A consensus protocol for the standardization of cerebrospinal fluid collection and biobanking

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ABSTRACT

There is a long history of research into body fluid biomarkers in neurodegenerative and neuroinflammatory diseases. However, only a few biomarkers in CSF are being used in clinical practice. One of the most critical factors in CSF biomarker research is the inadequate powering of studies because of the lack of sufficient samples that can be obtained in single-center studies. Therefore, collaboration between investigators is needed to establish large biobanks of well-defined samples. Standardized protocols for biobanking are a prerequisite to ensure that the statistical power gained by increasing the numbers of CSF samples is not compromised by preanalytical factors. Here, a consensus report on recommendations for CSF collection and biobanking is presented, formed by the BioMS-eu network for CSF biomarker research in multiple sclerosis. We focus on CSF collection procedures, preanalytical factors, and high-quality clinical and paraclinical information. The biobanking protocols are applicable for CSF biobanks for research targeting any neurologic disease. ***Neurology*® 2009;73:1914–1922**

GLOSSARY

CIS = clinically isolated syndrome; **EDSS** = Expanded Disability Status Scale; **IgG** = immunoglobulin G; **MALDI-TOF** = matrix-assisted laser desorption/ionization time-of-flight; **MS** = multiple sclerosis; **MSFC** = Multiple Sclerosis Functional Composite; **SPMS** = secondary progressive multiple sclerosis.

There is a long history to the search for body fluid biomarkers in neurodegenerative and neuroinflammatory diseases, such as multiple sclerosis (MS). CSF has major advantages in the study of neurologic conditions, although sampling CSF is more invasive than sampling blood or urine.[1] Because of its close proximity to the CNS, the CSF may more accurately reflect ongoing pathology of the brain, spinal cord, and meninges, and therefore may provide important and novel information.

Currently, the most frequently used CSF biomarker in MS is the detection of oligoclonal immunoglobulin G (IgG) bands or quantitative intrathecal IgG synthesis. Despite extensive research efforts, no other markers have been adopted into clinical practice in MS. Reviews on the state-of-the-art of biomarker research in MS have shown that the majority of studies are underpowered.[2,3] One of the most critical is the lack of sufficient CSF samples that can be obtained by a single research center. Therefore, collaboration between investigators is needed.

WHY IS STANDARDIZATION OF CSF COLLECTION PROTOCOLS NEEDED? Standardized collection protocols should be established to ensure that the statistical power gained by large numbers of samples is not compromised by preanalytical factors. Furthermore, standardization of collection protocols allows investigators to replicate studies with samples that match the initial pilot data.

Here, we provide protocols for the standardized collection, biobanking, and exchange of CSF samples. This is a consensus protocol obtained during meetings of the European network for biomarkers in MS, BioMS-eu, held in London in March 2007. Large differences were present between collection protocols (figure and table 1). In the discussions, we have sought a balance between practicality and scientific rationale. Particular attention has been focused on preanalytic procedures, because errors in the collection, storage, and exchange of biofluids account for 60% of total laboratory errors.[4] Last, for optimal CSF research in MS, high-quality clinical and paraclinical data such as MRI are also needed. Such data will have great importance for the estimation of the prognostic value of a candidate marker.

Supplemental data at www.neurology.org

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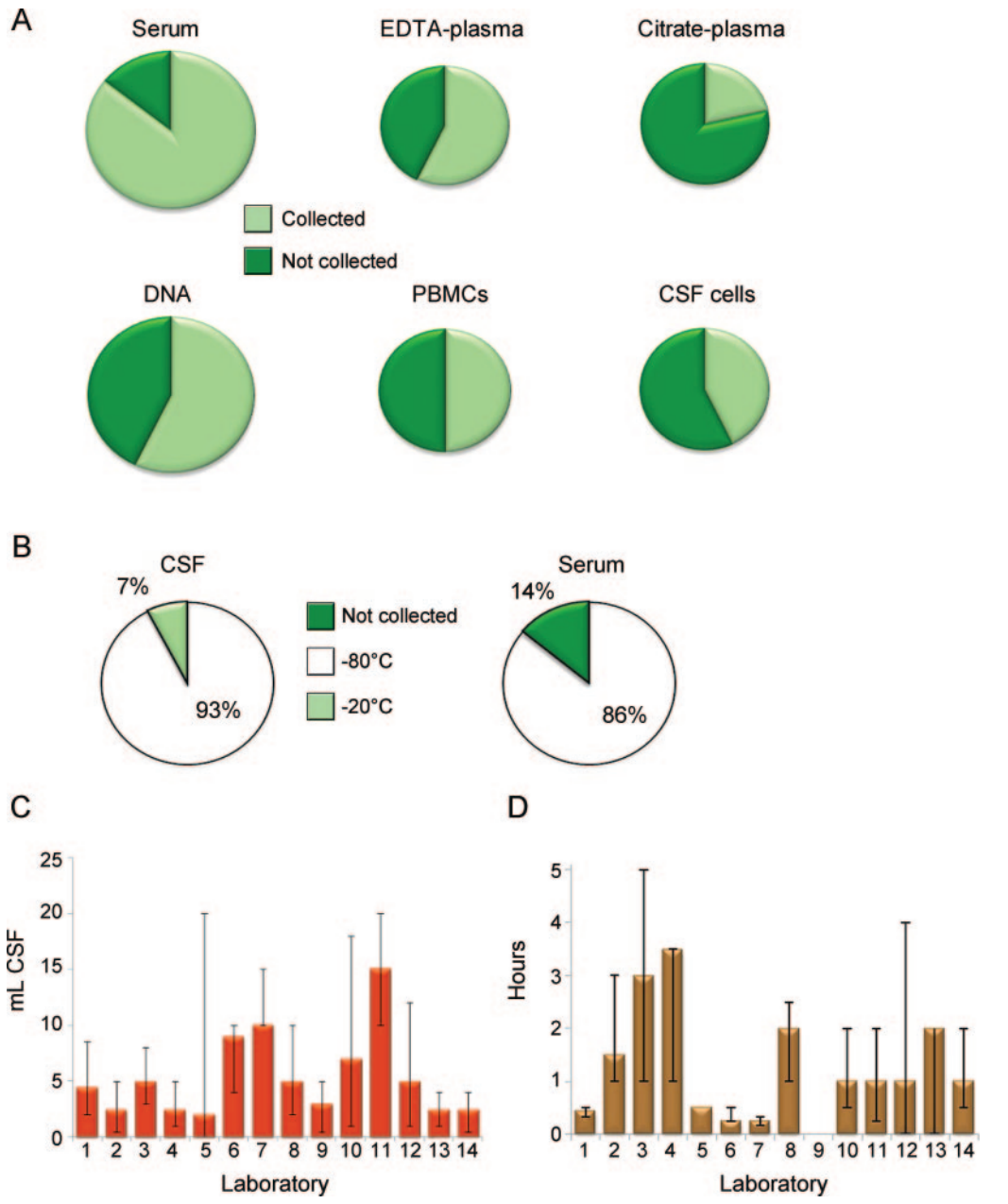
Figure Results of inventory of collection procedures among 14 European centers with CSF biobanks for multiple sclerosis research in 2006



(A) Other body fluids that are collected simultaneously with CSF. (B) Storage temperature of CSF and serum. (C) Average volume of CSF that is collected per patient per CSF withdrawal. Bars indicate the average and range of volume per center. (D) Time delay between CSF withdrawal, spinning, and storage in the freezer. Bars indicate the average and range of time per center. EDTA = ethylenediaminetetraacetic acid; PBMC = peripheral blood mononuclear cell.

We would like to stress that researchers should adhere to these protocols for optimal collaboration in the field of CSF biomarker research. We suggest using tables 2 and 3 as a checklist for CSF biomarker research and recommend that future studies of CSF biomarker take these issues into account. In discovery-based biomarker research, all these items should be considered carefully before initiating a study. Although some procedures may not be possible in everyday clinical practice and less stringent requirements may suffice for specific research questions, careful documentation of these issues is crucial to facilitate retrieval of appropriate samples dictated by specific study aims.

Importantly, the procedures for withdrawal and storage of CSF (table 2) are broadly applicable for any neurologic disease.

PROCEDURE FOR CSF COLLECTION **Item 1: Volume of withdrawal of at least 12 mL.** The CSF volume taken can influence the concentration of biomarkers. Most

Table 1 Results of inventory on collection protocols among 14 multiple sclerosis biomarker research centers

Procedure for CSF withdrawal	Previous status among European CSF centers
Type of needle	71% atraumatic, 21% traumatic, 8% both
Time of day of withdrawal (important for markers that are sensitive to circadian rhythm)	71% no specific day/time of withdrawal, 29% in the afternoon only
Temperature until storage	57% at room temperature, 43% at 4°C
Type of tube	50% Sarstedt, 29% Eppendorf, 21% other
Dividing into aliquots	Range 0.2–2 mL
Surveillance of freezers	Present at 93% of the centers
Several freezers to split the samples (backup)	Present at 14% of the centers

molecules and cell numbers have a rostrocaudal concentration gradient.[5,6] If a small volume is taken, the CSF will reflect the composition of the lumbar dural sac, whereas large volumes may reflect the rostral spinal or even ventricular CSF. Therefore, if biomarker concentrations in a sample from a puncture of 2 mL are compared with that in a puncture of 15 mL, this can lead to erroneous results. Also, collecting different portions of the CSF for biobanking (e.g., initial and final volumes of the puncture) may introduce errors. Thus, a standard volume of CSF should be collected during lumbar puncture; the first 2 mL can be used for basic CSF analysis (item 33), and the remainder of the sample should be pooled before being divided into aliquot parts. At least, the procedure must be recorded. The volume of collected CSF does not correlate with the risk of post–lumbar puncture headache.[7,8]

Item 2: Location of puncture vertebral body L3–L5. Usually, diagnostic CSF is obtained by lumbar puncture. Because of the increasing gradient in protein concentration from ventricular to lumbar CSF,[9] the site of CSF withdrawal must be recorded. When CSF is taken from other locations, such as the cervical cisterns or the lateral ventricles (e.g., ventricular drainage), this should be documented.

Item 3: Removal of bloody CSF samples. A traumatic tap causing blood contamination of CSF occurs in approximately 14% to 20% of standard lumbar punctures.[10] For biomarkers that have high serum concentrations, such as coagulation factors, blood contamination can lead to false-positive results. In addition, blood proteins lead to suppressed matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF)/MS proteomics patterns in CSF. This suppression by blood proteins is, however, highly reduced after removal of the blood cells by centrifugation before initial freezing.[11,12] Recording of erythrocyte count is essential to select CSF samples appropriate for these measurements. CSF samples with an erythrocyte count above 500/μL should not be used for biomarker studies.

Item 4: Use of atraumatic needle (Sprotte or Whitacre needle). There is no evidence that the type of lumbar puncture needle influences biomarker concentrations. However, atraumatic needles are best tolerated by patients and are associated with a lower risk for post–lumbar puncture headache, i.e., approximately 12% for a needle size of 20–22 gauge compared with approximately 70% for a needle size of 16–19 gauge.[13,14]

Item 5: Use of polypropylene collection tubes. There are several reports showing that the type of collection tube influences biomarker outcomes, e.g., total tau proteins and amyloid-β peptides.[15] Therefore, standardization is important. We propose to use polypropylene tubes, with their low protein binding potential, for collecting CSF. No additives should be used. Glass tubes should be avoided because of safety reasons for personnel.

Item 6: Time of day of withdrawal. For biomarkers that are influenced by circadian rhythms, time of withdrawal is important.[16] Because it is often difficult to accomplish standardization of withdrawal time in everyday clinical practice, documentation is necessary to select the appropriate samples to minimize the effect of this variable.

Items 7 and 8: Serum, plasma, and DNA linked to the CSF sample. It is important to collect matched serum and/or plasma samples for evaluation of CSF biomarkers because the concentration of the marker in blood often influences that in CSF.[1] Further, serum/plasma pairs are essential to study the intrathecal origin of a biomarker and its CNS specificity. Furthermore, the presence of CNS markers in serum/plasma may aid in disease monitoring. Vacuum tubes that use ethylenediaminetetraacetic acid (in dried format) are preferred over those that use citrate (in solution), because if tubes containing a standard volume of citrate are filled incompletely, the final biomarker concentration is diluted artificially. Depending on the type of biomarkers and methods of study, we recommend collecting both serum and plasma[17]; for some methods, plasma is preferred over serum and vice versa. Serum/plasma samples should not be hemolytic.

Last, DNA collection expands the possibilities for studying the phenotypes and genotypes within individuals. A protocol for storage and handling of DNA can be found in appendix e-1 on the *Neurology*® Web site at www.neurology.org.

Item 9: Storage at room temperature until spinning and dividing into aliquots. For CSF, there are no data available yet that support a preference for leaving the

Table 2 Consensus-based recommendations for CSF withdrawal procedure

Item	Procedure	Ideal situation
1	Preferred volume	At least 12 mL; first 1–2 mL for basic CSF assessment (see issue 33); last 10 mL for biobanking
		Record volume taken and fraction used for biobanking
2	Location	Vertebral body L3–L5
3	If bloody	Do not process further
		Criteria for bloody: more than 500 red blood cells/μL
		Record number of blood cells in diagnostic samples
4	Type of needle	Atraumatic
5	Type of collection tube	Polypropylene tubes, screw cap, volume 1–2 mL
6	Time of day of withdrawal and storage	Preferably standardized within each center, allowing for intercenter differences in local logistics
		Record date and time of collection
7	Other body fluids that should be collected simultaneously	Serum
8	Other body fluids that should be collected simultaneously	Plasma: EDTA (preferred over citrate)
9	Storage temperature until freezing	Room temperature before, during, and after spinning
10	Spinning conditions	Serum: 2,000*g*, 10 min at room temperature
		CSF: 400*g*, 10 min at room temperature/2,000*g* if no cells are to be preserved
11	Time delay between withdrawal and spinning and freezing	Optimal for CSF: 1–2 h
		Optimal for serum: 30–60 min
		Thus doing both body fluids simultaneously, ideally within 1 h
		After spinning, samples must be divided into aliquots and frozen immediately for storage at −80°C
12	Type of tube for aliquots	Small polypropylene tubes (1–2 mL) with screw caps; record manufacturer
13	Aliquots	A minimum of 2 aliquots is recommended; the advised research sample volume of 10 mL should be enough for >10 aliquots
14	Volume of aliquots	Minimum 0.1 mL; depending on total volume of tube: 0.2, 0.5, and 1 mL; preferably, the tubes are filled up to 75%
15	Coding	Unique codes; freezing-proof labels; ideally barcodes to facilitate searching, to aid in blinding the analysis and to protect the privacy of patients
16	Freezing temperature	−80°C
17	Additional items on sample collection protocols that must be recorded	Location of samples
18	Additional items on sample collection protocols that must be recorded	Surveillance of freezers
19	Additional items on sample collection protocols that must be recorded	Splitting of samples over 2 or more freezers

EDTA = ethylenediaminetetraacetic acid.

samples at room temperature or at 4°C until processing. For serum/plasma, it is more crucial. To avoid platelet activation,[18] serum/plasma samples should be kept at room temperature before centrifugation. Therefore, processing at room temperature for both serum/plasma and CSF, including during and after spinning, is suitable for most studies. Relatively few systematic studies have been performed on this issue. We would recommend exploratory studies to define the effect of temperature on specific biomarkers.

Item 10: Standardized spinning conditions. We propose to adhere to a standardized spinning protocol of 400 *g* for 10 minutes at room temperature when fragile cells need to be preserved for RNA of cell isolation, and otherwise at 2,000 *g*. For serum, we propose to spin at 2,000 *g* for 10 minutes at room temperature. Standardization of spinning temperature and speed may be important for some biomarkers, although no studies have addressed these specific preanalytical variables for CSF. For plasma and serum, temperature of processing is known to be critical for specific biomarkers.[19] After centrifugation, the supernatant must be divided into aliquots and stored immediately. If this is not done, the processing time should be documented.

Item 11: Standardization of time delay between withdrawal, spinning, and freezing. Studies of the effects of preanalytical variables by MALDI-TOF/MS proteomics (proteins/peptides <20 kD) have shown that the time between sampling and storage is more crucial for specific serum proteins or peptides than for CSF.[11,12,20] For CSF, it was observed that processing within 2 hours does not lead to artifactual results.[11,12] For serum, it was observed that small differences in processing time (approximately 10–30 minutes) can result in different proteomics spectra.[17] Some biomarkers, such as antibodies or specific cytokines, are not very sensitive to sampling and storage conditions.[21] For practical reasons and in view of the standard of 30- to 60-minute clotting time for serum, we recommend a time delay of 1.5 hours (±30 minutes) for both matrices. When CSF cells are to be preserved, processing as soon as possible is advised because cell numbers decrease quickly. However, in most of the centers, processing of the body fluid samples within 1 hour is not common practice. Therefore, documentation of time of withdrawal and storage is required to select uniform samples. For newly discovered biomarkers, these preanalytical variables should be evaluated.

Item 12: Use of small polypropylene tubes for aliquots. Because of the same rationale as for CSF withdrawal (item 5), we recommend that polypropylene tubes should be used for division into aliquots and storage. Furthermore, vials with screw caps should be used for a secure sealing.

Table 3	Consensus-based recommendations for information requirements in databases of patients with multiple sclerosis
Item	**The following characteristics should be recorded:**
	Basic demographics
20	Date of birth (age if date of birth is not available)
21	Gender
22	Ethnicity
	Outcome measurements
	Clinical characteristics
23	Clinical subtype at time of sampling according to McDonald criteria[32]
24	Date of first symptoms
25	Date of diagnosis according to McDonald criteria, date of first and second events
26	Date of conversion from RRMS to SPMS (if possible)
27	EDSS at sampling; if possible, MSFC and other validated functional outcome measures at sampling
28	EDSS and other functional scores (e.g., MSFC) at follow-up (i.e., the patients should be followed up); include the date of measurement
29	Relapses
	Number and, if possible, dates of relapses in the 2 y before collection of sample
	Time between the start of last relapse and collection of sample
	Relapse at the time of sampling according to Schumacher criteria (≥1 increase in EDSS > 24 h on stable background for at least 30 days) [41]
30	Number and, if possible, dates of relapses at each year of follow-up
31	Glucocorticoid therapies, at sampling and year before sampling
32	Use of other drugs, at sampling and year before sampling
33	Basic CSF analysis (CSF cell count, differential cytology, erythrocyte count, oligoclonal IgG bands [which is at least 2 bands by definition], albumin ratio, total protein [if albumin is not measured], and IgG index)
	Record the methods of routine analysis
	MRI characteristics
34	MRI scan of brain and spinal cord; record date
35	Number and volume of Gd-contrast enhancing MRI lesions, T1 and T2 lesion volumes, and brain/spinal cord atrophy, when available
36	Follow-up MRI scans, if possible
	General database requirements
37	The data in the CSF database should be in English and use standardized international units

RRMS = relapsing-remitting multiple sclerosis; SPMS = secondary progressive multiple sclerosis; EDSS = Expanded Disability Status Scale; MSFC = Multiple Sclerosis Functional Composite; IgG = immunoglobulin G; Gd = gadolinium.

Item 13: Aliquots. Freeze/thaw cycles can influence biomarker concentrations.[22] For example, 1-time freezing of CSF samples can lead to a highly significant loss of amyloid-β, which is decreased a further 20% after 3 more thawing cycles.[23,24] By contrast, no effects on CSF proteome profiles obtained by MALDI-TOF/MS have been observed after up to 4 freeze/thaw cycles.[12]

In principle, repeated freezing/thawing of samples should be avoided, because data addressing this topic are available for only a few biomarkers and the response to freeze/thaw cycles of new biomarkers is not known. Thus, splitting the pooled sample into multiple small aliquots is optimal, and eventual freeze/thaw cycles should be recorded.

Item 14: Volumes of aliquots of 0.2, 0.5, and 1 mL. Small aliquot volumes are optimal to avoid freezing/thawing and to avoid waste of CSF. The proposed *tube* sizes are 0.25, 0.5, and 1 mL. Tubes should be filled up to 75% to prevent freeze-drying within the tube, which will affect the concentration of biomarkers, although it may only be a problem if the seal of the cryogenic tubes are not airtight. This issue has not been formally studied and is not referred to in related standard operating procedures.[25]

Item 15: Coding and use of freezing-proof labels. Unique codes are necessary to track samples and pair with clinical data. Ideally, bar codes should be used to facilitate searching, to aid in blinding the analysis, and to protect the privacy of patients. It is important to have center-unique codes, to track data retrospectively. Labels must be water and frost (−80°C) resistant.

Item 16: Freezing temperature of −80°C. Proteins may not be stable at −20°C for years. In one study, the effect of storing CSF at −20°C and −80°C on cystatin C, an abundant CSF protein, was investigated. Cleavage of this protein occurred in all samples stored at −20°C but not in samples stored at −80°C.[26] Apart from the cystatin C truncation, changes in the low molecular weight polypeptide profile due to CSF sample storage at −20°C for 3 months seemed to be minimal.[11,12] Oligoclonal bands in CSF may be recovered after several years of storage at −20°C, indicating a high stability of immunoglobulins.[27] No data are available showing the benefit of storage of CSF or serum in liquid nitrogen. Because this is expensive and not practical for CSF biobanking, there is no basis yet to recommend storage in liquid nitrogen.

Taking these data together, we recommend that samples are stored at −80°C to ensure long-term stability of biomarkers.

ADDITIONAL ITEMS OF SAMPLE COLLECTION PROTOCOLS THAT MUST BE RECORDED IN MS BIOMARKER RESEARCH

Item 17: Location of samples. To enable easy tracking and fast relocation of samples, storage information should include freezer location, freezer identification, and sample location within the freezer.

Items 18 and 19: Surveillance of freezers and splitting of samples. Freezers should be alarm controlled, and a sample rescue plan should be established and documented. All freezers must be registered in a freezer log file. Ideally, daily temperature logs should be available for all freezers. Aliquots of samples should

be distributed among different freezers. Ideally, an empty backup freezer should be available.

INFORMATION REQUIREMENT IN DATABASE IN THE CONTEXT OF MS

Items 20 and 21: Basic demographics, such as age and gender. Information on the age at sampling is needed to allow comparability to age-matched reference values, because many proteins show age-dependent changes, e.g., albumin or IgG.[28] Ideally, date of birth and date of sampling are recorded (table 3). Gender must be provided because of variability of markers influenced by hormones.

Item 22: Ethnicity. Reference ranges of biomarkers can be influenced by the genetic status.[29] For example, a recent study observed a higher IgG index in African Americans than in Caucasians, unrelated to socioeconomic status.[30] Criteria for race and ethnicity are available via the Web site of the NIH.[31]

STANDARDIZATION OF OUTCOME MEASUREMENTS IN MS

Items 23–26: Clinical subtype at time of sampling, date of onset, and date of diagnosis. A goal of biomarker research is to identify surrogate endpoints for relevant disease characteristics such as clinical subtype, disease duration, disease activity, and progression. Therefore, it is crucial that diagnosis is made according to standard criteria[32,33] and that the correct disease subtype at sampling is recorded. The date of first and second events should also be recorded to define the date of conversion from clinically isolated syndrome (CIS) to clinically definite MS.[32,33]

The following clinical subtypes (stages) of MS are commonly differentiated: CIS, relapsing-remitting MS, relapsing secondary progressive MS (SPMS), nonrelapsing SPMS, primary progressive MS, and progressive relapsing MS.[34] The time point of conversion to SPMS may be helpful to distinguish between slow and rapidly progressive MS or to develop biomarkers to predict conversion to the SPMS phase.

Item 27: Expanded Disability Status Scale and functional scores at sampling. We recommend using appropriate and well-validated outcome measures. Although Expanded Disability Status Scale (EDSS) scores and functional scores[35] are not linear disease severity scores and do not necessarily reflect progression rate, inflammatory activity, and lesion load,[36,37] they are important for stratification purposes and as a measure of severity. However, it is advised to include other clinical scales too, such as the Multiple Sclerosis Functional Composite (MSFC) and its subscores.[38,39] The MSFC also accounts for cognitive functioning, which is affected in 30% to 70% of MS patients.[40]

Item 28: Clinical scores at follow-up. Follow-up EDSS, functional system scores, and preferably MSFC and its subscores are helpful to determine disease progression rate, which is an important clinical endpoint required for evaluation of candidate biomarkers.

Item 29: Number of relapses in the preceding years before collection of sample and time between last relapse and lumbar puncture. Numbers of relapses is an indicator for retrospective clinical activity that may influence biomarker status. Relapses should be defined according to the Schumacher criteria,[41] and the dates should also be recorded to determine the time interval between the start of the last relapse and the time of sampling. It is important to relate number of relapses to a defined retrospective time window, preferably 2 years, to obtain comparable and reliable data on annual relapse frequency.

Item 30: Number of relapses at each year of follow-up. Because annual relapse rates are often used to describe the clinical activity and most MS therapies mainly affect the number of relapses, this is an important target variable for biomarker research.[42,43] Ideally, dates of relapses should be recorded, which allows for studying whether a biomarker predicts early vs late relapses.

Items 31 and 32: Treatment at sampling and year before sampling. It is well known that commonly used drugs for treatment of MS, including immunomodulatory agents and methylprednisolone for treatment or prevention of relapses, have an influence on expression of biomarkers.[44,45] Therefore, type and duration of treatment, also not related to MS therapy, should be documented in detail, preferably beginning at least 1 year before CSF collection.

Item 33: Basic CSF analysis (protein, cell counts, erythrocytes, and so on). To enable stratification of patients according to their CSF findings and to evaluate suitability of samples for further analysis, results of basic CSF analysis should be recorded. Primarily, the CSF profile serves for exclusion of other diseases. In addition, quantitative changes of immunologic markers are likely to occur, depending on disease stage, relapse activity, and medication. Inflammatory processes may influence the blood-CSF barrier function and thereby biomarker concentrations.[1]

Oligoclonal IgG bands are important to test the value of a new diagnostic biomarker. The sensitivity of oligoclonal IgG bands is strongly dependent on the method used. We strongly recommend isoelectric focusing followed by immunoblotting and staining for IgG.[46,47] Preferably, the methods of all routine diagnostic procedures, including oligoclonal banding, should be documented.

Items 34 and 35: MRI characteristics. This information should contain the following items: whether a brain and/or spinal cord MRI has been performed, the date the study was performed, and where it was performed (to access the source data if required). Preferably, the data set should be available for later analysis. It is questionable whether the number of lesions and total lesion load are reliably recorded with routine diagnostic studies, but these are valuable parameters for estimating disease activity. There is great variation between different imaging centers regarding which routine sequences are obtained (axial vs sagittal, T2 vs proton density vs fluid-attenuated inversion recovery techniques, slice thickness, and so on). A valuable and reliable parameter to collect is the number of gadolinium enhancing lesions, because the presence of gadolinium enhancing lesions reflects the inflammatory activity at the time of the scan and ideally also of the CSF or blood collection. In the context of studies on biomarkers for neurodegeneration and neuroprotection in MS, information regarding brain atrophy is valuable, although several outcome measures of atrophy exist in various centers. A common MRI protocol would be desirable.[48,49]

Item 36: Longitudinal MRI scans. Longitudinal MRI scans would be desirable to monitor disease progression, and they may be possible in some centers. However, because of the lack of using standardized MRI protocols in routine investigations, regular follow-up MRIs cannot be recommended at present.

Item 37: Data in the CSF database in English. The mask on the database screen could be in the local language, but the underlying files will need to be in English. It is strongly suggested to use a commercially available program, if not a common database for networks such as BioMS-eu. The database should also adhere to standardized international units.

ETHICAL ISSUES

For collaboration in Biomarker research, the presence of good ethical protocols that comply with national and international ethical and other legal regulations is of utmost importance. Most, if not all, centers already have a good ethical protocol for CSF biobanking and biomarker research. The most important issues are that the protocol allows exchange of (coded or pseudoanonymized) samples and relevant patient information, and patient consent. To address the needs of investigators, samples should initially be pseudoanonymized, i.e., stored with a code that can be linked to subject identifiers so that clinical details could be updated after the sample has been collected. However, when samples are extracted from the biobank for the purposes of research, they should be released as anonymized samples, i.e., stripped of their link with personal identifiers. This is to protect the privacy of individuals participating in research.

Researchers may have to give notice of new research projects to their ethical office and make material transfer agreements. Because rules differ among centers and countries, it is the responsibility of the research centers to adapt their procedures according to local rules.

CONCLUDING REMARKS

The lists provided in table 2 can be used as an easy checklist for CSF biobanking for any CNS disease, applicable during setup of the procedures and also as a checklist for recording sample characteristics. It is expected that these standardizations will pave the way for large biomarker studies and fruitful collaborations. Ultimately, these endeavors are to arrive at validated biomarker assays for diagnosis, prognosis, and treatment of CNS diseases and a potential to elucidate relevant disease mechanisms.

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DISCLOSURE

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