The Clinical Trial Pathology Advisory Group (CT-PAG)
Enhancing UK biomarker-led research

Reuben Tooze, Susan Richman, Guy Betts, Maggie Cheang, the CT-PAG advisory group members, Jessica Lee, Karin Oien, Gareth Thomas, Craig Robson

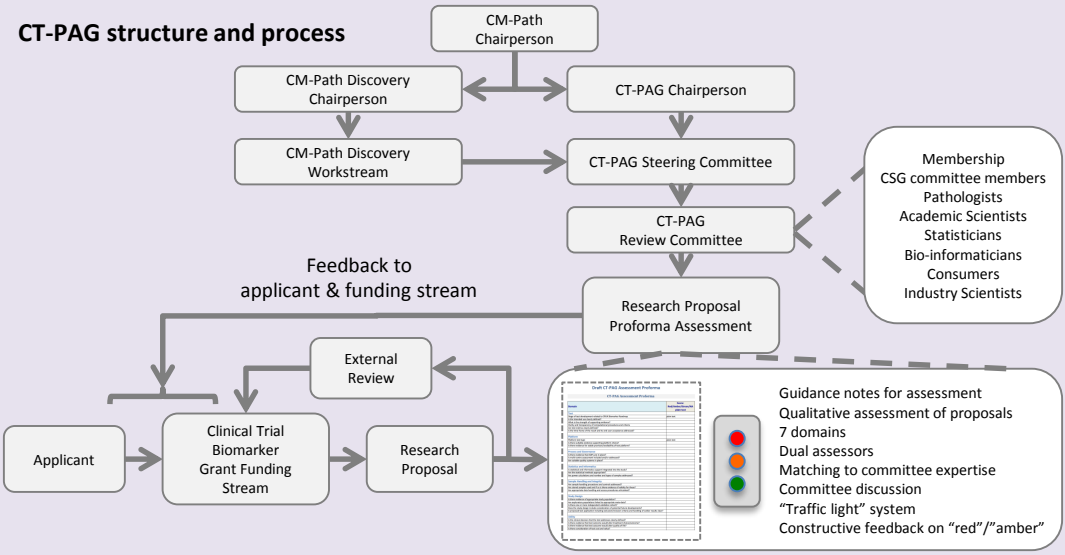
https://cmpath.ncri.org.uk/

Background

A strong pipeline linking biomarker discovery and validation to targeted therapeutic development is essential to deliver rational evidence-based therapeutic decisions in the emerging era of targeted therapy.

The recently formed Clinical Trial Pathology Advisory Group (CT-PAG) sits within the NCRI initiative in cellular molecular pathology, CM-Path. Aligned with the biomarker roadmap, CT-PAG aims to provide guidance and technical critique of pathology and biomarker components in clinical trials. To this end, CT-PAG has developed a proforma to help standardization of assessment and provide guidance for enhancing biomarker-led research supported via NCRI. This proforma aims to provide the basis for a succinct assessment and checklist for technical issues relating to biomarker research across the "biomarker roadmap". The proforma has been developed drawing on related efforts from NCI, the National Academies (USA), CRUK and other sources.

CT-PAG structure and process

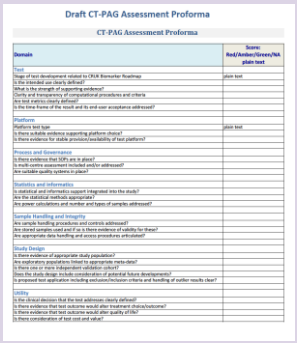


CT-PAG Proforma

Domain 1: Test
Stage of test development
Clarity of defined usage
Strength of supporting evidence
Definition of metrics/procedures
Time-frames & end-user usage

Domain 2: Platform
Type of test/platform
Evidence supporting platform
Evidence for stable provision/availability of platform

Domain 3: Process and Governance
SOPs
Multi-centre assessment
Suitability of quality systems


Draft CT-PAG Assessment Proforma

CT-PAG Assessment Proforma

Domain	Score: Red/Amber/Green/NA plain text
Test	
Stage of test development related to CRUK Biomarker Roadmap	plain text
Is the intended use clearly defined?	
What is the strength of supporting evidence?	
Clarity and transparency of computational procedures and criteria	
Are test metrics clearly defined?	
Is the time frame of the result and its end-user acceptance addressed?	
Platform	
Platform test type	plain text
Is there suitable evidence supporting platform choice?	
Is there evidence for stable provision/availability of test platform?	
Process and Governance	
Is there evidence that SOPs are in place?	
Is multi-centre assessment included and/or addressed?	
Are suitable quality systems in place?	
Statistics and Informatics	
Is there evidence that support integrated into the study?	
Are the statistical methods appropriate?	
Are power calculations and number and types of samples addressed?	
Sample Handling and Integrity	
Are sample handling procedures and controls addressed?	
Are stored samples used and if so is there evidence of validity for these?	
Are appropriate data handling and access procedures enforceded?	
Study Design	
Is there evidence of appropriate study population?	
Are exploratory populations linked to appropriate meta-data?	
Are validation cohorts described in sufficient detail?	
Does the study design include consideration of potential future developments?	
Is proposed test application including exclusion/inclusion criteria and handling of outlier results clear?	
Utility	
Is the clinical decision that the test addresses clearly defined?	
Is there evidence that test outcome would alter treatment choice/outcome?	
Is there evidence that test outcome would alter quality of life?	
Is there consideration of test cost and value?	

Domain 4: Statistics & Informatics
Integration of support in study
Statistical methods
Power calculations, sample types, numbers and controls

Domain 5: Sample handling and integrity
Sample handling procedures & controls
Storage & utility
Data & access procedures

Domain 6: Study design
Study population
Exploratory populations meta-data
Validation cohorts
Future proofing
Inclusion/exclusion/outliers

Domain 7: Utility
Definition of clinical decision
Impact on treatment choice
Impact on quality of life
Test cost and value

Conclusions

CT-PAG aims to support the continued enhancement of excellence in biomarker-led clinical investigation in the UK. Through dialogue with stakeholders we aim to facilitate and support best practice in biomarker-led pathology research, hence improving the delivery of cellular and molecular pathology in research and ultimately in clinical application. We have developed and applied our version-1 CT-PAG proforma as a starting point in a process which we hope to see develop in an iterative cycle.