnostic criteria utilized are listed below.

The elements on this form are classified as Supplemental (unless otherwise specified by an asterisk as indicated below) and should only be collected if the research team considers them appropriate for their study.

\*This element is classified as Core

## Specific Instructions

Please see the Data Dictionary for definitions for each of the data elements included in this CRF Module.

* Current Diagnosis – Choose only one.
* MS Clinical Course Onset – For participant/subjects with a diagnosis of multiple sclerosis only indicate whether the onset was relapsing (i.e. due to “attack” or “relapse”), or progressive (i.e. without evidence of an attack but rather due to insidious neurological worsening).
* MS Current Disease Course – For participant/subjects with relapsing onset, please specify whether participant/subject’s current clinical course is relapsing-remitting MS, secondary progressive MS or uncertain. For participant/subjects with progressive onset, please specify whether participant/subject’s current clinical course is primary progressive MS (i.e. no history of relapse), progressive relapsing MS or uncertain (i.e. history of relapse[s] at some point in time after the initially progressive onset).
* NMO Spectrum Disorder Type – For participant/subjects with a diagnosis of NMO Spectrum Disorder only, indicate the type of that the participant/subject currently has: monophasic, relapsing, recurrent optic neuritis, recurrent myelitis, unknown, or “other” (please specify type).
* NMO Spectrum Disorder Details –Indicate which clinical, imaging and/or laboratory characteristics apply –select all that apply from this list of five:
	+ Optic neuritis (also specify whether unilateral, bilateral or unknown)
	+ Acute myelitis (also specify whether cervical, thoracic and/or lumbar segments were involved (check all that apply)
	+ Contiguous spinal cord lesion >3 vertebral segments on MRI
	+ Brain MRI does not meet diagnostic criteria for multiple sclerosis
	+ NMO-IgG status (either seropositive, seronegative or unknown – only one of these boxes should be checked) [Supplemental]
* Time between onset of first optic neuritis and first myelitis – Indicate the elapsed time between onset of the first optic neuritis and the first myelitis (in months) only if applicable, i.e. only if both the optic neuritis and acute myelitis boxes (in 3 b) have been checked. [Supplemental]
* ADEM Type – Indicate the type of ADEM that the participant/subject currently has: monophasic, recurrent, multiphasic, unknown, or “other” (please specify type).
* ADEM Signs/Characteristics – Indicate which clinical or imaging characteristics apply by selecting all that apply.
* Other CNS demyelinating disorder – Specify type of disorder *and* check only one box to indicate whether monophasic, recurrent, unknown, or “other” (please specify).
* Diagnostic Criteria – For MS only, indicate which diagnostic criteria the participant/subject fulfills.
* Onset History – Complete all as accurately as possible
* Family History of MS – Refers to first or second degree relative
1. Lublin, F. D., Reingold, S. C., Cohen, J. A., Cutter, G. R., Sørensen, P. S., Thompson, A. J., … Polman, C. H. (2014). Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*, *83*(3), 278–286. [↑](#footnote-ref-1)
2. Lublin FD, Reingold SC, Cohen JA, et al. Defining the clinical course of multiple sclerosis: the 2013 revisions. Neurology. 2014;83(3):278-286. [↑](#footnote-ref-2)
3. Wingerchuck, D.M., Banwell, B., Bennett, J.L., Cabre, P., Carroll, W., Chitnis, T., …Weinshenker, B.G. (2015) International consensus diagnostic criteria for neuromyelitis optica spectrum disorders [*Neurology*](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4515040/), 85(2): 177-189. [↑](#footnote-ref-3)
4. see NMO 2006 criteria for details [↑](#footnote-ref-4)
5. Krupp LB, Banwell B and Tenembaum S. Consensus definitions proposed for pediatric multiple sclerosis and related disorders. *Neurology*. 2007; 68: S7-12. [↑](#footnote-ref-5)
6. Thompson AJ, Banwell BL, Barkhof F, et al. Diagnosis of multiple sclerosis: 2017 revisions of the McDonald criteria. Lancet Neurol. 2018 Feb;17(2):162-173. [↑](#footnote-ref-6)
7. Lublin, FD, Reingold, SC, Cohen, JA, et al. (2014). Defining the clinical course of multiple sclerosis: the 2013 revisions. *Neurology*, *83*(3), 278-286. [↑](#footnote-ref-7)