ENMC Impact Report 2021

Our year in highlights

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Contents

1 Message from Dr Arpad von Moers, Chair of the Executive Committee

Just as in 2020, the year 2021 was dominated by the waves of pandemic.

Again the ENMC team in Baarn had to be very flexible and resourceful in order to prepare and perform the workshops, and with success: in 2021 the ENMC hosted eight workshops in different formats, both fully online in the "Zoom rooms" and in a professional hybrid setting.

Notwithstanding these challenging circumstances, the Mid-Career Mentoring Programme was implemented successfully. This programme provides an important contribution for the next generation of leaders in the neuromuscular field. Four mentees were selected for an ENMC mentorship and 20 international experts were registered as a mentor. Furthermore, the Young Scientist Programme has been updated and is now called Early-Career Programme, to be in line with the Mid-Career Mentoring Programme.

The members of the Executive Committee (EC) and the Research Committee (RC) had an inspiring face-to-face meeting, where both committees jointly met in the workshop hotel in Hoofddorp on 5 and 6 November. This was a highlight in 2021.
On 7 November 2021 the EC-Chair responsibilities were transferred from me to Dr Alexandre Méjat, International Scientific Affairs manager at AFM-Téléthon, France.

In 2021 we said goodbye to two much valued colleagues. The unrivaled Ms Annelies Zittersteijn retired. She organised workshops for the ENMC for more than 16 years and enabled everybody to feel most welcome and connected with the ENMC.
Dr Jes Rahbek had been the Danish representative within the EC from the early days of the ENMC. He always stressed the patients' point of view and the importance to engage them in our activities. He transferred the Danish representation to Mr Henrik Ib Jørgensen, Director of Muskelsvind-fonden.

Your unwavering commitment to the mission of the ENMC is much valued and ensures that the ENMC can continue to improve the care and treatments for NMD patients. I would like to thank the ENMC team in Baarn, the members of the RC and EC, the Associated Partners, the workshop organisers and participants and the Company Forum for their supporting contributions.

Dr Arpad von Moers,
Chair of the Executive Committee

The members of the RC and EC committees during the joint meeting in November, with two staff members of the ENMC.

2 The mission of the ENMC

In 1992, a group of scientists and clinicians, together with parents of children affected by neuromuscular conditions, launched the European Neuromuscular Centre (ENMC). They had in mind the ultimate goal to improve diagnosis, accelerate the search for effective treatments and improve the quality of life of people with neuromuscular conditions. To achieve this goal, it was, and still is, of utmost importance that experts in the field of rare and ultra-rare disorders share their knowledge and experience and collaborate in research worldwide.

The ENMC encourages and facilitates this collaborative aim through the organisation of small interactive workshops for multidisciplinary groups of researchers, clinicians and persons affected by a neuromuscular condition, a unique concept in the scientific community.

ENMC Mission Statement

The mission of ENMC is to encourage and facilitate communication and collaboration in the field of neuromuscular research with the aim of improving diagnosis and prognosis, finding effective treatments and optimising standards of care to improve the quality of life of people affected by neuromuscular disorders.

“Connecting people”

3 The ENMC workshops in 2021

Many ENMC workshops that were planned to take place in 2020 were postponed to 2021 due to Covid-19. But again in 2021 the pandemic prevented the ENMC from organising face-to-face workshops in Hoofddorp. Last year, two ENMC workshops took place in a hybrid format, with a professional videoconferencing setup in the meeting room. Six other workshops were organised virtually, sometimes spread over a couple of afternoons to enable people to call in from different time zones. Most of these online meetings were in preparation of the face-to-face meetings that had been postponed to 2022. One workshop, 259, was held fully online.

We express the hope that in 2022 we will be able to organise most workshops in a face-to-face setting, because social interactions contribute to a trusted atmosphere and create lifelong collaborations and are therefore an important assett of the ENMC workshops. The professional hybrid setup has proven to work well and enabled us to continue to organise our workshops.

In 2021 three workshop applications were submitted, two regular applications and one themed workshop application. All three were selected for financing by the ENMC and are planned to take place in 2022.

3.1 Themed workshops

THEMED WORKSHOPS

In addition to the regular ENMC workshop applications, where topics of the workshops originate from the workshop organisers, ENMC launched a call for themed workshops applications. This programme was set up to prepare the stepping stones for the future by listening to the needs of the neuromuscular patients and research community. With a "Themed Call", the ENMC provides workshop funding opportunities for 1 or 2 themed workshops per year, focusing on a pre-identified topic which:

- is of broader interest to more than one condition (transversal workshops)
- requires a multidisciplinary approach
- is not often discussed in a workshop
- is groundbreaking and strategic and requires the development of a sustainable platform in the future

For upcoming years (2022 and beyond), themes for the calls will be chosen by the ENMC every two years and will be announced in September. The application deadline will be the first of March in the year following the announcement.

3.2 Summary of ENMC workshops held in 2021

Workshop no./date and format	Topic	Workshop leaders
Workshop no. 253 30-31 October 2020 (virtual) 19-20 February 2021 (virtual) Every two months virtual meetings were planned in 2021 24-26 June 2022 (face-to-face)	Striated muscle laminopathies; natural history and clinical trial readiness	Dr G. Bonne, Dr L. Maggi, Prof. S. Quijano-Roy, Dr C. Bönnemann
Workshop no. 255 15 January 2021 (virtual) 16 January 2021 (virtual) 22 January 2021 (virtual) September 2022 (face-to-face)	Muscle imaging in idiopathic inflammatory myopathies	Prof. M. de Visser, Prof. J. Vencovský, Prof. P.G. Carlier
Workshop no. 256 8-10 October 2021 (hybrid)	Myositis specific and associated autoantibodies (MSA-ab)	Dr Y. Allenbach, Prof. O. Benveniste, Dr J. Damoiseaux, Dr A. Mammen
Workshop no. 258 16 October 2020 (virtual) 4 December 2020 (virtual) 9 July 2021 (virtual) 25-27 March 2022 (face-to-face)	Genetic epidemiology and clinical trial readiness in encephalomyopathy of Leigh syndrome	Prof. E. Bertini, Prof. S. Rahman, Prof. M. Schiff, Prof. B. Cohen
Workshop no. 259 11 December 2020 (virtual) 28 May 2021 (virtual) 29 May 2021 (virtual)	Anaesthetic management in neuromuscular disorders	Dr N. Voermans, Dr M. Snoeck, Prof. H. Jungbluth
Workshop no. 261 19 March 2021 (virtual) 17-19 June 2022 (face-to-face)	Management of safety issues arising following AAV gene therapy	Prof. L. Servais, Prof. F. Muntoni, Prof. C. Bönnemann
Workshop no. 262 16 July 2021 (virtual) 17 December 2021 (virtual) 11-13 February 2022 (face-to-face)	Standards of Care for the Dysferlinopathies	Prof. V. Straub, Dr A. Mayhew, Dr T. Stojkovic, Dr L. Bello
Workshop no. 263 25 June 2021 (virtual) 26 November 2021 (virtual) 13-15 May 2022 (face-to-face)	Focus on female carriers of dystrophinopathy: refining recommendations for prevention, diagnosis, surveillance and treatment	Prof. A. Ferlini, Dr J. Bourke, Dr R. Quinlivan, Dr A. Sarkozy
Workshop no. 264 19-21 November 2021 (hybrid)	Multi-system involvement in Spinal Muscular Atrophy	Prof. G. Baranello, Dr T. Gilllingwater, Prof. K. Swoboda, Dr R. Kothary

Note: The workshop number (no.) is given once an application is officially approved and hence dates can be reserved. It does not always precisely reflect the timing of the execution of the workshop. Workshops 257 and 260 will take place in 2022 and are therefore not listed here.

Two out of the eight planned workshops, 256 and 264, took place in a hybrid setup in the Marriott Hotel, Hoofddorp, The Netherlands in the autumn of 2021. One workshop, 259, was held fully online.

Six workshops, 253, 255, 258, 261, 262 and 263 were held virtually in 2021 and will be followed by a face-to-face meeting in 2022. The workshops are listed in the table on the left page.

253rd virtual ENMC International Workshop: Striated Muscle Laminopathies

Due to the worldwide pandemic, the 253rd ENMC international workshop on Striated Muscle Laminopathies (SML), scheduled initially in March 2020, was postponed.
After a first virtual conference held during two afternoons on 30 and 31 October 2020, the organisers proposed a second round of virtual sessions on 19-20 February 2021 in order to progress in the preparative work necessary to reach the initial aims of the workshop which are

1. to share available data on natural history in adult and pediatric SMLs among experts and
2. to create working groups focused on the identification of clinical outcome measures and biochemical, molecular and imaging biomarkers useful for natural history studies and future clinical trials.

Before the second meeting, a survey was circulated among the workshop participants to collect the current status of the basic science research as well as the available data and knowledge related to clinical management of SML patients.

The workshop gathered 30 participants from Europe and America, including healthcare providers and researchers from Argentina, France, Italy, The Netherlands, Spain, Germany, Poland, UK and USA, as well as patients and representatives from four advocacy associations (Cure-CMD, Fundacion Andrès Marcio niños contra la laminopatía (FAM), Muscular Dystrophy UK (MD-UK), Associazione Italiana Distrofia Muscolare di Emery-Dreifuss (AIMED).

In the second meeting Dr G. Bonne organised three parallel working groups with the aim to summarize the answers of the survey for three topics: clinical aspects, biomarkers and perspective of patients and patient representatives.
The meeting ended with the proposition to hold virtual sessions of 1h30 every other month to allow each working group to further exchange data, knowledge and advances on preparative work on the specific topics that would be presented at the face-to-face meeting scheduled on 10-12 December 2021.

Once again in December 2021, the worldwide pandemic prevented a face-to-face meeting as scheduled. Therefore, the 253rd international ENMC workshop was converted into a virtual session on 10 December 2021 and the face-to-face meeting was rescheduled for 24-26 June, 2022.

Dr G. Bonne:

> “All these virtual meetings have been an excellent opportunity to update and deepen our knowledge of natural history of laminopathies, laminopathies, promoting the international research and collaborative studies to better characterise and follow our patients, while we all really hope to meet again in person on 24-26 June 2022.”

The virtual session in December was dedicated to the patients' perspectives, with reports from patient representatives on patients' expectations and needs. The discussions between clinicians, researchers and patient representatives highlighted the difficulties faced by patients and their families to get a correct diagnosis and an adapted care once diagnosed. This helped in prioritizing the scientific and clinical questions that need to be tackled for SML.

256th ENMC International workshop: Myositis specific and associated autoantibodies


On site (left) and online (right) participants of workshop 256.

Workshop attendees included a multidisciplinary group of 20 participants from 10 countries comprising clinicians from different disciplines, laboratory specialists, researchers and two patients. Due to Covid-19 restrictions this was a hybrid meeting with about half of the participants attending on site and the other half attending online.

Background

Idiopathic inflammatory myopathies (IIM) represent different subtypes: dermatomyositis (DM), Immune-Mediated Necrotizing Myopathy (IMNM), Anti-Synthetase Syndrome (ASyS), Inclusion Body Myositis (IBM), Overlap Myositis (OM), and Polymyositis (PM). These subtypes differ in clinical manifestations, prognosis, and therapeutic options. In the last decades multiple markers in IIM patient's blood called 'autoantibodies' have been discovered that support the diagnosis and add information on subtype and prognosis. Detection of Myositis-Specific Autoantibodies (MSA) was originally restricted to research laboratories, but nowadays several commercial assays have become available, enabling widespread introduction of the assays in clinical laboratories.

Workshop deliverables and their outcomes

The following workshop deliverables were set to enable optimal interpretation of the test results of the assays for MSA: (i) Define the clinical indications that suggest screening for MSA, (ii) Define the optimal testing strategy for patients suspected of

The patient's voice was well represented at this important meeting by Mr R. Mischke and Mrs I. de Groot.

IIM; (iii) Harmonise the way of reporting results to the clinician in order to enable optimal interpretation.

Outcome for the patients and their families

The patients will benefit from a better understanding of the clinical usefulness of MSA in terms of diagnosis, subtyping and prognosis by their treating clinician.

Next steps

A multi-centre study will be designed in order to better determine the test-characteristics of the individual MSA in relation to the associated clinical manifestations. This will improve the interpretation of the test results.

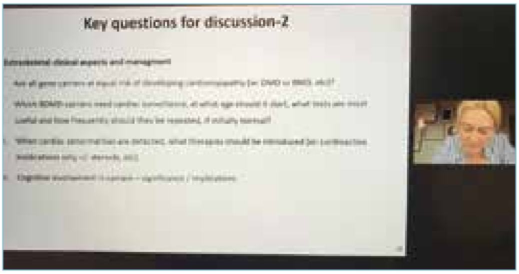
Social interactions are an important part of the ENMC face-to-face workshops. Here Mr Y. Piette (Early-Career Researcher) and Mrs I. de Groot (patient) are having a chat during one of the breaks of workshop 256.

263rd ENMC international workshop: Focus on female carriers of dystrophinopathy: refining recommendations for prevention, diagnosis, surveillance and treatment

Two virtual meetings took place in 2021, on 25 June and on 27 November. A face-to-face meeting is planned for 13-15 May 2022.
In the virtual meetings, 16 participants from France, UK, Italy, Germany, Spain, Belgium and the Czech Republic were present in the Zoom room. Participants were medical doctors and/or researchers in the field of neurology, cardiology and medical genetics. Also two patient representatives and two Early-Career Researchers attended the meeting.

Background

Dystrophinopathy (DMD) female carriers are a clinically complex and still neglected patient group. These individuals carry the gene for Duchenne muscular dystrophy on one of the X-chromosomes, which can be potentially inherited by their sons, but are themselves protected by the fact that the second X-chromosome has the 'healthy' gene. Sometimes, female carriers do present with symptoms, which require attention and research. Management and research for DMD female carriers are still considered as "low priority". There is poor definition of "female carrier status" and "manifesting carrier", of clinical outcome measures, assessment and management of non-muscle symptoms and use of various novel therapies.



Key questions for discussion-2

Mrs E. Rueben talking about what it means to be a female carrier.

The deliverables of the workshop are to:

1. Raise priority and need for much greater clinical and research focus on DMD female carriers.
2. Highlight unmet needs of dystrophinopathy female carriers.
3. Propose a clinically useful classification of carrier status.
4. Demonstrate how available preventative and therapeutic approaches can improve patient outcomes.

Participants of workshop 263 in the Zoom room.

255th ENMC International Workshop: Muscle Imaging in idiopathic inflammatory myopathies

This summary covers the work done in the three virtual meetings in January 2021. The workshop will be followed up by a face-to-face consensus meeting in September 2022.

The first three virtual meetings held on 15, 16 and 22 January gathered 23 clinicians, researchers and patients from France, Denmark, Belgium, The Netherlands, UK, USA, Italy, Germany, Poland and Czech Republic.

Background

Muscle imaging plays an important role in the diagnostic process in Idiopathic inflammatory myopathies (IIMs) and might also be helpful for monitoring disease progression as part of natural history studies and clinical trials. Despite the advantage of visualization of a large muscle volume and its capability to differentiate active inflammation from chronic damage, there is still no generally accepted recommendation for the performance and evaluation of the imaging modalities.

Participants of workshop 255 in the Zoom room.

Main objectives

The main objective of this workshop was to define recommendations concerning main technical parameters and propose a universally applicable evaluation system.
An overview on the current classification of IIMs was given, followed by an overview of published qualitative and quantitative magnetic resonance imaging (MRI) protocols. A review of established scoring systems showed how significantly the individual scoring methodologies differ across published studies.
Both patients attending the workshop expressed their wish that muscle imaging becomes a reliable outcome instrument, its potential being enormous since it is non-invasive, painless and widely available.

Talks in the preparatory virtual meetings focused on different myositis subtypes and their patterns on MRI or other imaging modalities, MRI as a biomarker to be used to monitor disease progression or as outcome measure in clinical trials, the preferential use of quantitative imaging methods and their technical challenges, usefulness and limitations of the imaging technique DEXA, and correlation of imaging with other assessment methods of muscle involvement, such as muscle strength and muscle function.

259th ENMC International Workshop: Anaesthesia and neuromuscular disorders

This workshop was held fully virtually. Part 1 started in December 2020 and part 2 continued on the weekend of 28 and 29 May 2021. This summary covers the second part of the workshop with 29 experts in the field from four different continents. The full report of this workshop has been published in Neuromuscular Disorders, Vol. 32-1 January 2022.

Background

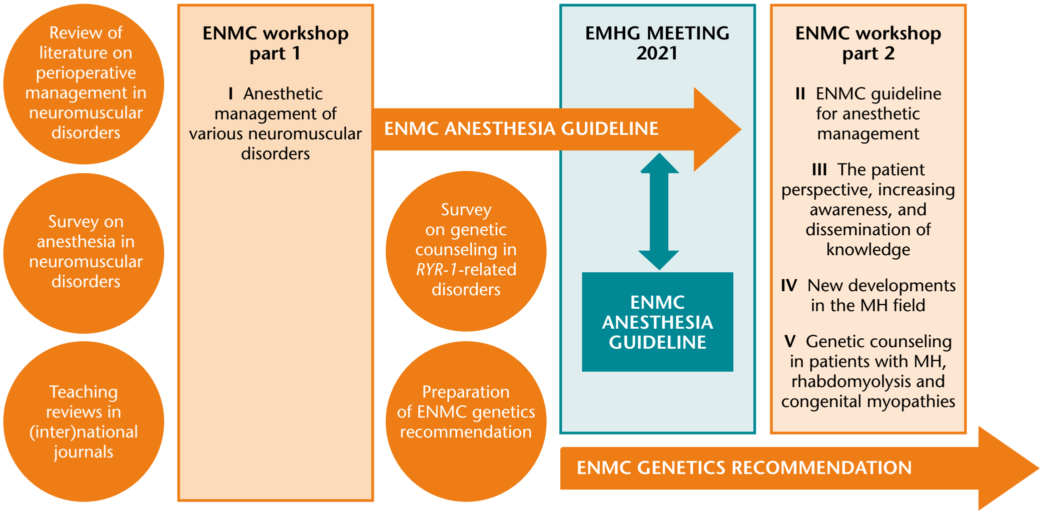
The first day was about new developments in the field of malignant hyperthermia, differences and similarities between malignant hyperthermia and anaesthesia induced rhabdomyolysis, and an overview on the evolving spectrum of *RYR-1*-related myopathies, malignant hyperthermia and exertional rhabdomyolysis including the the use of dantrolene, a druge that blocks the release of calcium from the sarcoplasmic reticulum of skeletal muscle cells.

The Dutch patient organisation of neuromuscular disorders, Spierziekten Nederland, illustrated the process of development and implementation of emergency warning cards for patients with neuromuscular disorders (Project ALERT).

Genetic counselling of patients with malignant hyperthermia, rhabdomyolysis and *RYR-1*-related myopathies, with its challenges and limitation, was another topic of the workshop.

Main objectives

The goal of this workshop was to create consensus for the anaesthetic management of patients with neuromuscular disorders. The virtual meetings have been a great opportunity to exchange knowledge about the anaesthetic management of patients with neuromuscular disorders amongst experts from the NMD research field and experts from other disciplines. The goal of this workshop was to create consensus and draft ENMC recommendations for genetic counselling in *RYR-1*-related disorders and for the anaesthetic management of patients with neuromuscular disorders. These recommendations are now in preparation.



ENMC workshop part 1 and 2, the connection to the EMHG meeting in 2021, and the preparatory activities and projects.

Onsite and online participants of workshop 264.

264th ENMC International Workshop: Multi-system involvement in Spinal Muscular Atrophy

The 264th ENMC workshop, multi-system involvement in SMA, took place in a hybrid set-up in The Netherlands on the weekend of 19-21 November 2021. With 13 participants onsite and 17 participants joining remotely from 11 different countries, knowledge and data could be shared in a confidential manner and lively discussions took place.

Background

Spinal muscular atrophy (SMA) has classically been viewed as a motoneuron disease caused by loss of the Survival Motor Neuron 1 (SMN1) gene and low SMN protein levels. SMN is expressed in all cells and tissues and ubiquitously reduced in SMA patients. Not surprisingly, there is growing evidence of multi-system involvement in SMA.

Recently approved SMN-enhancing therapies impressively ameliorate the neuromuscular presentation resulting in an increased survival of severely affected patients. However, limited peripheral drug availability in some of the treated patients may set the focus on previously overseen peripheral organ phenotypes.

The most important issue to adress is the concern that now longer living patients will develop signs of systemic non-neuronal manifestations over time. It is not fully understood whether patients receiving treatment after the onset of symptoms have developed peripheral organ defects that cannot be rescued by SMN restoration. With the evolving landscape of therapeutics in SMA and the ever-changing natural history of the disease, there is an urgent need for broader systemic monitoring of SMA progression.

Main objectives

The objectives of this workshop were:

1. to provide a comprehensive evaluation of the different aspects characterising the multi-system involvement in SMA patients.
2. to establish a framework for an integrated and collaborative approach across a variety of stakeholders to identify and monitor possible multi-system manifestations in SMA with potential implications for the therapeutic strategies.

Workshop outcomes

SMN levels largely differ between organs and cells and the workshop participants agreed that it is crucial to carefully measure the SMN amounts in different organs. This should contribute to the development of a second generation of animal models which better represent the current clinical landscape of treated SMA.

It was agreed that efforts should be directed to the identification of reliable outcome measures, which can be standardised in many centres, for instance, to clarify the prevalence and nuances of brain-associated comorbidities including cognitive impairment and/or autistic spectrum disorders in patients affected by SMA. Patients being treated with drugs that increase SMN protein levels may require additional medications to treat other peripheral symptoms. However, too many hospital visits may result in additional burdens for the patients.
In addition to clinical monitoring, data collection by international and national patient registries and patient organisations may be beneficial for a better understanding of the patients' needs.

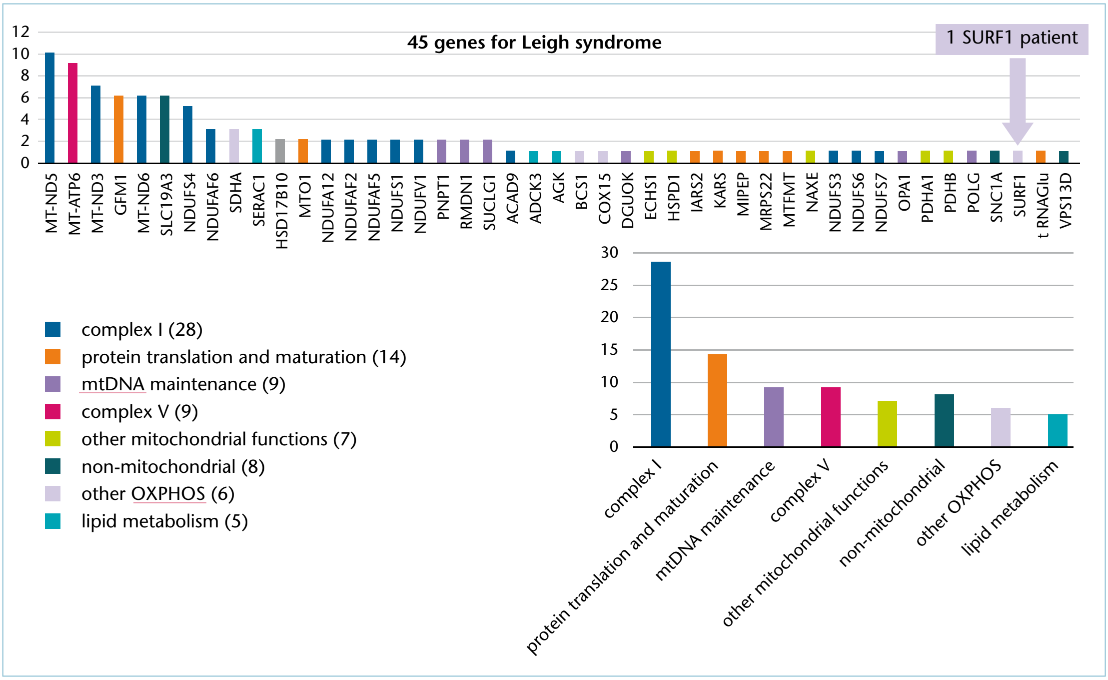
258th ENMC International Workshop: genetic epidemiology and clinical trial readiness in encephalomyopathy of Leigh Syndrome spectrum

This summary covers the work done in three virtual meetings in 2020 and 2021. The face-to-face consensus meeting will take place in March 2022. In total, 25 international experts and patients from 11 different countries virtually met to discuss the main objectives of this workshop.

Background

Leigh syndrome, also known as a "subacute necrotizing encephalomyopathy", is a genetically heterogeneous disease that primarily affects the central nervous system. This syndrome is characterised by focal and bilaterally symmetrical, necrotic (cell-death) lesions involving a few specific areas in the brain: the thalamus, brainstem, and posterior columns of the spinal cord. Leigh syndrome typically affects children; adult onset is rare. Leigh syndrome is a severe and progressive disorder.

Genetic heterogeneity in Leigh syndrome – by Agnès Rötig, research director of Imagine, Institut des maladies génétiques, Paris



Main objectives

The objectives of this workshop were:

1. to increase knowledge of the natural history of Leigh syndrome.
2. to improve its diagnosis.
3. to collect information on the genetic epidemiology of the syndrome.
4. to facilitate the identification of biomarkers.

The virtual meetings were dedicated to several issues concerning the diagnosis, clinical and genetic landscape of Leigh syndrome: the importance of developing biomarkers in order to set outcome measures for future trials. Major issues were discussed regarding definition of the Leigh syndrome spectrum, outcome measures, importance of metabolomics and proper functional scales to be used in clinical trials.
The participants experienced the virtual meetings as an excellent opportunity to update and deepen the knowledge of the genetic cause and natural history of Leigh syndrome, promoting international research and collaborative studies to better characterise and follow the patients.

261st ENMC International Workshop: Management of safety issues arising following AAV gene therapy

This workshop started with a virtual introduction meeting on 19 March 2021 and will be followed by a face-to-face meeting in June 2022.

Background

The overall aim of the meeting was to openly discuss and share information regarding serious adverse reactions observed after gene therapy administration, in order to work out the best strategy to decrease risk and manage these adverse reactions when they occur. The participants of this workshop included experts from pharmaceutical companies, regulators, clinicians, academics and patient advocacy representatives. There were participants from multiple specialities in order to gather the expert opinion on the types and mechanisms of adverse reaction. The group included immunologists, nephrologists and haematologists as well as neurologists.

Outcomes

A review of all of the publicly available information on safety and immunology concerns was compiled, and initial results have been shared with participants. Working groups were created to outline strategies for monitoring of treatment-related adverse events in AAV-mediated gene therapy, in preparation for the face-to-face meeting.

Main objective

To make AAV gene therapies safer for all patients and de-risk the use of promising therapies for clinicians, investigators and partners in academia and industry.

Participants of workshop 261 in the Zoom room.

3.3 Participants at ENMC workshops in 2021

The ENMC strives for diversity in its workshop participants, to ensure that a broad consensus can be reached at the meetings by having all relevant decision-makers around the table.

For each workshop that took place in 2021, the numbers of different stakeholders are shown in the table below.

No	Workshop Title	Participants	Clinicians	Basic researchers	Patients	Patient representatives	Industry	Early-Career researchers	Regulatory
253	Striated muscle laminopathies; natural history and clinical trial readiness	36	18	8	1	7	1	1	
255	Muscle Imaging in idiopathic inflammatory myopathies	22	15	3	2			2	
256	Myositis specific and associated autoantibodies	21	13	4	2			2	
257	The 3rd ENMC workshop on Dystroglycan and the Dystroglycanopathies	22	7	7		3	3	2	
258	Genetic epidemiology and clinical trial readiness in encephalopyopathy of Leigh Syndrome spectrum	27	15	6	1	2	2	1	
259	Anaesthetic management in NMD	30	20	7		1		2	
261	Management of Safety issues arising following AAV gene therapy	35	14	8	1	3	6	2	1
262	Standards of Care for the Dysferlinopathies	35	24	3	3	2		3	
263	Focus on female carriers of dystrophinopathy	24	13	5		3		3	
264	Multi-system involvement in Spinal Muscular Atrophy	28	12	11	1	1	1	2	
Average of 10 workshops (n)		**28**	**15**	**6**	**1**	**2**	**1**	**2**	**0**
%		100%	54%	22%	4%	8%	5%	7%	0%
Total of 10 workshops (n)		**280**	**151**	**62**	**11**	**22**	**13**	**20**	**1**

Clinicians and basic researchers formed the majority of the participants (76%), with an average of 54% clinicians and 22% basic researchers per meeting, which reflects the predominantly clinically-orientated nature of the workshops held in 2021. Connecting basic researchers with clinicians to bridge between the lab and the clinic and bring the fundamental science closer to the clinic is one of the aims of these workshops.

Through the ENMC Patient Participation Programme we aim to ensure that at least 10% of the participants of each workshop are persons affected by a neuromuscular condition, parents or advocates of these patients and/or representatives from a disease-specific patient or funding organisation. In 2021, these two groups made up 12% of total participants, the patient's voice was well-represented.

In addition, one or two and sometimes even three Early-Career researchers attended each ENMC workshop this year. ENMC supports the integration of young scientists in established neuromuscular networks via its Early-Career Programme and Mid-Career Mentoring Programme.

In five workshops, where it was relevant, we also had representatives from pharmaceutical companies and regulatory agencies.

New numbers to be proud of in 2021

Patients and patient representatives
This year we welcomed 11 patients and 22 patient representatives (parents, patient associations, patient advocates) to our workshops. They all gave a presentation, asked questions and intermingled in the discussions, which was very helpful for the researchers and clinicians in the workshops to learn the patient's needs and interests.

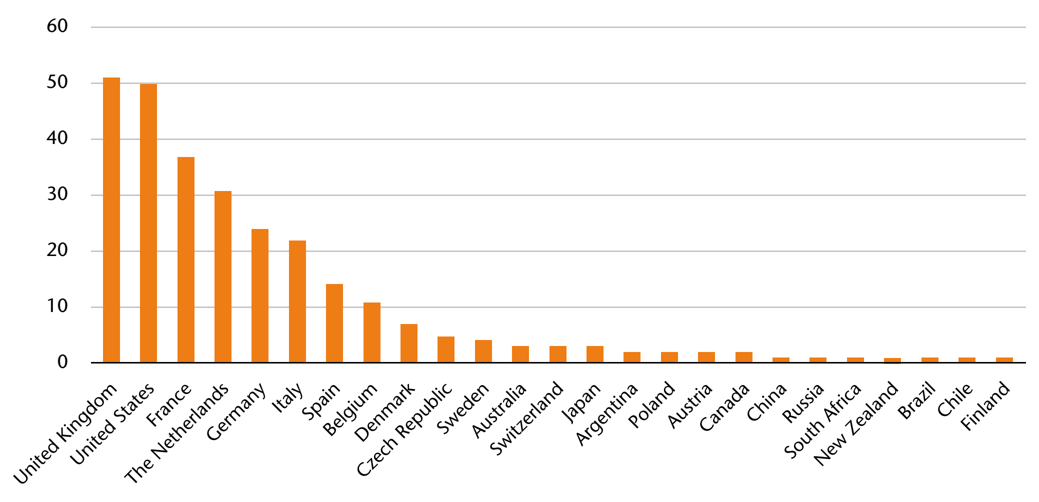
Researchers
We managed to hold 10 workshops in 2021 despite the pandemic, with the attendance of 62 basic researchers and 151 clinicians, respectively 22% and 54% of the total participants. The Early-Career Programme enabled 20 young researchers to attend the ENMC workshops and promote their entry in the neuromuscular network.

Sponsors
In 2021, the ENMC was sponsored by eight full partners and two associated partners. The ENMC Company Forum supported our activities through the contributions of seven pharmaceutical companies. We are very thankful for the support from all these partners and acknowledge them with gratitude.

3.4 Countries represented in ENMC workshops in 2021

One of the key criteria for a workshop approval by the ENMC is the geographical balance of the participants. The ENMC is convinced that a wide coverage of countries in the workshops is important, to make sure that broad consensus is reached at ENMC workshops. This will help to start international research collaborations, ensure the standardisation of healthcare provision for people affected by a neuromuscular condition, and improve the quality of diagnosis and treatment for patients worldwide. In 2021, many countries from all over the world were represented at the ENMC workshops (see diagram below), with a predominance of several ENMC member countries (United Kingdom, France, Italy, The Netherlands and Germany) and non-member countries like USA and Spain.

Total number of participants per country in ENMC workshops 2021



4 Creating global awareness about ENMC workshops

4.1 Publication and dissemination of workshop outcomes

Patients and families

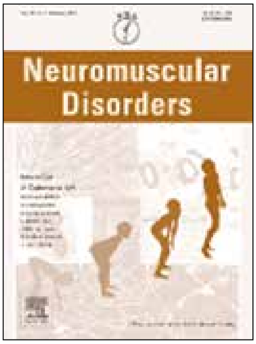
Informing patients and their families about the achievements of ENMC workshops is a key priority of the ENMC. For this purpose, a workshop lay report in English is written by workshop participants and published on the ENMC website within two weeks after the workshop. Lay reports are then translated into many different languages to increase their accessibility for people worldwide. The European partner organisations and other co-sponsors help to disseminate these translated lay reports via their local patient networks and the ENMC creates awareness on social media (Twittername: _ENMC; LinkedIn: ENMC group) during the workshops and whenever lay reports are published on its website.

Follow, like and retweet us!

The ENMC maintains an online archive of all workshops organised since 2000, which provides access for the general public to the outcome of the workshops over the years:

https://www.enmc.org/publications/workshop-reports/

Research community



Researchers, clinicians and healthcare providers who are active in the research field of rare neuromuscular disorders need to be able to read about the scientific results of ENMC workshops in the literature. Therefore, it is mandatory that workshop organisers submit a full workshop report to Neuromuscular Disorders within 6 months after the workshop.

Since 2021, Early-Career Researchers who made a significant contribution to the organisation of the workshop and the writing of the lay and full report, can become co-authors on the full report.

Citation score

124%

ENMC-workshop derived publications are cited 24% more than average (100%). In bibliometric terms this means that they have a "high impact"in the research field.

4.2 International conferences in 2021

ENMC representatives have attended the following international virtual congresses:

- The International Congress on Neuromuscular Diseases (ICNMD), May 2021
- PNS (Peripheral Nerve Society) Annual meeting, June 2021
- International Congress of the World Muscle Society (WMS), September 2021

5 The ENMC Mid-Career Mentoring Programme

This programme has been developed for people who seek mentoring in order to become independent researchers and/or potential future leaders in the NMD field. These individuals typically are in the stage in their careers where they are developing their own research plans and have a proven track record in the neuromuscular field. They have established research teams and collaborative networks.
The guidelines and the mentee and mentor forms can be found on the ENMC website:

https://www.enmc.org/mid-career-mentoring-programme/introduction/

Mid-Career Mentoring Programme

5.1 Interview with an ENMC mentee and her mentors

The first mentorships started in 2021. We spoke with mentee Dr Rossella Avagliano Trezza and both of her mentors, Dr Selma Tromp and Prof. Annemieke Aartsma-Rus.

DR S. TROMP is a clinical neurophysiologist at the Leiden University Medical Center, The Netherlands. She has held several board functions, such as the Chair of the Dutch Society for Neurology from 2014 to 2017 and is currently a member of The Netherlands Federation of Medical Specialists, with her special focus on quality of care.

PROF. A. AARTSMA-RUS is a Professor of Translational Genetics at the Department of Human Genetics of the Leiden University Medical Center. She has several board functions, such as vice-chair of COST Action "Delivery of antisense RNA therapies" and Chair of the TREAT-NMD Advisory board for Therapeutics (TACT). Thus far, she has published over 200 peer reviewed papers and 11 book chapters, as well as 15 patents and has edited one book. She has given many invited lectures at meetings, symposia and workshops as well as patient/parent organisations meetings, where she is known for her ability to present science in a clear and understandable way.

DR R. AVAGLIANO received her Master's degree in Naples, Italy and has worked in The Netherlands since May 2010. She recently moved to the field of neuromuscular diseases in the lab of Prof. B. Smeets at the Maastricht University in The Netherlands.

Q: **Selma,** why did you become a mentor?

SELMA I had personal contacts within the ENMC and was asked to be a mentor. In the early phase of my career, I could have used someone to help guide me. Since I now have the possibility to help someone else, I applied.

Q: **Annemieke,** why did you become a mentor?

ANNEMIEKE I like to help people reach their potential. I have been fortunate to have several informal mentors myself during my career, who were very helpful, motivating and supportive. I want to pay it forward. It is very useful to get advice on strategic choices in science and career planning, and to have someone to reach out to if you have a "I'm doing this for the first time, but you are an expert" related question. However, it is equally useful to be able to do a reality check sometimes.

Q: **Rossella,** why did you apply for the Mentoring Programme?

ROSSELLA I felt that I could use an outside perspective on my career trajectory. I specifically looked for a female perspective, as I have been struggling with work-life balance since the birth of my son. Also, I was looking to embed myself well in the neuromuscular field. I want to find my own path and my niche, to do something important and make a difference for people living with neuromuscular diseases. The Mentoring Programme will help me with those goals.

Q: What will the Mentoring Programme look like for you?

ROSSELLA I will schedule regular meetings with both of my mentors, online and hopefully live as well. I would like to work on my management skills (mainly for delegating tasks and responsibilities) and my academic skills (clinical trials and related issues) and I think I need some guidance in how to collaborate with industry. Also it would be very helpful for me to discuss grant submissions for instance. I hope the mentors can provide me with support and guidance and it's helpful for me to hear their perspectives. I hope to find my place in the NMD community; especially during Covid-19 it has been hard, because there were no events to network at.

Q: Do you have a comment for people considering becoming a mentor or a mentee?

ANNEMIEKE It is very rewarding to see mentees reach their potential and realize what their talents are and improve them. One has to be careful however, not to see a mentee as a mini-you. What worked for you will not necessarily work for the mentee. Listen to the mentee, what are his/her needs and how can you help and advice? Often it is not your job to give advice to the mentee on what to do, but rather, with careful questions, to make the mentee realize his/her own best choice him/herself.

SELMA I fully agree, and that makes us as mentors get a lot of energy from the programme. If you are considering becoming a mentor and are questioning 'why me?', like I did, I recommend you just do it!

ROSSELLA My advice? Apply! There is so much to be gained from being a mentee and even completing the application itself helps you focus on your strengths and needs"

5.2 Call for Ambassadors

The ENMC asks you to help create awareness about this important Mid-Career Mentoring Programme within your own local and international networks. Perhaps you are interested in becoming a mentor yourself or you may be or know a suitable candidate mentee for this programme. Please, feel free to contact us at enmc@enmc.org for any questions or materials to share.

Dr Rossella Avagliano:

> "I want to find my own path and my niche, to do something important and make a difference for people living with neuromuscular diseases. The Mentoring Programme will help me with these goals."

6 Resources and financial management in 2021

Financial summary 2021

Annual accounts for the year 2021 were compiled in accordance with Guideline C1 for the reporting of small-sized non-profit organisations as published by the Dutch Accounting Standards Board.
The financial accounts are drawn up in Euros.

In the summary table below, the overall income and expenses over the year 2021 are shown in comparison with the figures for the previous financial year 2020.

Statement of income and expenses for the year 2021 in Euros (€)

	2021	2020
INCOME		
Full partner contributions	231.000	231.000
Associated partner contributions	10.000	10.000
Company Forum contributions	84.204	75.791
Other contributions	5.000	1.000
Total income	**330.204**	**317.791**
EXPENSES		
Personnel expenses	183.075	156.237
Rental expenses	11.574	11.326
Activity (workshop) expenses	22.716	68.059
Organisational expenses	53.801	37.996
Total operating expenses	**271.166**	**273.618**
Operating result	59.038	44.173
Interest income	– 946	– 106
Net result	**58.092**	**44.067**
APPROPRIATION OF RESULTS		
Development reserve	–	80.000
Development reserve withdrawal*	20.746	– 3.652
Other free reserves	78.838	– 32.281
CASH AT BANKS ON 31 DECEMBER	**631.374**	**573.745**

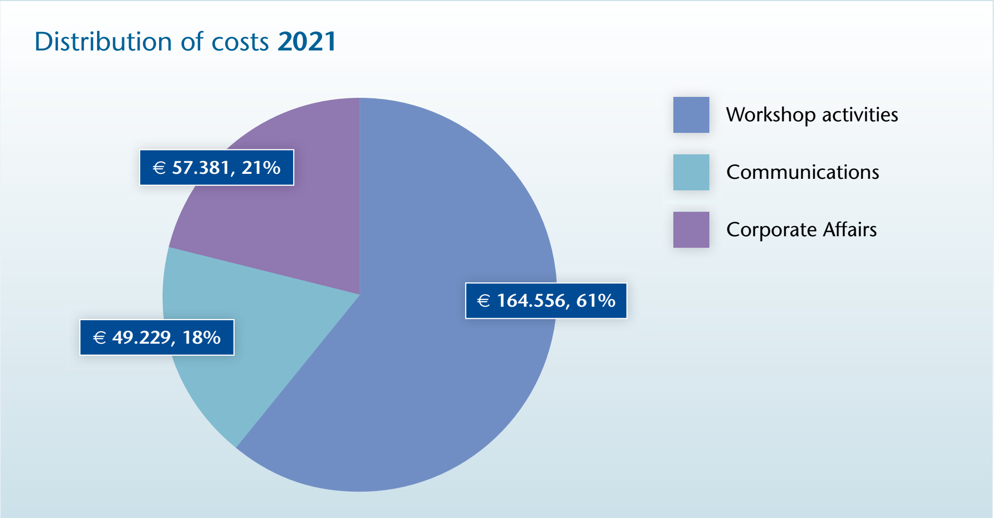
**Note: Withdrawal means that these costs were made in 2021 and could be taken from this provision.*

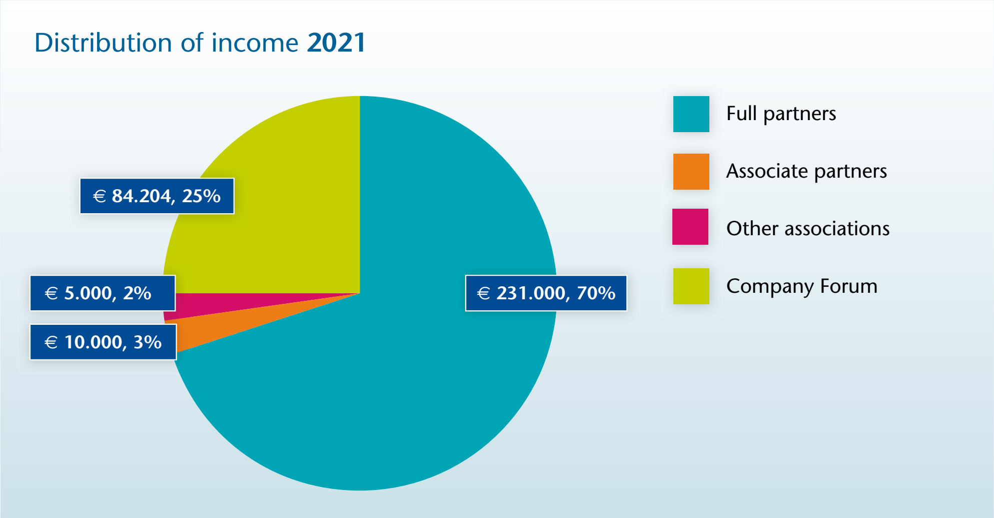
The distribution of income from the different ENMC supporters and the distribution of costs over the key accounts: workshop activities, corporate affairs and communications, are provided in the two diagrams below. Outside the ENMC administration, SMA Europe supported International flights of four participants in the 264th ENMC workshop. They originated from non-ENMC countries, namely, Belgium, Canada, and Spain.

Opinion of the auditors

The independent accountants have verified and approved the annual accounts. For a full PDF version of the annual accounts report of 2021, please visit the ENMC website:

https://www.enmc.org/about-us/annual-report/





7 Governance in 2021

The European Neuromuscular Centre was founded as a non-profit organisation on 24 November 1992 under Dutch law. The foundation is supported by financial contributions of European patient organisations for neuromuscular disorders and many other related organisations. The statutory location is in Baarn, The Netherlands, in the building of the Dutch Neuromuscular Diseases Patient Association.

7.1 The ENMC Executive Committee

The ENMC is governed by an Executive Committee consisting of representatives of ENMC partner organisations.

Composition of the ENMC Executive Committee on 31 December 2021
Dr K. Adcock (United Kingdom)
Dr A. Ambrosini (Italy)
Dr S. van den Berge (The Netherlands)
Dr I. Meijer (The Netherlands)
Dr A. Méjat (vice-Chair, France)
Dr A. von Moers (Chair, Germany)
Dr J. Rahbek (Denmark)
Dr R. Willmann (Switzerland)

7.2 The ENMC Research Committee

The ENMC Research Committee is responsible for reviewing the scientific content and quality of the workshop applications and advises the Executive Committee on awarding the grants for ENMC workshops.

Composition of the ENMC Research Committee on 31 December 2021
Dr A. Buj-Bello (France)
Dr A. Ferreiro (Chair, France)
Prof. Dr N. Goemans (Belgium)
Prof. Dr E. Gomes (Portugal)
Prof. Dr H. Jungbluth (United Kingdom)
Prof. Dr C. Kornblum (Germany)
Dr M. Olivé (Spain)
Prof. Dr T. Sejersen (Sweden)
Prof. Dr W. Stenzel (Germany)
Prof. Dr V. Timmerman (Belgium)
Dr N. Voermans (The Netherlands)

7.3 The ENMC Office

The office takes care of the daily business of the ENMC.

ENMC Office staff on 31 December 2021
Dr A. Breukel (Managing Director)
Mrs F. Ott (Operational Manager)
Mrs E. Smit-Branderhorst (Operational Manager)
Ms T. van Esch (Workshop Assistant)
Dr A. Ferreiro (Research Director)

Welcome to our new workshop and management assistant: Ms Tamara van Esch
Tamara van Esch finished her first year in Medical Natural Sciences and worked in the entertainment industry over the past 10 years. She founded The Mevrouw Tamara Foundation that initializes projects in which artists from different disciplines and societal organisations meet each other, to create more awareness for those who are often not heard.

As a management assistant, Tamara helps to organise workshops and is a staff member of the ENMC office.

Henrik Ib Jørgensen (left) and Jes Rahbek during the EC meeting in November 2021.

7.4 Transfer of the Muskelsvindfonden representative

After representing the Muskelsvindfonden at ENMC for 28 year (from 1993-2021) Jes Rahbek passed this task to Henrik Ib Jørgensen in November 2021. Jes, a specialist in neuromuscular rehabilitation, supported the ENMC activities from its beginning and strongly contributed to the shape and strategy of the ENMC we know today. For instance, the highly regarded and constructive patient participation programme goes back to Jes' initiative in 2012 at a meeting in Musholm, Denmark.
This was the first time that patient participation in research activities was discussed extensively. Jes is also a long-term member of the TREAT-NMD task force. We will miss Jes' insightful comments and his extensive memory of the developments in the neuromuscular network.
Henrik is Chief Executive Officer of Muskelsvindfonden, member of the board at Danish National Rehabilitation Centre for Neuromuscular Diseases and has been delegate in SMA Europe since 2018. The ENMC welcomes him in the Executive Committee and looks forward to a great collaboration.

8 A special thank-you to all our partners and supporters

It is thanks to the continuous support of the eight European patient organisations that the ENMC is able to facilitate and organise, on average, eight workshops per year. With support from additional partner organisations, such as condition-specific associations, associated partners and members of the ENMC Company Forum, we are also able to invite participants from non-ENMC countries and facilitate the attendance of Early-Career Researchers, patients and patient representatives.

ENMC full partners

FONDAZIONE Telethon

AFMTELETHON
INNOVER POUR GUÉRIR

Muscular Dystrophy UK
Fighting muscle-wasting conditions

SPIERZIEKTEN NEDERLAND

MUSKELSVINDFONDEN

fsrmm
fondation suisse de recherche sur les maladies musculaires
fondazione svizzera per la ricerca sulle malattie muscolari
schweiz. stiftung für die erforschung der muskelkrankheiten

PRINSES BEATRIX SPIER FONDS
KRACHTIG TEGEN SPIERZIEKTEN

Deutsche Gesellschaft für
Muskelkranke e.V. DGM

ENMC associated partners

Finnish Neuromuscular Disorders Association

Österreichische
MuskelForschung

Members of the Company Forum

PerkinElmer
For the Better

LUPIN
NEUROSCIENCES

NOVARTIS

SANOFI GENZYME

Amicus
Therapeutics

IONIS

Biogen

Roche

Workshop-specific sponsors in 2021

SMA
EUR
OPE

9 Looking forward to 2022 and beyond

9.1 Workshops in 2022

Twelve ENMC workshops in several separate (virtual, hybrid and/or face-to-face) meetings are planned to take place in 2022 (see table below). Despite the Covid-19 pandemic and the consequent travel and event restrictions, we hope to be able to organise these workshops, albeit in separate settings and on different dates. In 2023 we hope to get back to fully face-to-face workshops. We herewith would like to thank all organisers and participants for their flexibility in changing the dates in their calendars and for being cooperative and very active in the online meetings in 2021.

Two review rounds for workshop applications are scheduled in 2022: one in the spring (submission deadline 1 March 2022) and one in the autumn (submission deadline 1 September 2022).

The workshops that are selected at these review rounds will all be planned for 2022 or 2023.

Preliminary ENMC programme 2022

Workshop no. and date	Topic	Workshop leaders
Workshop no. 254 28-30 January 2022 (virtual)	Formation of a European Network to initiate a European data collection, along with development and sharing of treatment guidelines for adult SMA patients	Prof. P. Laforêt, Dr E. Pegoraro, Dr L. van der Pol, Prof. M. Walter
Workshop no. 262 11-12 February 2022 (virtual) 4 July 2022 (face-to-face)	Standards of Care for the Dysferlinopathies	Prof. V. Straub, Dr A. Mayhew, Dr T. Stojkovic, Dr L. Bello
Workshop no. 260 11-13 March 2022 (face-to-face)	Congenital Myasthenic syndromes	Prof. L. Maggi, Dr P. Rodriguez-Cruz, Dr D. Beeson, Prof. H. Lochmüller
Workshop no. 258 25-27 March 2022 (face-to-face)	Genetic epidemiology and clinical trial Readiness in encephalomyopathy of Leigh Syndrome spectrum	Prof. E. Bertini, Prof. S. Rahman, Prof. B. Cohen, Prof. M. Schiff
Workshop no. 266 1-3 April 2022 (face-to-face) ENMC Themed workshop	Remote delivery of clinical care and validation of remote clinical outcome assessments in neuromuscular disorders: a response to Covid-19 and proactive planning for the future	Dr L. Lowes, Mrs. M. James, Dr L. Alfano
Workshop no. 265 13-15 May 2022 (face-to-face)	Muscle Imaging in Facioscapulohumeral Muscular Dystrophy (FSHD): relevance for clinical trials	Dr G. Tasca, Dr S. Attarian, Prof. J. Vissing, Prof. J. Díaz-Manera

Workshop no. and date	Topic	Workshop leaders
Workshop no. 263 13-15 May 2022 (face-to-face)	Focus on female carriers of dystrophinopathy: refining recommendations for prevention, diagnosis, surveillance and treatment	Prof. A. Ferlini, Dr J. Bourke, Dr R. Quinlivan, Dr A. Sarkozy
Workshop no. 267 20-22 May 2022 (face-to-face)	Psychological interventions for improving quality of life in slowly progressive neuromuscular disorders	Dr N. Voet, Dr C. Graham, Dr B. Gallais
Workshop no. 257 10-12 June 2022 (face-to-face)	The 3rd ENMC workshop on Dystroglycan and the Dystroglycanopathies	Prof. S. Winder, Prof. V. Straub, Prof. K. Campbell
Workshop no. 261 17-19 June 2022 (face-to-face)	Management of safety issues arising following AAV gene therapy	Prof. L. Servais, Prof. F. Muntoni, Dr C. Bönnemann
Workshop no. 253 24-26 June 2022 (face-to-face)	Striated muscle laminopathies; natural history and clinical trial readiness	Dr G. Bonne, Dr L. Maggi, Prof. S. Quijano-Roy, Dr C. Bönnemann
Workshop no. 255 (face-to-face)	Muscle imaging in idiopathic inflammatory myopathies	Prof. M. de Visser, Prof. J. Vencovský, Dr P. Carlier
Workshop no. 268 30 September-2 October 2022 (face-to-face)	Genetic diagnosis, clinical classification, outcome measures, and biomarkers in Facioscapulohumeral Muscular Dystrophy (FSHD): relevance for clinical trials	Dr G. Bonne, Dr L. Maggi, Prof. S. Quijano-Roy, Dr C. Bönnemann
Workshop no. 269 Date to be established (face-to-face)	Clinical trials in DMD: Ten years on, what have we learned? How can we optimize future trial design?	Prof. F. Muntoni, Prof. N. Goemans, Prof. C. McDonald, Prof. E. Mercuri

For updates please visit the ENMC website: https://www.enmc.org/workshops/upcoming-workshops/

9.2 International conferences in 2022

ENMC ambassadors will attend the following international congresses with a booth.

- The International Congress on Neuromuscular Diseases (ICNMD), 5-9 July 2022
- The Myology Meeting, 12-17 September 2022
- The Treat-NMD Conference, 7-9 December 2022

9.3 Budget for 2022

This table presents the budget forecast for 2022 as of 31 December 2021.

Budget 2022 in Euros (€)	Actuals 2021	Budget 2022
INCOME		
Full Partner contributions	231.000	231.000
Associated Partner contributions	10.000	15.000
Company Forum contributions	84.204	85.000
Other contributions	5.000	10.000
Total income	**330.204**	**341.000**
EXPENSES		
Personnel expenses	183.075	165.500
Rental expenses	11.574	11.300
Activity expenses	22.716	140.000
Organisational expenses	53.801	60.000
Total operating expenses	**270.892**	**376.800**
Interest income	– 946	– 700
NET RESULT	**58.366**	**-36.500**

Colophon

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