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Committee for Medicinal Products for Human Use (CHMP)

# Concept paper on the need for revision of the guideline on clinical investigation of medicinal products in the treatment of Parkinson's disease

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| Agreed by Central Nervous System Working Party | 25 September 2025 |
| Adopted by CHMP for release for consultation | 04 November 2025 |
| Start of public consultation | 30 November 2025 |
| End of consultation (deadline for comments) | 31 March 2026 |

The proposed guideline will replace the Guideline on clinical investigation of medicinal products in the treatment of Parkison's disease (EMA/CHMP/330418/2012 rev. 2, 7 July 2012).

Comments should be provided using this EUSurvey form. For any technical issues, please contact the EUSurvey Support.

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| **Keywords** | ***Parkinson's Disease, Parkinsonism, Guideline, Confirmatory trials, Multiple System Atrophy, Corticobasal degeneration, Progressive Supranuclear Palsy, essential tremor*** |

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# 1. Introduction

Neurodegenerative movement disorders (NMDs) are age-dependent disorders characterised by neuronal loss, accumulation of pathological proteins, and syndromes dominated – at least initially – by disturbances of movement.

The most common NMD is Parkinson's Disease (PD), which is neuropathologically characterised by the degeneration of heterogeneous populations of neural cells (particularly dopaminergic neurons) involving different neurotransmitter systems and different regions of the Nervous System. The degeneration of the pigmented neurons in the *pars compacta* of the *substantia nigra* accounts for most of the distinctive motor symptoms. The presence of alpha-synuclein rich eosinophilic cytoplasmatic inclusions (Lewy bodies) in the lesioned cells of pigmented nuclei and other brain regions is the hallmark for the neuropathological diagnosis (Bloem et al, 2021). Recently, different biomarker algorithms have been proposed to identify early-stage Parkinson's disease pathology, for research purposes (Höglinger et al, 2024 and Simuni et al, 2024).

The guideline proposed will extend the scope of the current one: other NMDs in scope for this revision are Multiple System Atrophy, Corticobasal degeneration and Progressive Supranuclear Palsy. In addition, this guideline will provide guidance on the developments for essential tremor.

# 2. Problem statement

The current guideline predates some recent developments in the field. As such, it does not adequately reflect recent developments related to the use of newly proposed biomarker algorithms for the selection of patients in clinical trials, it does not address specific considerations that may be applicable to the development of targeted agents, and it does not give adequate guidance for developments addressing (also) non-motor symptoms. Advanced PD and other movement disorders patients are increasingly being treated with treatments such as parenteral levodopa / agonists, deep brain stimulation, and focused ultrasounds (FUS). These patients have usually been excluded from clinical trials with medicines; discussion on strategies to include this population in studies is needed. The guideline is not expected to address co-development of device-drug combinations.

Furthermore, the current guideline does not provide guidance on developments for the treatment of other non-rare NMDs and of essential tremor.

# 3. Discussion (on the problem statement)

The following critical aspects should be discussed in the update of the guidance document:

- Utility and role of clinical and non-clinical biomarkers for Patients' enrolment in neurodegenerative movement disorders clinical trials, for both targeted and non-targeted treatments;
- Primary and secondary endpoints (including digital) for non-motor and motor symptoms, especially when addressing refractory aspects of disease (freezing, falls, dementia, apathy);
- Considerations on the inclusion, in clinical trials for medicinal products, of patients being treated with medical devices, including but not limited to implantable devices, or with long-term formulations of symptomatic treatments;
- Design elements for randomised studies targeting the underlying pathophysiological process(es) (on top of symptomatic treatment), including for the demonstration of durability of effect;

- The scientific questions of interest and corresponding Estimands of interest should be clearly defined in the different settings. In line with the ICH E9(R1) Addendum on Estimands and Sensitivity Analysis, the guideline will address considerations on intercurrent events such as concomitant medication and their adjustments and nondrug treatments such as deep brain surgery, focused ultrasound, physiotherapy;
- The role of decentralised elements for clinical trials in this area, including data collection occurring outside clinical trial sites;
- Specific consideration for developments for the treatment of other NMDs and of essential tremor.

# 4. Recommendation

The Central Nervous System Working Party (CNSWP) recommends drafting a revision of Parkinson's disease guideline including the utility and role of new biomarkers to inform enrolment in clinical trials / enrichment approach and other forms of Parkinsonism and related disorders.

# 5. Proposed timetable

It is planned to release for consultation a draft CHMP guidance document not later than Q4 2026.

# 6. Resource requirements for preparation

The preparation of this guideline will involve the CNSWP. A draft version of the document will be discussed in a workshop planned when the draft is at the commenting phase, with the SAWP, the MWP, and other relevant WPs and committees.

# 7. Impact assessment (anticipated)

It is aimed that this guideline will improve regulatory consistency and alignment for medicinal products in PD and related disorders.

# 8. Interested parties

The interested parties in the guidance document include learned societies and academia – The Movement Disorders Society (MDS), European Academy of Neurology (EAN), The International Society for CNS Clinical Trials and Methodology (ISCTM), The European College of Neuropsychopharmacology, pharmaceutical industry (e.g. EFPIA and others) and other regulatory agencies.

# 9. References to literature, guidelines, etc.


- Guideline on clinical investigation of medicinal products in the treatment of Parkinson's disease https://www.ema.europa.eu/en/clinical-investigation-medicinal-products-treatment-parkinsons-disease-scientific-guideline
- Procedure for European Union guidelines and related documents within the pharmaceutical legislative framework (EMEA/P/24143/2004): https://www.ema.europa.eu/en/documents/scientific-guideline/procedure-european-union-guidelines-and-related-documents-within-pharmaceutical-legislative-framework_en.pdf

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