ColonAiQ® Clinical Evidence Package

CE Marked, China NMPA registered and Singapore HSA-cleared ColonAiQ®

Compiled on August 14, 2025

ColonAiQ® Clinical Evidence Package

Executive Summary

ColonAiQ® represents a breakthrough in colorectal cancer (CRC) detection and monitoring, utilizing a multi-gene methylation approach targeting circulating tumor DNA (ctDNA) in blood samples. This comprehensive evidence package demonstrates the clinical utility of ColonAiQ® across multiple applications: early detection, molecular residual disease (MRD) monitoring, and recurrence prediction.

Key Performance Metrics:

- **Sensitivity**: 86.1% for CRC detection (all stages)
- **Specificity**: 91.9% for healthy controls
- **Early Stage Detection**: 78.3% sensitivity for Stage I CRC
- **MRD Detection**: 78.0% sensitivity with 90.2% specificity at postoperative month 1
- **Recurrence Prediction**: 17.5x higher risk of relapse for ctDNA-positive patients

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1. Technology Overview

Multi-Gene Methylation Platform

ColonAiQ® employs a simplified multiplex quantitative PCR (qPCR) assay targeting six DNA methylation markers:

Target Genes:

- **SEPTIN9** (2 loci): Well-established CRC methylation marker
- **BCAT1**: Branched-chain amino acid transaminase 1
- **IKZF1**: Ikaros family zinc finger 1
- **VAV3**: Vav guanine nucleotide exchange factor 3
- **BCAN**: Brevican

Technical Advantages

1 **Multi-locus Detection**: Captures fuller spectrum of tumor epigenetic heterogeneity
2 **Co-methylation Patterns**: Analyzes adjacent CpG sites from the same DNA molecule
3 **Simplified Workflow**: Single-reaction PCR-based assay deployable in clinical settings
4 **Cost-Effective**: More accessible than next-generation sequencing approaches
5 **Rapid Turnaround**: Results available within days, not weeks

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2. Pivotal Clinical Studies

2.1 Gastroenterology Study (2021) - Early Detection

Study Design: Multicenter case-control study

Population: 507 plasma samples from multiple centers

Primary Endpoint: CRC and advanced adenoma detection

Key Findings:

Category	Sensitivity	Specificity	Sample Size
All CRC	86.1%	91.9%	173 CRC, 136 controls
Stage I	78.3%	-	23 patients
Stage II	82.0%	-	50 patients
Stage III	86.0%	-	72 patients
Stage IV	100%	-	16 patients
Advanced Adenoma	42.1%	-	107 patients

Comparative Performance:

- **vs. Fecal Immunochemical Test (FIT)**: 88.3% vs 59.7% overall sensitivity
- **vs. CEA**: 80-92% vs 17-47% for early-stage CRC
- **vs. SEPT9 alone**: Superior performance across all stages

2.2 JAMA Oncology Study (2023) - Molecular Residual Disease

Study Design: Multicenter prospective longitudinal cohort study

Population: 299 patients with stage I-III CRC

Study Period: December 2019 - February 2022

Follow-up: Median 21 months (range 8-27 months)

Primary Findings:

Postoperative Month 1 Results

- **ctDNA-positive patients**: 17.5x higher relapse risk (HR 17.5; 95% CI: 8.9-34.4; P<0.001)
- **Sensitivity**: 78.0% for relapse detection
- **Specificity**: 90.2%
- **Negative Predictive Value**: 94.4%

Longitudinal Monitoring

- **Median Lead Time**: 3.3 months (IQR: 0.5-6.5 months) ahead of radiological detection
- **Sustained ctDNA-positive**: 68.8x higher recurrence risk (HR 68.8; 95% CI: 18.4-257.7; P<0.001)
- **Post-adjuvant chemotherapy**: 13.8x higher recurrence risk for ctDNA-positive patients

Clinical Risk Stratification

Stage III Patients:

- ctDNA status superior to traditional clinical risk factors
- May guide adjuvant chemotherapy duration decisions
- 6-month vs 3-month chemotherapy benefit observed in high-risk ctDNA-positive patients

2.3 Performance Evaluation Study (Alternative Therapies)

Study Design: Performance validation study

Population: 88 participants (47 CRC patients, 41 controls)

Objective: Comprehensive kit performance assessment

Performance Metrics:

- **Overall Accuracy**: 93.18% (82/88 samples)
- **CRC Sensitivity**: 89.36% (42/47 patients)
- Stage I: 100% (8/8)
- Stage II: 81.25% (13/16)
- Stage III: 87.5% (14/16)
- Stage IV: 100% (7/7)
- **Specificity**: 97.56% (40/41 controls)

Technical Validation:

- **Precision**: 100% reproducibility (intra-day and inter-day)
- **Detection Limit**: 0.5% methylated DNA
- **Minimum DNA Input**: 10 ng
- **Interference**: No effect from common clinical substances

2.4 PreC Real-World Study (Annals of Oncology 2023)

Study Design: Prospective community screening study

Population: 105,285 participants (ages 40-80)

Study Period: January 2021 - December 2022

Setting: Community-based screening program

Screening Results:

- **ColonAiQ® Positive Rate**: 6.42% (6,759/105,285)
- **Colonoscopy Compliance**: 48.56% (3,282/6,759) vs 17.25% national average
- **Positive Predictive Value**:
- CRC: 1.92% (63/3,282)
- Advanced Adenoma: 13.44% (441/3,282)
- Any Adenoma: 36.41%
- **Early Detection Rate**: 90.28% for early colorectal neoplasms

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3. Regulatory Status and Approvals

3.1 China NMPA Approval

- **Registration Number**: ■■■■20243400902
- **Approval Date**: May 14, 2024
- **Valid Until**: May 13, 2029
- **Classification**: Class C IVD
- **Intended Use**: Qualitative detection of gene methylation in human plasma samples for CRC auxiliary diagnosis and recurrence risk assessment

3.2 Singapore HSA Registration

- **Device Registration**: DE0510590

- **Listing Date**: November 4, 2025
- **Expiry Date**: October 4, 2026
- **Classification**: Class C IVD
- **Quality System**: ISO13485 certified (expires March 9, 2028)

3.3 European CE Marking

- **Registration**: NL-CA002-2021-63348
- **Notification Date**: December 6, 2021
- **Authorized Representative**: SUNGO Europe B.V.
- **Compliance**: EU Directive 98/79/EG for IVD medical devices

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4. Clinical Applications and Utility

4.1 Primary Screening

Target Population: Asymptomatic individuals aged 40-80

Clinical Scenario: Alternative to invasive colonoscopy for initial screening

Benefits:

- Non-invasive blood test
- Higher patient compliance
- Cost-effective first-line screening
- Effective risk stratification

4.2 Molecular Residual Disease Detection

Target Population: Post-surgical CRC patients (stages I-III)

Clinical Scenario: Early detection of microscopic residual disease

Optimal Timing: Postoperative month 1

Clinical Impact:

- Guides adjuvant chemotherapy decisions
- Identifies high-risk patients requiring intensive monitoring
- Enables personalized treatment approaches

4.3 Recurrence Monitoring

Target Population: CRC survivors under surveillance

Clinical Scenario: Serial monitoring during follow-up

Benefits:

- Earlier detection than imaging (3.3-month lead time)
- Guides frequency of radiological examinations
- Enables early intervention strategies

4.4 Treatment Response Assessment

Target Population: Patients receiving adjuvant chemotherapy

Clinical Scenario: Monitoring treatment effectiveness

Applications:

- Duration of adjuvant therapy guidance
- Treatment escalation decisions
- Response assessment

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5. Proposed Clinical Decision Framework

5.1 ctDNA-Guided Management Protocol

Positive ctDNA at POM1:

1 Recommend adjuvant chemotherapy regardless of stage

2 Consider extended duration for persistently positive patients

3 Increase surveillance frequency

4 Earlier radiological follow-up

Negative ctDNA at POM1:

1 Potential de-escalation of standard adjuvant chemotherapy (research setting)

2 Standard surveillance protocol

3 Continued serial ctDNA monitoring

During Surveillance:

1 Positive ctDNA $\rightarrow$ Intensify imaging studies

2 Persistent positivity $\rightarrow$ Consider early intervention

3 Serial monitoring every 3 months for up to 2 years

5.2 Integration with Standard Care

Complementary to CEA Testing:

- Combined approach improves diagnostic accuracy (AUC: 0.849)
- Addresses CEA limitations (65.9% of patients CEA-negative preoperatively)
- Enhanced sensitivity (83.3%) and specificity (86.5%) when combined

Colonoscopy Guidance:

- Positive ColonAiQ® → Prioritize colonoscopy
- Improved compliance rates (48.56% vs 17.25% national average)
- Cost-effective two-step screening approach

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6. Comparative Performance Analysis

6.1 vs. Current Screening Methods

Method	Sensitivity (CRC)	Specificity	Notes
ColonAiQ®	86.1%	91.9%	All stages, blood-based
FIT	59.7%	-	Stool-based, affected by bleeding
CEA	17-47%	-	Limited early-stage sensitivity
SEPT9 alone	Lower	-	Single-marker limitation
Colonoscopy	~95%	~95%	Gold standard but invasive

6.2 vs. Other ctDNA Methods

Advantages over NGS-based approaches:

- Simplified workflow (hours vs days)
- Lower cost and complexity
- Broader clinical applicability
- Standardized methylation targets
- Reduced technical expertise requirements

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7. Health Economic Considerations

7.1 Cost-Effectiveness Factors

Screening Benefits:

- Reduced colonoscopy burden for negative tests
- Earlier detection leading to better outcomes
- Improved patient compliance and participation

MRD Monitoring Value:

- Prevents unnecessary chemotherapy in low-risk patients
- Enables early intervention in high-risk patients
- Reduces long-term healthcare costs through prevention

Healthcare System Impact:

- Streamlined patient pathways
- Resource optimization
- Improved population health outcomes

7.2 Real-World Implementation

PreC Study Economics:

- Large-scale feasibility demonstrated (>100,000 participants)
- Sustainable compliance rates
- Effective risk stratification in community settings
- Integration with existing healthcare infrastructure

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8. Future Development and Research

8.1 Ongoing Clinical Trials

- Interventional trials incorporating ctDNA-guided management
- Larger prospective validation studies
- Health economic outcome studies

8.2 Potential Expansions

- Additional cancer types using similar methylation approach
- Integration with artificial intelligence for enhanced prediction
- Point-of-care testing development

8.3 Personalized Medicine Integration

- Companion diagnostic development
- Treatment selection algorithms
- Risk-adapted surveillance protocols

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9. Conclusions

ColonAiQ® represents a significant advancement in colorectal cancer management, offering clinically validated performance across the entire disease spectrum from screening through surveillance. The comprehensive clinical evidence demonstrates:

1 **Robust Early Detection**: Superior performance compared to existing non-invasive methods
2 **Effective MRD Monitoring**: Clinically actionable results with significant prognostic value
3 **Practical Implementation**: Simplified workflow suitable for routine clinical practice
4 **Regulatory Support**: Multiple international approvals confirming safety and efficacy
5 **Real-World Validation**: Large-scale community implementation demonstrating feasibility

The multi-gene methylation approach addresses key limitations of single-marker assays while maintaining the practical advantages of PCR-based detection. With proven clinical utility across screening, MRD detection, and surveillance applications, ColonAiQ® is positioned to transform colorectal cancer management and improve patient outcomes.

References and Supporting Documents

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1 Ding Y, et al. Two-year update of the prospective evaluation of ColonAiQ (PreC) study. Annals of Oncology. 2023;34(S2):S426.

1 NMPA Medical Device Registration Certificate. Registration No.: ■■■■20243400902. Approved May 14, 2024.

1 HSA Singapore Medical Device Registration. Device Registration No.: DE0510590. Listed November 4, 2025.

1 European CE Marking Notification. Registration No.: NL-CA002-2021-63348. December 6, 2021.

This clinical evidence package was compiled on August 14, 2025, based on peer-reviewed publications, regulatory approvals, and clinical study data available at the time of preparation.

Note: This document summarises published and supplied data as of the compilation date. For external communications, always verify the latest official regulatory listings.