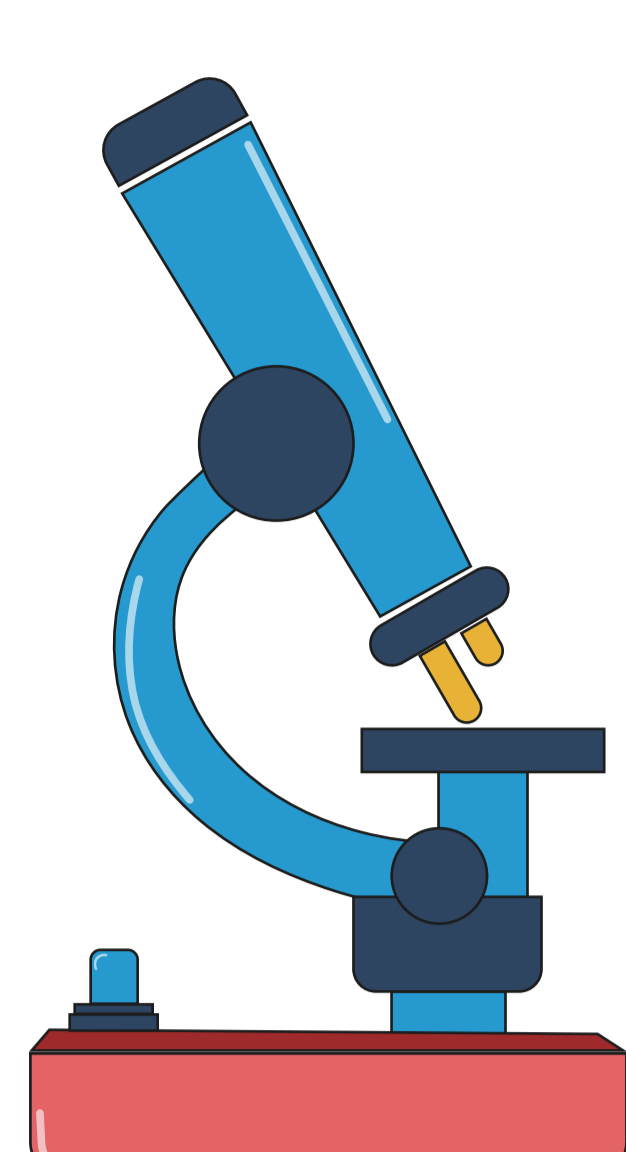


Framework for the development and validation of new fluid biomarkers for Alzheimer's disease (AD) diagnosis

Colour codes indicate the levels of evidence for each blood-based biomarker:

Blue: mostly accomplished for this marker; **Purple:** somewhat accomplished for this marker; **Red:** no results that address this aspect for this marker.



Phase 1

Preclinical exploratory studies

Biomarker identification and leads prioritisation:

- Hypothesis driven (A β , pTau, GFAP, NfL)
- Unbiased -omics data (proteomics, transcriptomics)



Phase 2

Clinical assay development and validation

Technical:
LDTs and RUO assay development and validation (A β , pTau, GFAP, NfL)

Clinical:
Analysis of diagnostic accuracy in case-control studies (A β , pTau, GFAP, NfL)



Phase 3

Retrospective and longitudinal studies

Technical:
Define criteria for a positive test e.g., cut-offs (A β , pTau, GFAP, NfL)

Clinical:
Diagnostic accuracy for early disease detection e.g., preclinical, prodromal (A β , pTau, GFAP, NfL)

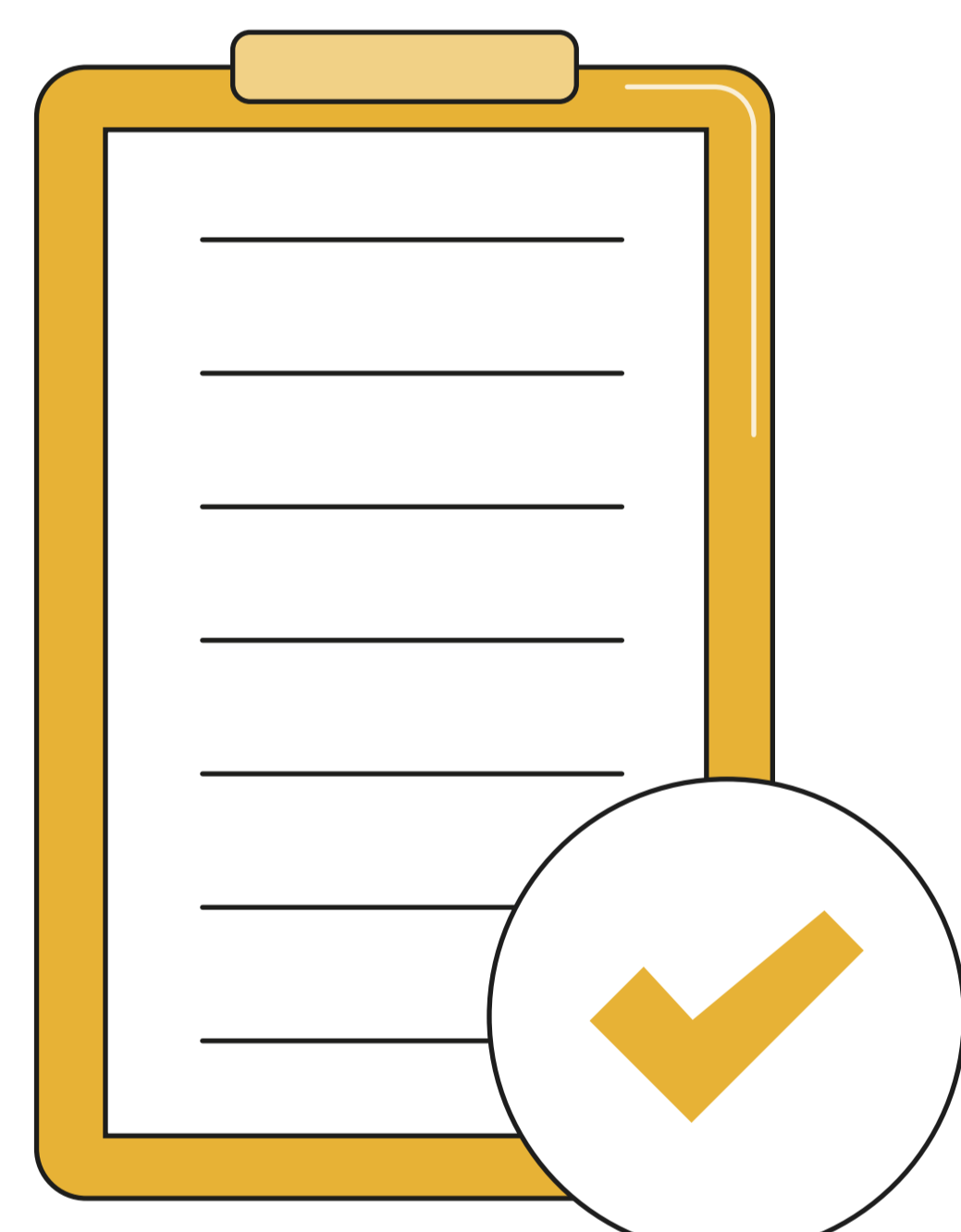


Phase 4

Prospective studies and real-world performance

Technical:
IVD assay development and validation (A β , pTau, GFAP, NfL)

Clinical:
Establish diagnostic performance prospectively (A β , pTau, GFAP, NfL)



Phase 5

Implementation and impact on clinical outcomes

Regulatory:
Integration in clinical guidelines (A β , pTau, GFAP, NfL)

Clinical:
Impact of biomarker testing on clinical decision making (A β , pTau, GFAP, NfL)

Phase 2 secondary aims and levels of achievement of blood-based biomarker development and validation for AD

Technical secondary aims

- Reproducibility of assays between laboratories (A β , pTau, GFAP, NfL)
- Pre-analytical factor assessment (A β , pTau, GFAP, NfL)
- SOPs for sample handling and storage (A β , pTau, GFAP, NfL)

Clinical secondary aims

- Relation with gold standard measures; e.g., CSF, autopsy (A β , pTau, GFAP, NfL)
- Identification of covariates (age, sex, ethnicity, lifestyle) influencing biomarker concentrations in patients and healthy controls (A β , pTau, GFAP, NfL)
- Relation with disease characteristics; e.g., cognitive performance (A β , pTau, GFAP, NfL)
- Disease specificity assessment for differential diagnosis (A β , pTau, GFAP, NfL)

Progress achieved in the biomarker implementation roadmap

- Phases 1 and 2 of the roadmap have largely been achieved for A β , pTau, and NfL
- Research continues on phases 1 and 2 for GFAP, and phase 3 for all biomarkers
- Phases 4 and 5 need to be undertaken for all biomarkers

Abbreviations: A β , amyloid β ; CSF, cerebrospinal fluid; GFAP, glial fibrillary acidic protein; IVD, in vitro diagnostic; LDT, laboratory-developed test; NfL, neurofilament light chain; pTau, phosphorylated tau; RUO, research use only; SOP, standard operating procedure

Reference: Teunissen CE, et al. Blood-based biomarkers for Alzheimer's disease: towards clinical implementation. *Lancet Neurol.* 2022;21(1):66–77.

Developed by EPG Health, an IQVIA business. This content has been developed independently of the sponsor Roche Diagnostics International Ltd, who have had no editorial input into the content. EPG Health received unrestricted educational funding from the sponsor in order to help provide its healthcare professional members with access to the highest quality medical and scientific information, education and associated relevant content.

