

Case study | Mumbai, India

Featured analytical validation team:

Varun Bagai, Dr. Manoj Vyas, Hersh Parikh, and Pravin Nilawe

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Introduction

Founded in 2020, Karkinos Healthcare is a privately owned oncology company whose goal is to build a technology-led, managed-care platform that addresses accessibility and affordability gaps in cancer care across India. Headquartered in Mumbai, Karkinos is focused on providing innovative cancer research, early detection, advanced diagnostics, and treatment of common cancers through its nationwide distributed cancer care network.

To support this mission, the molecular diagnostics team at Karkinos required highly advanced next-generation sequencing (NGS) capabilities in their laboratory. Given their prior positive experience using Applied Biosystems™ real-time PCR (qPCR) systems from Thermo Fisher Scientific, they turned to Thermo Fisher to provide Ion Torrent™ instruments and Ion Torrent™ Oncomine™ assays to meet their lab's NGS needs.

A critically important step in implementing NGS for clinical research is validation of the assays and instruments. This process would be particularly challenging because it involved three simultaneous projects. Rather than take on the risk involved in performing the work themselves, Karkinos turned to Thermo Fisher's analytical validation (AV) consulting services.

The analytical validations were supported by a Thermo Fisher project manager in collaboration with a field application scientist (FAS) and bioinformatics team, providing coordinated direct and remote support that enabled fast and successful projects and valuable training for Karkinos' lab managers and technicians.

For going above and beyond to accomplish India's first-ever NGS analytical validations using an Ion Torrent instrument, the Thermo Fisher AV team responsible for providing the service—project manager Varun Bagai, FAS manager Dr. Manoj Vyas, senior bioinformatics specialist Hersh Parikh, and field bioinformatics scientist Pravin Nilawe—has been honored with the Thermo Fisher Global Support Services Guardians of Your Science award. We connected with this impressive team, and with Dr. Prerana Jha, senior scientist of molecular oncology at Karkinos, to learn more about the successful project and how the team earned this honor.



Can you provide some background on yourself and the project?

Dr. Prerana Jha:

As senior scientist in molecular oncology, I lead Karkinos Healthcare's molecular lab in Mumbai. I came to Karkinos after working at one of the top private hospitals in India, and joined the company when it was in the thought-process stage. I've been with Karkinos now for two-and-a-half years. In our lab, we do molecular diagnostics for oncology, but we are also expanding toward research on other diseases, such as rare diseases.



Dr. Prerana Jha
Senior Research Scientist,
Molecular Oncology,
Karkinos Healthcare,
Mumbai, India

We have had several cases now where we have identified rare variants of fusion or compound mutations and published our results; so, in fact, we are a research-oriented diagnostic center.

We built the backbone of our main lab on Thermo Fisher platforms. Thermo Fisher set up our entire qPCR, Sanger sequencing, and NGS platforms.

Our NGS setup includes an Ion Torrent™ Genexus™ System and Ion GeneStudio™ S5 System. With NGS, we analyze both FFPE solid-tumor samples and liquid biopsy samples, running 50-gene Oncomine™ Precision Assay panels on the Genexus System, and the 500-gene Ion Torrent™ Oncomine™ Comprehensive Assay Plus on the Ion GeneStudio S5 System for comprehensive genomic profiling of key biomarkers.

As a new lab, we knew it would help us to have AV support. We chose the AV services from Thermo Fisher, and it was a great learning experience.

Varun Bagai:

As a senior technical project manager for the NGS AV team at Thermo Fisher, I managed all three NGS analytical validation projects for Karkinos. We performed all three projects concurrently, including the Oncomine Comprehensive Assay Plus on the Ion GeneStudio S5 System and the two Oncomine Precision Assays, solid and liquid, on the Genexus System.



Varun Bagai
Senior Technical Project Manager,
Analytical Validation Service,
Global Professional Services
Team, Thermo Fisher Scientific

As part of our AV service package, I delivered documentation—AV plan, run schedule, SOP template, AV data sheet, and the final AV report—in a timely manner for the three assays.

Performing three analytical validations simultaneously while working in different time zones made it critical for us to communicate effectively and collaborate with our service and support teams based in India. Dr. Jha and I would meet almost on a daily basis to discuss run plans, review data, and plan the next set of experiments. Our field team was always available to visit when needed on-site for wet lab and bioinformatics technical support, training new team members, or performing any instrument repairs. Working effectively as a team, we were able to complete all three projects on time, exceeding customer expectations.

Hersh Parikh:

Our initial discussions with the client were instrumental in gaining a deep understanding of their specific requirements. Although Karkinos initially contemplated conducting the project internally, they eventually recognized the value of our AV services for the Oncomine panels. Consequently, they made the decision to leverage our expertise. Throughout this collaboration, our AV service team played a pivotal role in establishing project timelines and expectations, thus enabling a seamless and successful collaboration.



Hersh Parikh
Manager, Bioinformatics,
Thermo Fisher Scientific,
South Asia

Can you tell us about how the team worked together on the project?**Varun Bagai:**

For the several months while we were running the three analytical validations, Hersh, Pravin, and Dr. Vyas acted as our dedicated field support team in India working directly with the customer. The standard AV process is for the AV project manager to host an AV kickoff call with the customer following successful instrument installation and qualification by our field service engineering (FSE) team. We present an overview of the AV service package overview, then review the AV plan, discussing training schedules and the timeline for finishing the project. We also provide a list of the controls and reagents that are included as part of the AV service package. The field support team then conducts a pretraining on-site visit to confirm that the customer has everything they need to be able to perform the training and analytical validation. In the Karkinos case, Dr. Vyas (FAS) later went on-site to train the customer on both Genexus and Ion GeneStudio instrument workflows along with the three assays. He then shadowed the customer and ran a training run with them using AV controls.

Sequencing is complex. To put it into context, a decade ago it would take three days and about 10 to 12 hours of manual work to be able to do one run using an Ion Torrent sequencer; but now, with automation, runs require just a few minutes of setup with a turnaround time of less than 24 hours. It has evolved a lot, but we still must explain to the customer what is happening at each step.

That's the role of the wet lab lead. They will go in, dilute samples, thaw reagents, and show the customer all the steps. Even with a fully automated system, you still need to put the right reagents and buffers in the right places; we show the customer how to put them in properly. The FAS also helps them with manual sample prep extractions, if needed.

Karkinos not only had a Genexus System, which is fully automated, but their third analytical validation was done on an Ion GeneStudio S5 System, which has some automation but requires more manual work. It required them to first do the prep on Ion Chef™ instruments, so Dr. Vyas also trained them on setting up their Ion Chef instruments for library preparation, which is the first essential part of sequencing.

Dr. Manoj Vyas:

I trained the Karkinos team on how to run the assays and did the troubleshooting in case something did not go right. The customer was new to the instruments and therefore faced a lot of challenges.

Before the Karkinos project, we had NGS systems running in the region, so I had firsthand experience and training on these instruments—but not for the analytical validation services. That was new for our team.



Manoj Vyas
FAS Manager,
Thermo Fisher Scientific

Dr. Prerana Jha:

We started working with the Genexus System before completion of the AV, so by then we didn't have much trouble with the wet lab process for the Genexus System. We did have more challenges with the Ion GeneStudio S5 System.

But overall, with the analytical validation for the assays on the Genexus System, we did not have much of an issue. The wet lab process was very fast, and although there were some hurdles, Dr. Vyas was available to help.

For the Oncomine Comprehensive Assay Plus, it took us a little more time because of a pool evaporation issue. And again, Dr. Vyas was here until we were able to have a satisfactory run replicated for the analysis.

Varun Bagai:

Once the sequencing runs were finished, the bioinformatics team—in this case Hersh and Pravin—troubleshooted the runs and walked the customer through the whole analysis pipeline, which is complex given the amount of data that come out of a sequencing run.

Hersh Parikh:

This was our first-ever AV service in India. There are occasions where we recommend customers do internal validations of an assay, and we have helped customers with that, but that's not the same as AV services.

At the lab level, we were involved in getting the experiments up and running. Over the course of about four to five months, as data were generated, the weekly calls with the Karkinos team allowed us to closely monitor their progress. The calls served as a platform to address any concerns and discuss the project status. By fostering transparent and open lines of communication, we helped ensure that both parties were well informed and actively involved in the project's progress. This approach helped us to establish a strong working relationship with the customer.

In addition to these meetings between our team and the customer, throughout the entire project we worked with them regarding data collection. If they ran into a problem with an assay, we stayed in touch and worked closely with them to help ensure that the correct data were being uploaded. All that close attention gave us an opportunity to engage with the customer for a long period of time. And all that support ultimately enabled their independence.

From my perspective, a lot of the learning happened when we started looking at data. For example, sometimes when you're looking at the data, you expect something to be present in the sample, and it may be there or not. One of the key issues I discussed with Karkinos was figuring out what could have gone wrong when we were not seeing expected results. I helped them understand why some variants were not getting picked up.

Regarding troubleshooting: is that always at the clients' site or are you also doing that remotely?**Hersh Parikh:**

While Pravin was often on-site at Karkinos, most of the work we do is remote. Our client base is widespread, and we are a small team serving the entire region, so most of the troubleshooting happens remotely since it requires a great deal of time, and we are also managing the IT infrastructure for the analysis in-house.

Can you elaborate more on the training process?**Varun Bagai:**

Once the customer has been trained, the AV project manager will host weekly meetings to review data, discuss the next set of experiments, monitor progress, and provide technical guidance about the NGS data. After wet-lab work is finished, we summarize all the AV data in an Excel™ spreadsheet and provide the final AV report. We review the data sheet and AV report with the customer and make any edits, if required, before signing off on the project.

Pravin Nilawe:

Since Karkinos was new to these NGS systems, they needed multiple trainings on handling them. The project began with Dr. Vyas training them across the entire pipeline; and the second part, the bioinformatics part, was where Hersh and I looked at and helped with troubleshooting the data, and then helped with the reporting part as well.

Hersh Parikh:

To empower the client to make the most of our services, we conducted several rounds of training sessions. These sessions were designed to familiarize the client with our software tools and workflows, enabling them to utilize our services effectively. We focused on providing comprehensive training, helping ensure that the client was equipped with the necessary knowledge and skills to maximize the benefits of our services. The client's enthusiastic participation and eagerness to learn greatly contributed to the success of these training sessions.



The Karkinos Healthcare team: Dr. Prerana Jha, Pooja Manesh, and Radhika Venkatakrishnan.

Pravin Nilawe:

The training was also a give-and-take process because unless we understand the customer's very specific requirements, we will not be able to train them well. So, we always need to interact with the customer, understand their doubts and concerns, and then make a plan to guide them going forward with specific trainings or hand-holding sessions. We did that with Karkinos, and it made us adjust our effort to provide training tailored to their needs.

What were some of the challenges in performing the analytical validations?**Hersh Parikh:**

The project presented a few challenges. The extensive nature of the simultaneous projects required consistent follow-up with the client. We also encountered occasional bottlenecks in the run/data process, which required diligent follow-up and prompt resolution.

However, our team's proactive approach and commitment to delivering high-quality results enabled us to overcome these challenges effectively. By offering effective solutions and demonstrating exceptional customer support, we helped the project remain on track and met the client's expectations.

Dr. Manoj Vyas:

One challenge was that Dr. Jha had hired some new graduates who didn't have much expertise with sequencing instrumentation, so they required a lot of hand-holding. The AV services helped us train them because we had to do so many runs for the project, with different dilutions and so on. That gave us a lot of time and opportunity to build the customers' confidence with both platforms.

Varun Bagai:

I think the biggest challenge was setting the right customer expectations both in terms of AV service package components and the timeline for finishing, as this was our first analytical validation project in India. For example, qPCR projects may take a couple of weeks since they are not as complex, so there may be an expectation that this type of project could also be done in few weeks. With sequencing, though, I've worked on projects that have taken as long as six to twelve months—and even with our expertise and lab experience, an average NGS analytical validation takes about three months. So, again, setting the right expectations for the customer was a key challenge from my standpoint. And then another challenge was working across cultures and different time zones. Third, it was a challenge performing three analytical validations simultaneously because that's a lot of data generated, running three different assays every week, and it requires dedicated resources to identify samples, perform sequencing runs, and analyze data.

Fortunately, Dr. Jha had dedicated molecular techs and access to good samples with orthogonal data, so that helped a lot. But if you ask any experienced NGS user across the globe, those who have done similar projects, they won't recommend performing three analytical validations at the same time.

Why won't they run them at the same time?**Varun Bagai:**

Because you need dedicated resources that must have the bandwidth for performing analytical validations along with managing their daily lab duties. You must have the right number of people on the team—and you don't want to get overburdened with running three different assays on two different sequencing platforms. Therefore, it's always a challenging task to run multiple projects, and we were initially discussing doing them one by one, as we have done with multiple AVs for a lot of other clients. This was also the first time for the AV team managing three analytical validations concurrently.

Was it surprising to you that they wanted to do all three at once?**Varun Bagai:**

Yes, and it was in fact surprising that the project came from India in the first place. We have done some in Japan, but this was the first time we had somebody choose the AV service in South Asia. They had an impressive collection of cancer specimens—not only solid biopsies, but also blood to run the liquid assay, and that's something that is not easily available across the globe. They are challenging samples to run, but it was exciting to see that there were that many samples available in India. And once the projects were finished, I think everyone at Karkinos saw the value of our service.

What was the driving force behind their decision to do the three analytical validations at once?

Varun Bagai:

It was due to their timelines. Karkinos' leadership had some strict timelines they had to meet, which made it necessary for us to run them at the same time.

Dr. Jha, can you tell us about your experience working with the AV service team, and share your thoughts on their effort to complete the projects for Karkinos?

Dr. Prerana Jha:

I'm very impressed with Thermo Fisher services and the way they have developed end-to-end solutions, from running the sample to the reporting. It can help a lot in starting up a lab in less time.

That documentation was great. I will tell you that it was a value addition because if a lab has not done much analytical validation before, they won't have the manpower to do the documentation. If I'm a lab head and I have to do the documentation myself, it will take a tremendous amount of time.

The documentation alone is worth the AV service—and every lab should use it.

“I'm very impressed with Thermo Fisher services and the way they have developed end-to-end solutions, from running the sample to the reporting. It can help a lot in starting up a lab in less time.”

—Dr. Prerana Jha

But it is more than the documentation. The process gave us an opportunity to learn about the assays comprehensively. For example, there was a lab issue for which the local FAS, Dr. Vyas, was available for many runs until we were able to resolve a pool evaporation and imbalance issue on the Ion GeneStudio S5 System by tricking the plates, so I would say it was a fantastic service, and it has provided me a great amount of learning.

And in addition to working with Dr. Vyas, Varun was conducting the AV services remotely with us. He was the main leader of the project, guiding me in many ways, and was always available. It never felt like Varun was not in India during the AV services.

He was helpful even when I wanted to do the AV services very fast. Sometimes after a run, I would call him and say I want the next run scheduled by tomorrow morning, and he would then work at night, sending me the next day's training schedule to help us finish faster.

And I am also thankful for Pravin and Hersh. Pravin specifically, as he was based in Mumbai, used to be here with me anytime—even at 8:30 a.m. or late nights—to troubleshoot and help me understand new systems and assays. Pravin helped whenever it was required, and there was never a delay from him. His physical presence on-site helped.

Hersh was not located in Mumbai, but since Pravin reports to Hersh, he was aware of all the work we were doing. He visited us twice, and whenever the issue was not resolved through Pravin, Hersh patched in. Or when Pravin was not available, Hersh helped us remotely. He was deeply involved during our AV services, and present on every call to resolve issues, particularly with the liquid assay. It was not a problem that he was remote and not on-site regularly.

Altogether, the team was excellent. I would say there were no gaps in service.

“The documentation alone is worth the AV service—and every lab should use it.”

—Dr. Prerana Jha

How much faster do you think it was having the team help you, rather than trying to do the analytical validations on your own?

Dr. Prerana Jha:

It took us 3–4 months to complete the AV services. I would say it took us around half of the time it would have taken if we had done it alone.

As recipients of the Guardians of Your Science award, what do you consider the keys to the success of this project?

Hersh Parikh:

Our collaborative approach played a vital role in the successful completion of the project over several months. We worked closely with the client, helping ensure that their requirements were fully understood and met. Our team's dedication to addressing any issues promptly and providing effective solutions further enhanced the collaboration. The diligent follow-up and regular training sessions fostered a strong partnership, leading to a successful outcome.

As a result of our efforts, the client expressed great satisfaction with the outcome of the project. Our ability to understand their needs, provide effective solutions, deliver exceptional customer support, and conduct thorough training sessions played a vital role in their overall satisfaction. The successful collaboration with Karkinos serves as a testament to our commitment to excellence and our ability to exceed client expectations.

Dr. Manoj Vyas:

Our team never let the customer down. We always kept morale high, tried to be on call, and, when it was required, everyone worked beyond regular office hours.

We did our best to run the site and do the project to meet the customer's expectations. And for months afterward, we continued to do our best to assist the customer in keeping the site up and running.



Dr. Manoj Vyas and the Karkinos Healthcare team: Dr. Prerana Jha, Pooja Manesh, and Radhika Venkatakrishnan.

Pravin Nilawe:

Whatever the issue, we were always timely in helping them. We worked with them closely, from clearing up their first basic-level concerns, to now where they are able to handle the technical use of the system themselves but can still turn to us with questions.

Varun Bagai:

I think the customer was not only impressed with timely execution, along with effective communication for this project, they were also impressed with the level of expertise that we bring to the table. I strongly believe Dr. Jha valued that we had the right technical expertise to provide her guidance around data analysis and feedback on sequencing performance metrics.

These are complex assays. We offered expertise that helped her gain confidence, and as it grew, she often looked to our team to offer recommendations around data quality and analytical studies. Over time, she started analyzing the data herself. She's technically very savvy, but with a new assay, having a team of dedicated professionals to rely on—that's helpful for building a strong working relationship. We have now done more than 500 analytical validation projects, but we haven't done a lot of projects in which three assays were going on at the same time. It was a big effort from the entire team. The journey was completed with the successful analytical validation of the assays in a few months rather than couple of years. To have been able to finish within that time span was outstanding. In fact, Dr. Jha has become an advocate for us, even speaking about our services at conferences.

Has that helped raise awareness of our AV service?

Hersh Parikh:

Absolutely, yes. Many of these conferences are workshops where we bring in prospective customers and show them what our products and services can enable them to do. For example, one conference that we held in the previous year brought in prospective customers from across the entire region—basically, all of India, and some of the attendees were completely new to NGS technology, so they were able to learn a lot about our systems.

But when a user of our services like Dr. Jha presents actual data sets to workshop attendees, they gain more confidence in our offer. So, currently, we are still in touch with Dr. Jha, talking with her and her team members on a regular basis.

Our AV service not only helped you with your lab's operations, Dr. Jha, but it also helped accelerate your work. In closing, can you tell us about the current promise and challenge of what you're working on?

Dr. Prerana Jha:

If I look back on my experience in the cancer field for almost 20 years now, we have moved forward very fast, but the knowledge that we have right now is still only a little.

Sequencing is the beginning. We need to know the mechanism of how disease works, how to check it at the early level.

It's an integrated science where obtaining information from each sample is valuable to helping identify the causes of diseases, and the implications for future cases. More and more research is being done and is needed.

The future really requires a great amount of work and dedication—from people in the field, in information technology, pathology, everyone—to integrate this information and use it wisely, to make this a science in which doing less gives more information and provides more benefit to patients in the future.

Note: Consulting services offered for the guidance in enabling the analytical validation in support of research efforts only.

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