
# Clinical and real-world insights

*an interview with* **Sheryl Elkin, QIAGEN**

QIAGEN Digital Insights offers a clinical and real-world insights portfolio that leverages two highly curated knowledgebases containing information from the medical and scientific literature, as well as real-world data from over 200,000 cancer cases. The QIAGEN Clinical Insights (QCI) portfolio supports precision medicine,[1] allowing users to customize specific content and to access on-demand variant assessments and standardized reporting workflows. QCI applies advanced analytics to provide laboratories with tools to prioritize and select variants as well as expert-curated content to populate reports for clinicians. QIAGEN Real World Insights combines population epidemiological data with curated information in partnership with pharmaceutical companies to drive more informed decisions faster during early drug and test development.

We reached Sheryl Elkin, Chief Scientific Officer of QIAGEN Digital Insights, a business division of QIAGEN, and a scientific lead for the QIAGEN Clinical Insights and Real-World Insights platforms. We focus for this Q&A on advancements in data analysis and clinical decision support tools that support fast and accurate clinical decision-making using increasingly larger diagnostic panels. Additionally, we will examine translation of clinical oncology data from patients back to the drug development pipeline for the upcoming generation of cancer treatments. In particular, we concentrate on how biomarkers and companion diagnostics can be used to stratify patients, identify cohorts, and design clinical trials for unmet medical needs.

**Q1. QIAGEN has formed a partnership with Quest to bring a myeloid assay to the clinic.[4]**

**Can you discuss the strategy of companies like QIAGEN to partner with clinical laboratory companies?**

- As the clinical and scientific literature grows every day, and particularly as laboratories move to larger and larger sequencing panels, researchers in these laboratories struggle to annotate their results with accurate and up-to-date information on a clinically relevant time scale. QIAGEN has an objective to provide "sample to insight" solutions through its large portfolio of products that laboratories use as reagents for their diagnostic assays. In addition, QIAGEN has also developed a portfolio of bioinformatic products that can help laboratories translate their raw data into meaningful information for health care providers. In particular, the interpretation solutions can relieve a significant barrier to entry for the laboratories. To address this need, QIAGEN has developed the following large knowledgebases to enable clinical decision support.

**The QIAGEN Knowledge Base**

- The QIAGEN Knowledge Base, underlying the QCI-Interpret application, is the result of over twenty years of curation by MD and PhD scientists. Over the years, these curators reviewed (and continue to review) the literature for relevant information that is extracted from an unstructured data format and converted into a structured data format. The QCI-Interpret (QCI-I) application applies rules and logic to the information stored in this knowledgebase to compute pathogenicity scores (based on American College of Medical Genetics guidelines) and actionability scores (based on Association for Medical Pathology guidelines) for any variant and presents this information to users. The scores are presented with links to the underlying evidence, providing full transparency to the logic utilized to generate the scores and allowing users to access this information to prioritize variants for reporting.

**QCI Precision Insights**

- The QCI Precision Insights knowledgebase joined the QCI portfolio as a result of the N-of-One acquisition in early 2019. QCI Precision Insights draws on a vast knowledgebase of catalogued and summarized information, curated by a team of PhD scientists and reviewed by a team of oncologists. The Precision Insights knowledgebase was built on real world cases; each variant and gene in the knowledgebase is assessed in the context of the specific cancer types in which they are observed. Curators review the evidence for each variant and for each gene in the context of each cancer type, and then write a report that includes referenced summaries. The interpretive comments are assembled based on logic and validation rules, and they include summaries of guidelines and account for interactions between variants. The QCI Precision Insights reports provide additional, transparent information to the clinician, saving them the time of diving into the literature and extracting and evaluating all the evidence.

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**QCI Interpret One**

- QIAGEN has recently released a new product, QCI Interpret One, that seamlessly combines the power of both QCI Interpret and QCI Precision Insights. QCI Interpret One will allow clinical laboratories to quickly go from a large Variant Call Format file (vcf) to a fully annotated variant analysis report. The QCI-Interpret application also allows users to select and report therapies and trials that are associated with the variants and to generate a report. QCI-Interpret One accelerates variant analysis and reporting, helping diagnostic laboratories to reduce the reporting bottleneck and scale their operations.
- These knowledgebases allow users in clinical laboratories to entrust QIAGEN with knowledge acquisition and report writing and allows the laboratories to focus on the technical aspects of the test and the final decisions. Laboratory Directors maintain the responsibility for selecting variants and reviewing the reports, but their process is accelerated using the QIAGEN tools, helping them to scale and achieve faster turnaround times.

**Does QIAGEN gain access to the clinical data generated by Quest with QIAGEN-developed assays?**

- QIAGEN acquires limited demographic data from its clinical partners: specific diagnosis, age, gender, location (by state or physician's zip code); this information is used to enhance specificity of trial matching. At this time, QIAGEN does not have access to any clinical data associated with these cases. QIAGEN is working with various partners to expand the clinical information that is collected in order to expand the scope of potential analysis and collaboration.

**Q2. Following up on the Quest and QIAGEN partnership, the recent announcement highlighted a focus on myeloid malignancies. Along these lines:**

**Could you please provide some background on how QIAGEN analytics will be used to create clinical knowledge for this area?**

- As next-generation sequencing diagnostics expanded for hematologic malignancies, QIAGEN expanded its coverage of these diseases, particularly focusing on the diagnostic and prognostic significance of the markers. QIAGEN engaged with hematologic oncology specialists and leaders in the field to help us adapt our systems to cover the aspects of myeloid and lymphoid malignancies that are distinct from solid tumors. The cases we receive from Quest and other hematologic oncology laboratory partners help to focus the knowledge acquisition and enhance our coverage in this area. Our on-demand variant curation service helps Quest to scale their testing; myeloid malignancies often harbor high numbers of novel variants, and QIAGEN rapidly distinguishes the biologically-relevant variants from variants of unknown significance and provides the evidence to support the classification.

**Q3. Does QIAGEN have plans to engage pharma companies about partnering? The gist of this question is around the notion of creating a full loop – from the lab to an assay to the clinic and back.**

- Yes! QIAGEN has engaged with several pharmaceutical companies to provide insights based on the mutational information in the cases processed. The demographic and epidemiological data aggregated from over 200,000 US-based somatic cancer cases provides a trove of information that pharmaceutical companies can use to inform their target selection, drug design, biomarkers and trial design and recruitment strategies.

For example, a pharma company that is working on a drug to target Gene X might want to know:

- Which mutations are most commonly observed in Gene X?
- What is known about these mutations? Are they likely to predict response to the drug?
- Which diseases are the mutations most prevalent in?
- Of all the positive cases, which disease represents the greatest proportion of cases?
- Are there any other genes for which mutations co-occur with mutations in Gene X in a statistically significant manner?
- What other genes might serve as biomarkers for a drug under development?
  - Are there synthetic lethal strategies that would be relevant based on the literature?
  - How prevalent are alterations in these genes in the disease of interest?
- Are there parts of the country that are testing more heavily for alterations in the biomarker of interest where we are seeing higher numbers of positive patients? Would this be a good location for a trial site? Are there competitors with trials open in this geographic region?

- QIAGEN scientists query the data and prepare reports to answer these and other questions. The design of the research questions and reports are highly collaborative, allowing the pharma company to focus on their specific questions of interest. In the future, QIAGEN hopes to make a portion of the data accessible through a subscription portal, so that pharma may access and manipulate the data themselves.

**Q4. Can you please comment on whether QIAGEN has plans to extend the real-world insights program to include other diseases and conditions beyond cancers – e.g., Cardiovascular? Diabetes? Other? How about broadening the program to include other 'omics data sets?**

- At this time, the Real-World Insights program is focused on oncology. In terms of other 'omics datasets, we are open to the concept and welcome the opportunity to interpret and analyze other types of diagnostic data input.

**Q5. What data and graphics are contained in a report for data generated on the QIAGEN platform? Can you cite examples online or in publication? What feedback have you received from users on the reports?**

- The Real-World Insights reports contain data presented in both graphic and tabular form, with text describing the data sources and the analysis methodology. In a recent example, QIAGEN collaborated with a pharmaceutical company that was working on a drug with three gene targets. The collaboration resulted in two projects:
  - A prospective population reporting strategy, wherein QIAGEN delivered a monthly report listing cases that contained the biomarkers of interest. The report listed the case, the cancer type (e.g., colorectal cancer), the specific alteration of interest that was observed, the gender, age, and location of the patient.
  - An extensive retrospective report examining:
    - The prevalence of the biomarkers across cancers and in specific cancer types of interest.
    - Distribution of alterations in the biomarkers of interest across cancer types, and identification of cancer types where alterations were most numerous.
    - Exploratory analysis to identify potential mutations that co-occur with the alteration of interest.
- The pharmaceutical company was very happy with the resulting report. They found the report to be very informative and the process to be collaborative.

**Q6. Does QIAGEN offer any courses or other support on using the platform? How to understand the report? How the data can be used for actionable decision-making?**

- Our customers often comment on how easy the software is to use to complete their workflows. That said, there are always specific workflows or use cases that need more support. QIAGEN's clinical decision support platform (QIAGEN Clinical Insight) is managed with user licenses, and users are trained in advance of gaining access to the platform. Technical and scientific support are also available to users. The clinical reports are configurable, and the users are walked through the report during both the sales and onboarding process, to ensure that they are familiar with the report components, as well as where they need to look for the critical information and the supporting evidence.
- The reports are delivered by the laboratory partners to the ordering oncologists. The oncologists then have the summarized information in front of them, including an explanation of clinical options supported by the identified mutations along with the underlying evidence. The clinician can weigh the evidence and make a decision for the patient's management.

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**Q7. How does QIAGEN support clients to develop Real World Insights projects?**

- For the Real World Insights analyses, the QIAGEN scientific team meets with the client to discuss each individual project and subsequently defines a Scope of Work that outlines all the analyses that will be done. The client does not have direct access to the data platform. The final report is delivered to the client and reviewed in detail with the QIAGEN scientific team, ensuring that all the analyses are clear and that the objectives of the analysis was met.

**Q8. More broadly, we note that the FDA lists several companion diagnostics licensed for specified cancers.[2] FDA also maintains a list of biomarkers on drug labels for possible adverse events.[3] A few questions along these lines:**

**What insights has QIAGEN gleaned from the real-world data of these CDx-Rx pairings? Do you foresee this platform enabling any QIAGEN plans for future listings in the table?**

- Absolutely. QIAGEN Real World Insights is uniquely positioned to help inform the design of companion diagnostics. Our Precision Insights knowledgebase has comprehensive variant assessments across a large complement of cancer genes. For a pharma company seeking to

design a companion diagnostic for their targeted therapy, QIAGEN can provide a list of variants observed in the gene of interest, together with the classification of each variant, the evidence underlying the classification, and the prevalence of the variant, across cancers or within a cancer type of focus. The pharma company can use that list to select variants with evidence that suggests they will be predictive and may wish to set a threshold for how frequently the mutations are observed in the population.

- The goal of any companion diagnostic is to strike the balance between recruiting as many likely responders as possible, while limiting the number of patients that are unlikely to respond. QIAGEN Real World Insights can help to develop a companion diagnostic that will refine this population.

### Q9. Any final comments or summary?

- QIAGEN has a twenty-year history of curating and standardizing scientific information that we mine and analyze to support precision medicine. The integration of the systems supported by the QIAGEN knowledgebase and the QCI Precision Insights knowledgebase represents a best-in-class product for the analysis of large diagnostic sequencing panels in oncology.
- QIAGEN has leveraged the information collected from over 200,000 oncology cases analyzed on these systems to provide a service to pharma companies. The customized data analysis accessed through QIAGEN Real-World Insights provides a unique source of data to drive and focus drug development, companion diagnostic development, and clinical trial design. JoPM


**References**

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**Sheryl Krevsky Elkin, PhD**, is the Chief Scientific Officer at QIAGEN Digital Insights, a business division of QIAGEN. Dr. Elkin joined QIAGEN through the acquisition of N-of-One, and has led the interpretation of thousands of patient cases, establishing a rigorous process for the analysis of scientific and clinical evidence and presentation of molecular and clinical evidence to physicians to help guide their therapeutic decisions. Dr. Elkin played a lead role in the development of the N-of-One clinical interpretation methodology to support clinicians in identifying therapeutic strategies specific to each patient and has been a key player in the integration of N-of-One with the QIAGEN Clinical Insights software. Prior to joining N-of-One, Dr. Elkin completed her postdoctoral fellowship at the Massachusetts Institute of Technology's Center for Cancer Research, where she earned a fellowship from the Leukemia and Lymphoma Society. She earned her doctorate in Biological and Biomedical Sciences from Harvard Medical School and an A.B. in Biology and Music from Amherst College, graduating Phi Beta Kappa and summa cum laude, with High Distinction in Biology.




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