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SECTION III.....NewCardio Partnerships



SECTION I: QTinno News

NewCardio is the first vendor to complete a blinded analysis for CSRC publication - clinical validation results expected for CSRC annual meeting in **Dec. 2010**.

Sep 16, 2010

Pharma Lynx signs MSA with NewCardio for Phase 1 QT studies using QTinno

Aug 05, 2010

Leading global Pharma. company selects QTinno for Phase 1 QT Studies

Aug 04, 2010

NewCardio completes QT study in Europe for Biotechnology company

Apr 08, 2010

Clinilabs signs MSA with NewCardio, Inc. for QTinno

Mar 18, 2010

NewCardio signs MSA with U.S.-Based CRO for QTinno

Sep 09, 2009

NewCardio announces MSA with Top-Five CRO

Aug 27, 2009

NewCardio announces MSA with Top-Three Contract Research Organization

Aug 05, 2009

NewCardio announces MSA with Dedicated Phase I

Jul 30, 2009

Top-Five global Pharma. Company names NewCardio as its provider of automated QT analyses

From the Editor

Welcome to NewCardio's first Quarterly newsletter! We are excited to share this newsletter with you and eager to express the progress of NewCardio's automatic cardiac safety solution, QTinno™. We want to convey with you insights regarding the industry's adoption of automatic cardiac safety analyses for early phase trials, specifically the shift from 'semi-automatic' cardiac safety analyses towards 'fully intelligent automation'. As this paradigm shift in the industry unfolds, our goal is to provide viewpoints from leading Medical/Scientific experts in cardiac safety while providing you with an update on the recent NewCardio milestones, including strategic Partnerships in support of early Phase drug trials.

We are grateful for your interest and sincerely hope you find this series informative and useful.

Vincent Renz
President and Chief Executive Officer
NewCardio, Inc.



SECTION II: QTinno™ Cardiac Safety

***By Ihor Gussak, MD, PhD, FACC**

**Accurate, Precise, Fully Automated:
How QTinno™ Achieves the Three Key
Goals for Early Cardiac Safety Assessment**

Some drugs delay cardiac repolarization, an unintended effect that can be measured as QT interval prolongation on the electrocardiogram (ECG). Repolarization delay may lead to potentially lethal cardiac arrhythmias, most notably torsade de pointes (TdP). Accordingly, the FDA now requires that all new systemically-administered drugs receive a thorough electrocardiographic evaluation early in clinical development, including a single trial dedicated to evaluating their effect on cardiac repolarization ("thorough QT study," or TQTS). The results of this evaluation may have profound effects on subsequent drug development. Thus, measurement accuracy and precision of paramount importance.

**QTinno™: A Fully Automated Solution
for Cardiac Safety Studies**

From the outset, QTinno was designed to meet the need for absolute accuracy and high precision in cardiac safety studies. To achieve these goals, it was not sufficient to simply automate existing manual and semi-automated approaches. Rather, new solutions were needed—solutions

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that took full advantage of modern computing power, and allow the computer to “look” at the ECG and make IDMs in ways that are beyond the abilities of the human mind.

QTinno Uses the Vector Magnitude Lead and Computational Power for IDMs

QTinno uses a “virtual” ECG lead, the Vector Magnitude lead (VM), which is calculated using information from *all 12 leads* and *all complexes* in each ECG. This confers important advantages over conventional approaches:

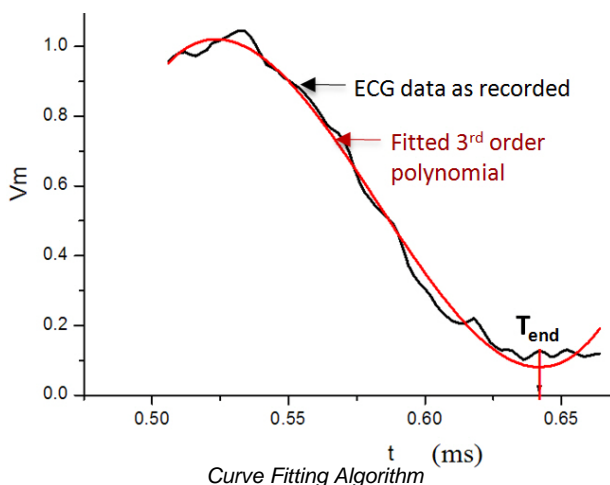
- The full QT interval is used for IDMs.
- The VM Lead substantially reduces electrical noise and improves the signal-to-noise ratio (SNR).

The VM lead is generated for all complexes in every ECG, allowing IDMs to be calculated from a much greater number of complexes than conventional approaches (which read 3 complexes per ECG).

QTinno Accurately Places Fiducial Points by Curve-Fitting to a Mathematical Function

Accurate, consistent placement of fiducial points is essential for automated ECG analysis. A second key feature of QTinno—curve-fitting to a 3rd order polynomial—further increases accuracy and consistency.

- To locate fiducial points (including T_{end}), QTinno fits recorded data for the peak and descending limb to a 3rd order polynomial, with fitting done in the Vector Magnitude lead.
- QTinno uses least-square fitting with multiple iterations done to optimize the fit between recorded data and the 3rd order polynomial. T_{end} is identified as the single minimum of the fitted 3rd order polynomial.

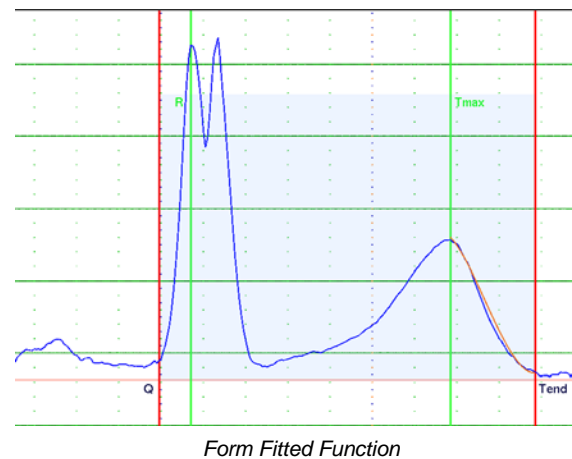


This novel approach provides at least 2 important advantages over existing automated algorithms.

Noise Resistance. QTinno is highly noise-resistant, not only because of the VM lead, but also because curve fitting is done using the entire T wave, not only the noise-prone data points surrounding T_{end} .

Baseline independence. Other automated algorithms usually localize T_{end} using the tangent-baseline intercept method. This approach has significant technical limitations, because of electrical noise, failure of T wave to return to baseline, and other factors—and often leads to significant QT interval errors.

QTinno determines T_{end} as the minimum of the fitted function without regard to the isoelectric baseline, which ensures accurate and precise IDM determinations.



QTinno Approach to Quality Control: Confidence Factor

Internal assessment of quality and reliability is a mandatory feature of automated ECG analysis—otherwise, the user is forced to accept all automated results on a “black box” basis, or overread all results to identify excessively noisy or misread files.

The QTinno solution incorporates a detailed quality control algorithm called Confidence Factor (CF). Factors examined by the CF algorithm include:

- Electrical noise content
- Missing or incomplete leads
- Arrhythmias, unstable heart rates, and excessive beat-to-beat variability
- Measurement quality, specifically “goodness of fit” to the 3rd order polynomial function

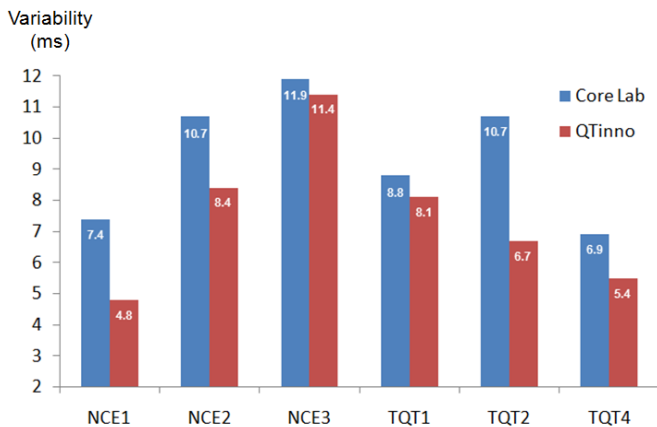
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These features enable CF to accurately identify problematic ECGs and flag them for human overread.

QTinno Clinical Validation

QTinno has undergone extensive clinical validation in partnership with pharma sponsors, CROs, academic institutions and regulatory agencies. The clinical validation includes analysis of 9 complete ECG datasets from 4 recent early-phase cardiac safety drug trials and 5 TQTs, and represents fully automated, blinded analysis of over 100,000 ECGs. In every case, QTinno returned highly accurate results with lower intrinsic variability and narrower confidence intervals than standard approaches.



Mixed Statistical Model with factors for period, age, gender, treatment and all interactions
 Variability data for TQT3 was not provided by Sponsor

Residual Variability Obtained from Fitting a Mixed Statistical Model to dQTcF by Method

Summary

- Measurement accuracy and precision are essential in all early-phase cardiac safety drug trials.
- QTinno does not simply automate existing measurement technologies, but instead provides a comprehensive and novel technical approach ensures high measurement accuracy and precision.
- QTinno's Confidence Factor algorithm reliably identifies the small percentage of problematic ECGs, and flags them for human inspection and overread.

**Part I of a two-part article by Ibor Gussak, MD, PhD, FACC
 Chief Medical Officer, NewCardio, Inc.
 Adjunct Professor of Cardiology, UMDNJ
 Executive Editor, Journal of Electrocardiology*



SECTION III: NewCardio Partnerships



Clinilabs, a leading provider of core laboratory services for clinical drug development since 2001, now offers ECG core laboratory services. High quality ECG analysis, delivered in a timelier and cost effective manner through our world class data center is made possible by the integration of QTINNO™, a fully-automated ECG analysis system from NewCardio. This solution gives our customers a validated, compliant, and cost-effective ECG solution for cardiac intensive and thorough QT studies. The integration of our ECG core laboratory with our state-of-the-art clinical research unit (CRU) in New York provides one-stop shopping for early-phase studies that involve cardiac assessment. Cardiac studies are completed quickly and efficiently by one CRO, one project manager, and one development team.

The industry has reached the "tipping point" in the transition from semi-manual reading of ECG intervals (e.g., QT) to fully-automated validated methods. Acceptability of such automated ECG data approaches, such as QTINNO™, has been determined by regulatory authorities when appropriately validated. New Cardio has rigorously validated QTINNO™ on seven different data sets and has worked closely with regulatory authorities on the validation analysis. Vincent Renz, CEO of New Cardio states "we are very excited to work with Clinilabs to offer QTINNO™, a significant improvement over current semi-automated approaches and greatly appreciate the FDA's favorable review of our QTINNO™ validation results". The QTINNO™ system used by Clinilabs has been independently validated and is designated as the preferred automated algorithm by one of the World's top five pharma companies.

Clinilabs has integrated a fully-automated solution into its data center based on empirical evidence of advantage provided through QTinno. Our system does not simply automate current manual methodologies, rather, through its vector magnitude approach the system synthesizes all twelve leads into a single vector magnitude lead that is exposed to analysis.

The benefits include:

- Enhanced reliability when measuring all timing interval, with special focus on the QT interval.
- Superiority in accuracy of key cardiac safety metrics.
- Provide more statistical robust studies, or the potential for smaller study sizes.
- Reduced turnaround times and costs.
- May enable us to examine additional cardiac safety markers.

While the robustness of its ECG signal processing system is the primary reason customers should consider Clinilabs, cost is a factor that will undoubtedly be of importance. Clinilabs' rates for automated ECG data processing are significantly lower than current industry pricing.

According to Dr. Gary Zammit, President and CEO of Clinilabs, "in order to enter this mature market, we had to create a competitive advantage. We do this by offering one-stop shopping at our integrated CRU and core laboratory, combining this with superior data processing technology, and delivering the package at a lower rate than customers have known in the past. We believe that this is a winning strategy for all stakeholders involved in drug development." For a limited time only, Clinilabs and New Cardio are offering to re-run data obtained from thorough QT or cardiac intensive studies at no cost to the client. This will enable clients to see first-hand how our technology provides high reliability and robust results within the client's existing study designs.



Pharma Lynx is a global CRO that provides comprehensive early Phase 1 QTc Trial services (PK/PD of Cardiac Repolarization) in Cancer patients and healthy subjects, Biomarker, Bioequivalence evaluations, Cardiac Safety analyses, and Phase 1 to Phase IV Clinical Studies. At Pharma Lynx, we support our customers with a 100% success rate in completing their clinical trials within a pre-defined timeline and cost effective budget. Pharma Lynx staff has extensive global experience with the ability to successfully conduct small to large projects in various therapeutic areas in the USA and globally in Europe, India and Japan.

Pharma Lynx provides full CRO services in the areas of:

- Cardiac Safety
- Project Management
- Clinical Data Management
- Clinical Monitoring
- Medical Monitoring
- Pharmacovigilance
- Patient Recruitment
- Biostatistics
- Clinical Development Plan
- EDC (as selected by the sponsor)
- Medical Writing

At Pharma Lynx we have clinically authoritative medical advisors from prestigious academic medical centers on the Medical Advisory Board that provide expert opinion in developing clinical development plan, clinical strategy, regulatory approval strategy and discussions with regulatory agencies.

Phama Lynx now offers Cardiac Safety services.

This past September, 2010, Pharma Lynx signed an agreement with NewCardio to license their QTInno™ cardiac safety solution for use in Phase 1 studies.

Pharma Lynx has exclusive collaborations with state-of-art facilities for phase 1 Clinical Pharmacology units in the USA and India, providing reliable QT and thorough QTc study data in healthy volunteers, special patient populations and BE studies per FDA guidelines. Dr. Ashok Srivastava, Chief Medical Officer, Global Executive Vice President Clinical and Medical Affairs at Pharma Lynx, emphasizes, "Adding cardiac safety to our breadth of services enables us to become the one-stop-shop for our drug development sponsors. With our global expertise and our robust service CRO infrastructure in over 25 countries in Americas, Europe, Japan and other Southeast Asian countries including India, we have the ability to successfully integrate cardiac safety to our services, offering a precise, cost-effective and timely solution to our sponsors for ECG data analysis".

In addition, Pharma Lynx has a comprehensive electronic safety reporting and EDC/Paper Data Capture facility with additional expertise in Japanese language.

The experienced global team at Pharma Lynx will not only help you execute clinical trials globally but also help you to navigate the regulatory approval of the study protocol.

For more information on Pharma Lynx, please call us directly at 732-694-3394, or visit our website at www.pharmalynx.com



A Symbol of Excellence

Development Solutions

ICON Development Solutions specializes in the strategy and delivery of early-phase clinical development services to enable informed, timely decision making for our clients. With industry-leading capabilities in clinical pharmacology, bioanalytical / immunoassay, biomarkers, PK PD modeling & simulation and the full range of support services – we incorporate scientific excellence and product development strategy in all that we do. The clinical pharmacology team at ICON has extensive experience in the design, study conduct and interpretation of Phase I, clinical pharmacology and translational medicine studies in all major therapeutic areas.

ICON has three state-of-the-art clinical pharmacology units in Omaha, Nebraska; San Antonio, Texas and Manchester, UK. In particular, our San Antonio facility is fully equipped for integrating QT assessments within sponsors' Phase I trials—providing the necessary insights to make critical decisions early in the development process. Our cardiac services include the 12-Lead Mortara Surveyor ECG System, providing 12-lead telemetry through a single device which acquires and transmits diagnostic 12-lead digital ECG data to a central system.

The utilization of our Mortara Surveyor Telemetry System provides the ease of ECG capture and telemetry coverage for up to 32 subjects simultaneously. Each of the 12-Lead Holter transmitters records and stores continuous wave forms. The capability of extracting and printing safety 12 lead ECGs at specified time points allows for immediate on-site evaluation. In addition, the system stores a 10 second 12-lead strip, and digitally transmits the waveform over a secure dedicated VPN connection to a Core Lab

for annotation of the QT interval by a Cardiologist. Alternatively, the waveform can be uploaded to a system such as QTInno™ for a fully automated correction of the QT interval.

For more information on ICON Development Solutions, please visit www.iconplc.com or email IDSinfo@iconplc.com



Contact NewCardio

To request a NewCardio presentation or a demo of QTInno™, please contact us at: sales@newcardio.com or call us directly at: 408.516.5000

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