NeurOmics Data Access Agreement

This agreement governs the terms on which access will be granted to the sequence and genotype data, "-omics" data (such as transcriptomics, proteomics and metabolomics / lipidomics data) as well as accompanying phenotype data generated by the NeurOmics Consortium (the "Data" as defined below).

For the sake of clarity, the terms of access set out in this agreement apply to all of the User, Authorised Personnel within the User's research group, and the User Institution (as defined below). Within the agreement "You" and "Your" shall be construed to refer to all these. In signing this agreement, You are agreeing to be bound by the terms and conditions of access set out in this agreement.

Title of research (120 characters maximum – this will be made public with your name and institution on access being granted):

Name of applicant (User), including affiliation and contact details:

Name with title:	
Position:	
User Institution:	
Institutional postal address:	
Institutional email address:	
Signature:	
Date:	

Name of authorised representative of the User Institution, including affiliation and contact details:

Name with title:	
Position:	
User Institution:	
Institutional postal address:	

Institutional email address:	
Signature:	
Date:	

For the NeurOmics Data Access Committee:

Name:	
Signature:	
Date:	

Data sets for which access is requested

Please list EGA data set ID(s) (EGAD number).

Version number of Appendix A that you are including: ....

Appendix A lists any specific conditions attached to individual data sets – you must be using a version that covers all the sets for which you are requesting access.

Description of proposed research

Please provide a clear description of Your project and its specific aims in no more than 500 words. This should include specific details of **what you plan to do with the data** and include key references.

If applying to use data sets that have restrictions on the way that they may be used (e.g. must only be used to investigate a specific condition, or may not be used for control purposes), then please clearly state how you plan to use [named data sets] as controls, and that you will respect the [specified] constraints on the use of [named] non-control data sets.

User's publication record

Please list up to 5 relevant publications of which you were an author or co-author, demonstrating your experience and competence to analyse data sets of this type. If you do not have relevant publications please demonstrate your expertise and responsibility with respect to human subjects genetic data analysis.

List of Authorised Personnel (please refer to definitions section)

Name with title:	
Position:	
Institutional email address:	

Name with title:	
Position:	
Institutional email address:	

Name with title:	
Position:	
Institutional email address:	

(Repeat as necessary)

Definitions

Authorised Personnel: Additional individuals who have an affiliation within the research group of the User at the User Institution including postdocs, students and any visitors. All Authorised Personnel must have an email address within the User Institution. If multiple research groups within the same institution require access they must each apply. Core IT and other administrative personnel at the User Institution who need to have access to the Data for data security and management purposes are automatically treated as Authorised Personnel and bound by the institutional acceptance of this agreement**.**

Collaborator: A collaborator of the User, including both someone working at a different institution from the User Institution and someone working in a separate research group in the same User Institution.

Consortium means the NeurOmics Consortium, a list of which can be found on the Project website www.rd-neuromics.eu.

Data: means all and any human data including but not limited to genomics, metabolomics, lipidomics and phenotype data obtained from the managed access datasets of the NeurOmics Project.

Data Access Committee (DAC): Access to NeurOmics Data will be managed with oversight from the NeurOmics DAC. The constitution of the DAC can be found on the Project website www.rd-neuromics.eu.

Data Producer(s): The NeurOmics Project partners and collaborators within the project, responsible for the development, organisation, and oversight of the Data.

Data Subject means a person, who has been informed of the purpose for which the Data is held and has given his/her informed consent thereto.

NeurOmics Project or Project: NeurOmics is a research project funded for five years from October 2012 until September 2017 from the European Union's Seventh Framework Programme for research, technological development and demonstration under grant agreement no. 2012-305121 (also see *Consortium).*

Publications: Includes, without limitation, articles published in print journals, electronic journals, reviews, books, abstracts submitted to conferences, posters and other written and verbal presentations of research.

Research Purposes: shall mean research that is seeking to advance the understanding of genetics and genomics, including the treatment and mechanisms of disorders, and work on

statistical methods that may be applied to such research. Further specific conditions apply to particular data sets as listed in Appendix A.

User: An applicant having signed this Data Access Agreement, whose User Institution has co-signed this Data Access Agreement, both of them having received acknowledgement of its acceptance.

User Institution: Institution(s) at which the User is employed, affiliated or enrolled. A representative of it has co-signed this Data Access Agreement with the User and received acknowledgement of its acceptance.

Terms and Conditions:

In signing this agreement, the User and the User Institutions(s):

1. Agree to only use the Data for Research Purposes, subject to any data set specific conditions listed in Appendix A, according to the consent obtained from sample donors.

2. Agree to preserve, at all times, the confidentiality of the information and Data. In particular, You undertake not to use, or attempt to use the Data to compromise or otherwise infringe the confidentiality of information on Data Subjects.

3. Agree to protect the confidentiality of Data Subjects in any Publications that you prepare by taking all reasonable care to limit the possibility of identification.

4. Agree not to attempt to link or combine the Data provided under this agreement to other information or archived data available for the Data sets provided, even if access to that Data has been formally granted to You, or it is freely available without restriction, unless specific permission to do so has been received from the relevant access committee(s) or sample custodians.

5. Agree not to transfer or disclose the Data, in whole or part, or any material derived from the Data beyond that in Publications, to any non-authorised personnel. Should the User or the User Institution(s) wish to share the Data with a Collaborator, the Collaborator must complete a separate *Application for Access to the Data*.

6. Agree to use the Data for the approved Research Purpose and project described in your application; use of the Data for a new purpose or project will require a new application and approval.

7. Accept that Data may be reissued from time to time, with suitable versioning. If the reissue is at the request of sample donors and/or other ethical scrutiny, You will remove earlier versions of the Data from subsequent analysis and Publication, and destroy/discard the earlier version unless obliged to retain Data for archival purposes in conformity with Institutional policy.

8. Agree to abide by the terms outlined in the "NeurOmics Project Publication Moratorium" (Appendix B). This includes respecting the moratorium period for Data Producers to first Publication of report(s) describing and analysing the Data.

9. You agree to acknowledge in any work based in whole or part on the Data, the published paper from which the Data derives, the version of the Data, and the role of the NeurOmics Consortium and the relevant primary collectors and their funders. Suitable wording for such acknowledgement is provided in the "NeurOmics Project Publication Moratorium".

10. Agree that the NeurOmics Consortium, the original Data Producers, Data depositors, copyright holders, and all other parties involved in the creation, funding or protection of any part of the Data supplied:

a) Make no warranty or representation, express or implied as to the accuracy, quality or comprehensiveness of the Data;

b) Exclude to the fullest extent permitted by law all liability for actions, claims, proceedings, demands, losses (including but not limited to loss of profit), costs, awards damages and payments made by You that may arise (whether directly or indirectly) in any way whatsoever from Your use of the Data or from the unavailability of, or break in access to, the Data for whatever reason and;

c) Bear no responsibility for the further analysis or interpretation of these Data.

11. Understand and acknowledge that the Data is protected by copyright and other intellectual property rights, and that duplication, except as reasonably required to carry out Your research with the Data, or sale of all or part of the Data on any media is not permitted.

12. Recognise that nothing in this agreement shall operate to transfer to the User Institution any intellectual property rights relating to the Data.

13. Accept that the User Institution has the right to develop intellectual property based on comparisons with their own data, but may not make intellectual property claims on the Data nor use intellectual property protection in ways that would prevent or block access to, or use of, any element of the Data, or conclusion drawn directly from the Data.

14. You agree that You will submit a report to the Data Access Committee, if requested, on completion of the agreed Research Purpose. The Data Access Committee agrees to treat the report and all information, data, results, and conclusions contained within such report as confidential information belonging to the User Institution.

15. If results arising from the User and the User Institution(s) use of the Data could provide health solutions for the benefit of people in the developing world, the User and the User Institution(s) agree to offer non-exclusive licenses to such results on a reasonable basis for use in low income and low-middle income countries (as defined by the World Bank) to any party that requests such a license solely for uses within these territories.

16. Agree to destroy/discard the Data held, once it is no longer used for the approved research, unless obliged to retain the Data for archival purposes in conformity with Institutional policy.

17. Agree to update the list of Authorised Personnel to reflect any changes or departures in affiliated researchers and personnel within 30 days of the changes made. These changes can be made by emailing info@rd-neuromics.eu.

18. Agree to distribute a copy of this agreement and explain its content to any person mentioned in the list of Authorised Personnel, including any additions made according to paragraph 17.

19. You will notify the Data Access Committee as soon as You become aware of a breach of the terms or conditions of this agreement.

20. Accept that this agreement will terminate upon any breach of this agreement by the User, the User Institution(s) or any Authorised Personnel listed in this application document. In this case, You will be required to destroy/discard any Data held, including copies and backup copies.

21. Accept that it may be necessary for the NeurOmics Consortium or its appointed agent to alter the terms of this agreement from time to time. In this event, the NeurOmics Consortium or its appointed agent will contact You to inform You of any changes, and You may be required to enter into a new version of the Agreement.

22. If requested, You will allow data security and management documentation to be inspected to verify that You comply with the terms of this agreement.

23. Understand that this agreement (and any dispute, controversy, proceedings or claim of whatever nature arising out of this agreement or its formation) shall be construed, interpreted and governed by the laws of Belgium and shall be subject to the exclusive jurisdiction of the Belgian courts.

WHEN SUBMITTING THIS DOCUMENT, PLEASE INCLUDE ALL PAGES OF THE AGREEMENT WITH THE SIGNATURE PAGE

Appendix A: Data Set Specific Conditions

Version 1

The patient samples for the NeurOmics Project were in some cases pre-existing prior to the start of the project but in most cases have been collected within the project. While they have all been approved for analysis and use in the Project, and for the resulting data to be used by others according to the NeurOmics Data Sharing Policy which this access agreement implements, in some cases the original consents restrict the uses to which the data can be put.

For the sake of clarity we list here all data sets, and any restrictions on use that apply. We also list the correct way to reference the origin of each sample set, as required in acknowledgements (see Appendix B).

Some of the NeurOmics disease (not cohort) studies have Research Ethical Committee approval to feedback to individual research participants genetic results that cause the clinical phenotype that is being studied. We encourage researchers who believe that they have identified a causal variant(s) for the disease under investigation by the NeurOmics project to contact the NeurOmics Project at info@rd-neuromics.eu who will ensure that the information is passed on to the relevant sample custodian, for their consideration.

Please note that NONE of the NeurOmics Projects have Research Ethical Committee approval to feedback to individual research participants genetic results that do not pertain to the clinical phenotype under investigation (so-called 'Incidental Findings'), and so such results SHOULD NOT be returned to the Data Access Committee, or directly to members of the NeurOmics Project or sample custodians.

If the data sets that you are requesting access for are not listed below, then you must obtain a more recent version of this appendix from www.rd-neuromics.eu and refer to that in your access application.

NeurOmics_SMA/LMND_GeneID-WES_V1	
EGA Study ID: EGAS00001000701. EGA data set ID: EGAD00001002694.	
Brief description:	This data set includes whole exome sequencing data. It comprises cases of spinal muscular atrophy (generally: lower motor neuron disease) patients. Deletion of the *SMN1* gene has been excluded as a disease cause. Samples are mostly affected individuals, but also unaffected parents or more distantly related family members. Patients did not belong to a specific race or are not from a defined or restricted geographic origin.
Conditions:	No additional constraints.
Data can be used as controls:	No.

Acknowledgement:	Corresponding PI: Prof. Dr. Brunhilde Wirth. This study makes use of data generated by the NeurOmics Consortium, derived from samples from the data set EGAD00001002694. A full list of the investigators who contributed to the generation of the data is available from www.rd-neuromics.eu. The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 2012-305121 "Integrated European –omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases (NEUROMICS)".

NeurOmics_HD_Modifier_V1	
EGA Study ID: EGAS00001000698. EGA data set ID: EGAD00001002695.	
Brief description:	48 samples from the TRACK-HD cohort. All samples carry the Huntington's disease expansion. The subjects were selected on the basis of rate of disease progression.
Conditions:	Data can only be used for Huntington's disease related research.
Data can be used as controls:	No.
Acknowledgement:	Prof. Sarah J Tabrizi This study makes use of data generated by the NeurOmics Consortium, derived from samples from the data set EGAD00001002699. A list of the investigators who contributed to the generation of the data is available from www.rd-neuromics.eu. The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 2012-305121 "Integrated European –omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases (NEUROMICS)". Funding for TRACK-HD was provided by the CHDI Foundation, and contributing authors are listed in the following publications. 1. Tabrizi, S. J. et al. Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: cross-sectional analysis of baseline data. The Lancet. Neurology 8, 791-801, doi:10.1016/s1474-4422(09)70170-x (2009). 2. Tabrizi, S. J. et al. Biological and clinical changes in premanifest and early stage Huntington's disease in the TRACK-HD study: the 12-month longitudinal analysis. The Lancet. Neurology 10, 31-42, doi:10.1016/s1474-4422(10)70276-3 (2011). 3. Tabrizi, S. J. et al. Potential endpoints for clinical trials in premanifest and early Huntington's disease in the TRACK-HD study: analysis of 24 month observational data. The Lancet. Neurology 11, 42-53, doi:10.1016/s1474-4422(11)70263-0 (2012).

	4. Tabrizi, S. J. et al. Predictors of phenotypic progression and disease onset in premanifest and early-stage Huntington's disease in the TRACK-HD study: analysis of 36-month observational data. The Lancet. Neurology 12, 637-649, doi:10.1016/s1474-4422(13)70088-7 (2013).

NeurOmics_HD_Biomarker-1_V1	
EGA Study ID: EGAS00001000698. EGA data set ID: EGAD00001002699.	
Brief description:	This data set includes RNAseq data from 136 samples from the TRACK-HD cohort including premanifest, manifest and control subjects.
Conditions:	Data can only be used for Huntington's disease related research.
Data can be used as controls:	No.
Acknowledgement:	Prof. Sarah J Tabrizi This study makes use of data generated by the NeurOmics Consortium, derived from samples from the data set EGAD00001002699. A list of the investigators who contributed to the generation of the data is available from www.rd-neuromics.eu. The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 2012-305121 "Integrated European –omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases (NEUROMICS)". Funding for TRACK-HD was provided by the CHDI Foundation, and contributing authors are listed in the following publications. 1. Tabrizi, S. J. et al. Biological and clinical manifestations of Huntington's disease in the longitudinal TRACK-HD study: cross-sectional analysis of baseline data. The Lancet. Neurology 8, 791-801, doi:10.1016/s1474-4422(09)70170-x (2009). 2. Tabrizi, S. J. et al. Biological and clinical changes in premanifest and early stage Huntington's disease in the TRACK-HD study: the 12-month longitudinal analysis. The Lancet. Neurology 10, 31-42, doi:10.1016/s1474-4422(10)70276-3 (2011). 3. Tabrizi, S. J. et al. Potential endpoints for clinical trials in premanifest and early Huntington's disease in the TRACK-HD study: analysis of 24 month observational data. The Lancet. Neurology 11, 42-53, doi:10.1016/s1474-4422(11)70263-0 (2012). 4. Tabrizi, S. J. et al. Predictors of phenotypic progression and disease onset in premanifest and early-stage Huntington's disease in the TRACK-HD study: analysis of 36-month observational data. The Lancet. Neurology 12, 637-649, doi:10.1016/s1474-4422(13)70088-7

	(2013).

NeurOmics_CMS_GeneID-WES_V1	
EGA Study ID: EGAS00001000693. EGA data set ID: EGAD00001002700.	
Brief description:	This data set includes whole exome sequencing data from cases clinically diagnosed as Congenital Myasthenic Syndrome (CMS) with the aim of finding new candidate genes. Patients had all been pre-screened for common hot spot mutations in known CMS genes. Samples are mostly affected individuals but also unaffected parents and other family members. Patients do not belong to any specific ethnic group.
Conditions:	No constraints
Data can be used as controls:	Yes
Acknowledgement:	Corresponding PI: Prof. Dr. Hanns Lochmüller. This study makes use of data generated by the NeurOmics Consortium, derived from samples from the data set EGAD00001002700. The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 2012-305121 "Integrated European – omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases (NEUROMICS)".

NeurOmics_CMS_GeneID-WGS_V1	
EGA Study ID: EGAS00001000693. EGA data set ID: EGAD00001002701.	
Brief description:	This data set includes whole genome sequencing from cases clinically diagnosed as Congenital Myasthenic Syndrome. These cases went through an initial run of WES but remained unsolved. All samples are affected individuals. Patients did not belong to any specific ethnic group.
Conditions:	No constraints
Data can be used as controls:	Yes
Acknowledgement:	Corresponding PI: Prof. Dr. Hanns Lochmüller. This study makes use of data generated by the NeurOmics Consortium, derived from samples from the data set EGAD00001002701. The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 2012-305121 "Integrated European – omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases (NEUROMICS)".

NeurOmics_CMS_Modifier-WGS_V1

EGA Study ID: EGAS00001000693. EGA data set ID: EGAD00001002702.	
Brief description:	This data set includes whole genome sequencing data for 20 Congenital Myasthenic syndrome patients. All these patients share the same *CHRNE* c.1267delG mutation in homozygosis and are of Romani ancestry. Their phenotypic presentation varies from mild to severe. The data set was used as part of an integrated approach to search for modifier genes.
Conditions:	No constraints
Data can be used as controls:	Yes
Acknowledgement:	Corresponding PI: Prof. Dr. Hanns Lochmüller. This study makes use of data generated by the NeurOmics Consortium, derived from samples from the data set EGAD00001002702. The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 2012-305121 "Integrated European – omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases" (NEUROMICS).

Appendix B: NeurOmics Project Publication Moratorium

Neurodegenerative (ND) and neuromuscular (NM) diseases are amongst the most frequent classes of rare diseases, affecting life and mobility of 500,000 patients in Europe and millions of their caregivers, family members and employers. This NeurOmics project brings together the leading research groups in Europe, five highly innovative SMEs and relevant oversea experts using the most sophisticated Omics technologies to revolutionize diagnostics and to develop pathomechanism-based treatment for ten major ND and NM diseases. Specifically we aim to:

a) use next generation WES to increase the number of known gene loci for the most heterogeneous disease groups from about 50% to 80%,

b) increase patient cohorts by large scale genotyping by enriched gene variant panels and NGS of so far unclassified patients and subsequent phenotyping,

c) develop biomarkers for clinical application with a strong emphasis on presymptomatic utility and cohort stratification,

d) combine -omics approaches to better understand pathophysiology and identify therapeutic targets,

e) identify disease modifiers in disease subgroups cohorts with extreme age of onset

f) develop targeted therapies (to groups or personalized) using antisense oligos and histone deacetylase inhibitors, translating the consortiums expertise in clinical development from ongoing trials toward other disease groups, notably the PolyQ diseases and other NMD.

To warrant that advances affect a large fraction of patients we limited the selection to a number of major categories, some of which are in a promising stage of etiological and therapeutic research while some others are in great need of further classification. The efforts will be connected through a NeurOmics platform for impact, communication and innovation that will provide tools and procedures for ensuring trial-readiness, WP performance, sustainability, interaction with the chosen Support IRDiRC and RD-Connect project and involvement of stakeholders in the NDD/NMD field.

This publication moratorium will protect the first publication rights of the sample custodians and data generators. The protected publication rights prohibit submission of papers by groups of authors not including the NeurOmics consortium that describe genetic variants or their use in association tests for the named phenotypes for which the samples were selected into the project, until one of the following criteria is met.

All data will no longer be subject to the publication moratorium once the data has been published, or two years after the end of the NeurOmics project i.e. after 30 September 2019.

This publication moratorium will be made available along with the data sets deposited in the EGA. Potential data users are encouraged to contact the NeurOmics data access committee if there is any doubt about how the data may be used. Where a breach of the moratorium takes place or is suspected, in addition to leading to potential termination of current and future data access, the Data Access Committee and/or the NeurOmics Steering Committee may contact

the appropriate journal editor with evidence that data use conditions have been breached and request that any manuscripts be withdrawn.

Principles for publications

Papers based on external users downloading NeurOmics data, should follow a core set of principles:

1. Authors who use data from the project must acknowledge the NeurOmics Consortium using the following wording, or close equivalent containing the same elements:

   "*This study makes use of data generated by the NeurOmics Consortium, derived from samples from <list each data set>. A full list of the PIs who contributed to the generation of the data is available in the data set description from www.rd-neuromics.eu. The research leading to these results has received funding from the European Community's Seventh Framework Programme (FP7/2007-2013) under grant agreement n° 2012-305121 "Integrated European –omics research project for diagnosis and therapy in rare neuromuscular and neurodegenerative diseases (NEUROMICS)".*

2. Authors who use data from the project must cite the relevant primary NeurOmics publication. Details of which can be found in data set description in Annex A and on www.rd-neuromics.eu.
3. Annex A provides further information on how to acknowledge the respective data set.
4. The NeurOmics PIs contributing data to the data set the User has been granted access to should be informed at least 2 weeks in advance about submission of a manuscript making use of this data set. Corresponding PIs are listed in the data set descriptions.

Users should note that the NeurOmics Consortium bears no responsibility for the further analysis or interpretation of these Data, over and above that published by the Consortium.