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SUPPLEMENT PREFACE

# Preclinical common data elements (CDEs) for epilepsy: A joint ILAE/AES and NINDS translational initiative

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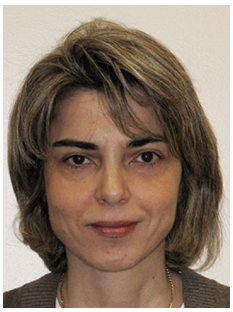

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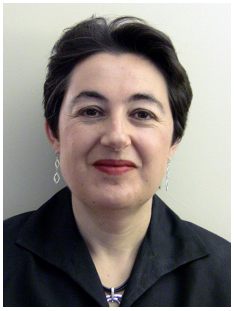

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This supplement reflects the efforts of a group of researchers with expertise in epilepsy to address several critical issues in preclinical epilepsy research today. In this case, "preclinical" refers to research in laboratory animals, mostly mice and rats, which aims to develop new treatments, biomarkers, or diagnostics for epilepsies with the ultimate goal of translating them into clinical testing and practice.

Common data elements (CDEs) are types of data that are common to many different research studies. CDEs refer to specific types of data, such as the sex or strain of an animal, or the age of an animal at the onset of an experiment about epilepsy. These types of data are commonly used by many investigators, and they reflect the units or elements of the data. This means the CDEs describe the units of data that are collected during experiments. The reason that CDEs are important, especially at the present time, is that they are emerging as very useful for comparison of datasets either in the same laboratory or different laboratories. At the present time, CDEs are not usually available from published working groups in preclinical epilepsy research, so many types of data that one would theoretically want to know about when reading a publication about a study, such as sex, strain, or age, are often unavailable. The consequence is that datasets are difficult to compare or cannot be compared at all. Meta-analyses are difficult or impossible. Another consequence of rare use of CDEs in preclinical epilepsy research is that data from many publications about one topic are hard to understand as a whole because one must read and interpret one study at a time. Datasets from different laboratories may lead investigators to come to different conclusions even if the differences are simply due to use of female instead of male subjects, or different strains/ages. Ultimately there are several problems: lack of transparency of methods/data, lack of reproducibility of one study by another group, and numerous published studies without a clear consensus driving the field forward.

The articles in this supplement were developed by 4 working groups that addressed 4 subareas: research about behavior, research about physiology in whole animals, pharmacological use of agents to determine their influence on acute seizures and chronic epilepsy, and electroencephalography (EEG). The working groups were conducted within a larger framework, a Task Force created jointly by the International League Against Epilepsy (ILAE) and the American Epilepsy Society (AES). This ILAE/AES Joint Translational Task Force was supported also by the National Institute of Neurological Disorders and Stroke (NINDS). The Task Force was chaired by AES [Jacqueline French (US) and Aristea Galanopoulou (US)] and ILAE [Terence O'Brien (Australia) and Michele Simonato (Italy)] members and comprised several investigators from the international epilepsy community: Amy Brooks-Kayal (US), Frances Jensen (US), Marco de Curtis (Italy), Akio Ikeda (Japan), Asla Pitkänen (Finland), and Helen Scharfman (US), whereas Solomon Moshé (US) was the liaison with the ILAE executive committee. Several large groups or "TASKs" were developed, with TASK3 focused on preclinical CDEs. This supplement describes the outcome of the TASK3 effort.

To address these needs, the 4 working groups groups (abbreviated here as Behavior, Physiology, Pharmacology, and EEG) started to consider how to draft CDEs, case report forms (CRFs), and companion papers for their subtopic of preclinical epilepsy research. The selected Co-chairs had international representation (Behavior: Nigel Jones and Andrey Mazarati; Physiology: Jan Gorter and Astrid Nehlig; Pharmacology: Melissa Barker-Haliski and Claudia Brandt; and EEG: Tomonori Ono, and Aristea Galanopoulou as TASK1 liaison) and were chosen to lead a group of 5 or more members with expertise in epilepsy. Each group worked separately but met at intervals to discuss progress and problems. The 4 groups were led by 4 of the Chairs of the Task Force: Jacqueline French, Aristea Galanopoulou, Asla Pitkänen, and Helen Scharfman. In addition, Brandy Fureman and subsequently Vicky Whittemore of the NINDS contributed.

Fortuitously, these efforts were coordinated and advanced with the help of Dr. Lauren Harte-Hargrove. She provided administrative help as well as assistance with writing, drafting tables, formatting and reconciling the

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CRFs and, most importantly, generating the CDE charts, which can be used eventually by the end users in the creation of their databases. Her outstanding efforts, including her outstanding availability at short notice, patience, and skill, as well as her congenial nature, were critical to the CDE effort and this supplement.

In the special issue of *Epilepsia Open*, there is an initial description of so-called Core CDEs, followed by working group reports describing the specific CDEs/CRFs that were developed:

1 *Core CDEs:* Harte-Hargrove et al.[1] Common Data Elements (CDEs) for Preclinical Epilepsy Research: Introduction to the Special Issue and Description of Core CDEs. A TASK3 report of the ILAE/AES Joint Translational Task Force.
2 *Behavior:* Mazarati et al.[2] A Companion to the Preclinical Common Data Elements on Neurobehavioral Comorbidities of Epilepsy. A report of the TASK3 Behavior Working Group of the ILAE/AES Joint Translational Task Force.
3. *Physiology:* Gorter et al.[3] A companion to the Preclinical Common Data Elements for Rodent Epilepsy Models. A report of the TASK3 Physiology Working Group of the ILAE/AES Joint Translational Task Force.
4 *Pharmacology:* Barker-Haliski et al.[4] A companion to the Preclinical Common Data Elements for Pharmacological Studies in Animal Models of Seizure and Epilepsy. A report of the TASK3 Pharmacology Working Group of the ILAE/AES Joint Translational Task Force.
5. *EEG:* Ono et al.[5] A companion to the Preclinical Common Data Elements and Case Report Forms for Rodent EEG Studies. A report of the TASK3 EEG Working Group of the ILAE/AES Joint Translational Task Force.

Each report is linked to the CDE charts (Excel files for use for creating databases) and CRFs (MS Word files for use by the investigators designing experiments and collecting data). These CDE and CRF files are included in folders and their links are given at the end of each manuscript (as supporting information).

The Core CDEs[1] refer to data that are collected for virtually all experiments in preclinical epilepsy. In contrast, for any given study, the CDEs for Behavior,[2] for example, may not be used because behavioral assays might not be part of the specific study. Similarly, some epilepsy research does not use the EEG. The Core CDEs are described by the Co-chairs of TASK3.[1]

The outcome of the working groups is not only a product of the working groups of TASK3, but also of others who have already reviewed and commented on the CDEs as they were developing. Most of this vetting was done in 2016. We offer these manuscripts and CDEs/CRFs as open access to facilitate review and hopefully feedback by the research community that would be interested in using them. Based on this community feedback, we will modify or update the current products. Future working groups will extend to additional epilepsy research areas, for example, models of epilepsies and seizures.

We invite the readers to contact Dr. Helen Scharfman with any feedback they would like to offer, which will be important to tailor these forms to the needs of the researchers involved in epilepsy research. Such feedback may include the accuracy or level of detail of the information contained or the prioritization of the CDEs as "high priority," "moderate," or "optional," meaning how important it is to obtain data on an element during an experiment using the specific technique. In this way we see this supplement as a beginning, not an end, to the efforts that will increasingly improve preclinical epilepsy research.

## Contributors

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working groups:

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*2. Physiology*

Co-chairs: Astrid Nehlig, Jan Gorter

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*3. Pharmacology*

Co-chairs: Melissa Barker-Haliski, Claudia Brandt

Members: Teresa Ravizza, Ilse Smolders, Bo Xiao, Michael Rogawski, Jeremy Barry

*4. EEG*

Chair: Tomonori Ono

TASK1 liaison: Aristea S. Galanopoulou

Members: Joost Wagenaar, Emmanuel Raffo, Ryosuke Hanaya, Filippo Sean Giorgi, Petr Fabera, John Jefferys.

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and the Segal Family Foundations and the Abbe Goldstein/Joshua Lurie and Laurie Marsh/Dan Levitz families. J. French receives funding from New York University, Epilepsy Research Consortium and Epilepsy Foundation. A. Pitkänen receives grant support from the Academy of Finland (272249 and 273909), European Union 7th Framework Program no:o 602102 EPITARGET, U54 NS1000064. H. Scharfman acknowledges the support of the NY State Office of Mental Health.

## Disclosure of Conflict of Interest

J. A. F., A. S. G., L. C. H., A. P., and H. E. S. received travel reimbursement from the ILAE, AES, and NINDS for meetings for the work done through the TASK3 of the ILAE/AES Joint Translational Task Force. L.H. is currently Associate Director of Research at Citizens United for Research in Epilepsy (CURE) but has no conflict of interest with regard to this manuscript. A. Galanopoulou has received royalties for publications from Elsevier, is a co-Editor-in-Chief of *Epilepsia Open* and has received an honorarium for a one-time advisory role to Mallinckrodt but has no conflicts of interest in regard to this manuscript. J. French receives New York University (NYU) salary support from the Epilepsy Foundation and for consulting work on behalf of the Epilepsy Study Consortium for Acorda, Adamas, Alexza, Anavex, Axcella Health, Biogen, BioPharm Solutions, Cerecor, Concert Pharmaceuticals, Engage, Eisai, GlaxoSmithKline, GW Pharma, Marinus, Nestle-Health Science, Neurelis, Novartis, Pfizer, Pfizer-Neusentis, Ovid, Sage, SK Life Sciences, Sunovion, Takeda, UCB Inc., Upsher Smith, Xenon Pharmaceuticals, Zogenix, and Zynerba. J. French has also received research grants from Acorda, Alexza, Eisai Medical Research, Lundbeck, Pfizer, SK Life Sciences, Sunovion, UCB Inc., Upsher-Smith, and Vertex, as well as grants from the Epilepsy Research Foundation, Epilepsy Study Consortium, Epilepsy Therapy Project, and NINDS. She is on the editorial board of *Lancet Neurology*, *Neurology Today*, and *Epileptic Disorders*. She is scientific officer for the Epilepsy Foundation for which NYU receives salary support. She has received travel reimbursement related to research, advisory meetings, or presentation of results at scientific meetings from the Epilepsy Study Consortium, the Epilepsy Foundation, Eisai, GW Pharma, Marinus, Nestle Life Sciences, Pfizer, Sage, SK life Sciences, Takeda, UCB Inc., Upsher-Smith, Zogenix, and Zynerba. H. Scharfman is a member of the Scientific Board of Advisors for Pyramid Biosciences. The remaining authors have no further conflicts of interest to disclose. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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