



Stilla Technologies Launches High-Throughput Digital PCR Chip, Plans Six-Color System

Feb 20, 2019 | [Madeleine Johnson](#)

This article has been updated from a previous version to clarify comments made by the company.

NEW YORK (GenomeWeb) – As digital PCR gains widespread acceptance as a workhorse research tool and begins pushing into the clinical market, French company Stilla Technologies is pushing the envelope with a new consumable chip that will enable its Naica digital PCR system to effectively triple its throughput.

In addition, the firm is progressing on development of a six-color system to bolster its current three-color detection capabilities, as well as pursuing long-term plans to enter the diagnostics space in collaboration with assay makers.

Officially launched earlier this month at the Society for Laboratory Automation and Screening conference, the new consumable chip, called the Opal, is able to test 240 samples per day on the [Naica](#) instrument, according to Caroline Charky, Stilla's vice-president of commercial operations. It [won](#) the New Product Award at the conference.

The Opal uses the same microfluidic technology as the original system which generates droplets within the chip itself, Charky said. The Naica HT platform and Opal chip also require less hands-on time than the original system, and are competitive in terms of pricing, she said.

Overall, the Naica system has three components. The Geode instrument combines droplet formation and thermal cycling on the consumable chip. PCR amplification on the self-assembled droplet array — which the firm calls a droplet crystal — takes one hour. The chip is then transferred to an instrument called the Prism3 for automated three-color fluorescence imaging readout. The Prism 3 can scan twelve samples in 10 minutes, according to Stilla. Finally, Stilla's software, called Crystal Miner, automatically identifies positive and negative droplets in each of the three fluorescence channels, ultimately generating an absolute concentration of target DNA.

The original chip, called the Sapphire, is able to run four samples, and the instrument can hold four chips, so the total throughput is about 60 samples per day, Charky said.

However, "We have a quite a few customers in Europe, Asia, and the US who are requiring higher throughputs for their applications, so now, on the same footprint of [one Sapphire] chip we are able to do 16 samples, and we can put three chips on one run, so 48 samples," she said.

Stilla made this assessment through a market survey of its customers, and found that labs particularly in food testing, and oncology applications like monitoring of cancer patients, as well as big qPCR labs that need digital PCR to confirm negative results, could all find higher throughputs useful.

The system also allows for three-color multiplexing, and the total run time per experiment is around two and a half hours. All told, the system can support five runs per day, Charky said, "so, it allows you to do 240 samples, and 720 targets, per day."

The Opal chip also requires much smaller volumes of sample than the Sapphire.

"We went from 25 microliters to 8 microliters of input volume in the chip," Charky said. "You're using much less reagents and have less dead volume, but still generating 20,000 partitions," she said, compared to up to 30,000 in the Sapphire chip, which still yields "a very good dynamic range." Furthermore, for applications that require higher sensitivity, the firm has a strategy for pooling two to three chambers which gives a limit of detection of 0.2 copies per microliter, and a 95 percent confidence interval, Charky said.

The Sapphire and Opal chips are both compatible with the higher throughput Naica system, so users do not need to invest in a new instrument. To use it just requires "a changing of the clamping system on the thermocycler," Charky said.

Stilla's major competitor in droplet-based digital PCR is Bio-Rad, whose BCR-ABL test and new QXDX instrument was CE-marked last year and [cleared](#) the US Food and Drug Administration last week.

Aric Joneja, a senior scientist at Abbott Labs' Rapid Diagnostics division, is using the Stilla digital PCR instrument as part of a product development workflow, creating assays for the Abbott ID NOW (formerly Alere i) point-of-care molecular diagnostics instrument. Joneja said his lab purchased the standard Naica system two years ago and uses it for droplet PCR and droplet RT-PCR. It plans to start using the Opal chip as well.

The lab demoed the Bio-Rad system, and found the two systems to have comparable data quality. However, Joneja said the lab preferred the Stilla workflow because it had "fewer manual steps, fewer consumables/disposables to keep track of, and easier to just push a button and walk away." In his opinion, the way in which the Stilla presents data by showing images of the droplets makes it easier to troubleshoot problems with an experiment, and, he noted, the Bio-Rad system does not provide this visual feedback. The option to have three colors, and potentially six, wasn't a significant factor, but Joneja also said the lab "definitely didn't want to buy a two-color system and later find a reason to use three colors."

In terms of throughput, the Bio-Rad QX200 system scales to run up to a 96-sample experiment in five hours, while the firm's new diagnostics instrument, the QXDx, is scalable and can process between 8 and 48 samples per run, also in approximately five hours.

For Joneja's purposes, 96-wells were more than the lab needed. "The BioRad might be better for clinics who are running really high throughput of samples; for our R&D purposes the throughput was not as important," he said.

In an email, a Bio-Rad representative noted that much research has been done using Droplet Digital PCR, with more than 3,500 peer reviewed articles published to date. The system also offers "thousands" of assays, multiplexing kits and master mixes, optimized and orderable directly from Bio-Rad, and the QX200 open system is also compatible with other vendors' assays. Additionally, Bio-Rad has made "major investments in the droplet space," including "hundreds of millions of dollars to develop and protect its foundational droplet intellectual property," the representative said. "Bio-Rad continues to leverage the innovations covered by this intellectual property to enhance its already outstanding portfolio of ddPCR and single cell product lines. This will continue to allow Bio-Rad to offer a host of products and features that competitors simply will not be able to offer."

Charky noted in a follow-up interview that Stilla's proprietary IP is unique from Bio-Rad's. "Everything is different," she said, "it is a different technology."

Stilla, meanwhile, is also planning to up the ante in terms of target multiplexing, as the firm has been developing six-color detection. "We are the first ones worldwide to demonstrate six-color digital PCR," Charky said.

An assay using the firm's three-color system to detect epidermal growth factor receptor (EGFR) mutations was published in 2017, as [previously reported](#), but a study published this month in [Oncotarget](#) describes a liquid biopsy assay that uses the new six-color methodology to detect a panel of mutations associated with non-small cell lung cancer, specifically sensitizing and resistance mutations in the EGFR gene.

The six-color platform is still an R&D product at this point, but Stilla expects to launch it in 2020 or 2021, Charky said.

"We are an instrumentation company, so we are cross-selling and co-marketing kits with companies that develop and validate the kits on the Naica," Charky said. Developers on the system include a German company developing an assay for GMOs with which Stilla plans to collaborate to launch a complete solution, and one in Montpellier designing circulating tumor cell liquid biopsy kits for CE-IVD use.

The firm also plans to pursue the clinical route on its own, Charky said, and has R&D projects for products that could ultimately obtain CE-IVD marking for clinical use.

Despite the throughput improvements to Naica, Stilla hopes to retain a competitive price. "We want to offer a digital PCR platform that is \$80,000 ... so any lab can have a digital PCR instrument," Charky said. She noted that almost half of the firm's customers are using the instrument for oncology applications, including translational research for cancer mutation monitoring.

The firm has also come a long way since launching Naica in 2016, Charky said, having recently won a second round of funding [from Illumina Ventures](#). It is also part of a European Consortium called Liquid Biopsies and Imaging for Improved Cancer Care, or [LIMA](#) with Royal Philips.

Stilla also won a public tender last year with Assistance Publique des Hôpitaux Paris, a system covering 39 hospitals in Paris that will acquire Naica systems over the next four years, Charky said.

To support all this growth, the firm is expanding, planning to triple in size by the end of the year, Charky said.

The firm has a distributor in China and has recently begun distributing in Japan and Korea, as well. These distributors have sold platforms to the Centers for Disease Control and the Centers for Inspection and Quarantine.

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