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16  
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18 UNITED STATES DISTRICT COURT  
19 CENTRAL DISTRICT OF CALIFORNIA

20  
21 CHROMACODE, INC. and  
22 CALIFORNIA INSTITUTE OF  
TECHNOLOGY,

23 Plaintiffs,

24  
25 v.

26 BIO-RAD LABORATORIES, INC.,

27 Defendant.  
28

CASE NO. 2:23-cv-08417-RGK-PD

**AMENDED COMPLAINT FOR  
PATENT INFRINGEMENT OF  
U.S. PATENT NOS. 10,068,051  
AND 10,770,170**

DEMAND FOR JURY TRIAL

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18 *And California Institute of Technology*  
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1 Plaintiffs ChromaCode, Inc. (“ChromaCode”) and California Institute of  
2 Technology (“Caltech”) (collectively, “Plaintiffs”), by and through their counsel,  
3 for their Amended Complaint against Defendant Bio-Rad Laboratories, Inc. (“Bio-  
4 Rad” or “Defendant”), allege as follows:

### 5 NATURE OF THE ACTION

6 1. This is an action for infringement of U.S. Patent Nos. 10,068,051 (the  
7 “’051 Patent”) and 10,770,170 (the “’170 Patent”).

8 2. Traditional methods of detecting the presence or absence of multiple  
9 targets (called “multiplexing”) in a biological sample require tagging every target  
10 with a different color—*i.e.*, target A is tagged with a “blue” signal, target B is  
11 tagged with a “red” signal, and so on. Although there may be an infinite number  
12 of unique colors in a rainbow, there are **not** an infinite number of colors that can be  
13 unambiguously **detected** by modern equipment. Accordingly, traditional assays  
14 were limited to only a few acceptable colors, which meant that only a small  
15 number of targets could be detected in a single test. ChromaCode’s co-founder,  
16 Dr. Aditya Rajagopal, together with his colleagues at Caltech, figured out how to  
17 break the paradigm and unambiguously identify multiple targets using the same  
18 color tag. Plaintiffs bring this action to stop Bio-Rad’s infringement of this  
19 valuable and groundbreaking intellectual property. Bio-Rad markets and uses  
20 ChromaCode’s exclusively licensed and patented multiplexing technologies in  
21 their digital Polymerase Chain Reaction (“PCR”) products without authorization  
22 and in violation of ChromaCode’s exclusive rights.

23 3. As a result of Bio-Rad’s infringement, and given the threat of its  
24 growing infringement, Plaintiffs will be irreparably harmed if such infringement is  
25 not halted.

### 26 THE PARTIES

27 4. Plaintiff ChromaCode is a Delaware corporation with its headquarters  
28 in Carlsbad, California. ChromaCode is a molecular diagnostics startup company

1 with a diagnostic and bioinformatics focus.

2 5. Plaintiff Caltech is a world-renowned science and engineering  
3 institute that marshals some of the world's brightest minds and most innovative  
4 tools to address fundamental scientific questions and pressing societal challenges.  
5 Caltech is a non-profit private university located in Pasadena, California in this  
6 District.

7 6. Defendant Bio-Rad is a Delaware corporation headquartered in  
8 Hercules, California. Bio-Rad is a developer and manufacturer of specialized  
9 technological products for the life science research and clinical diagnostics  
10 markets. Bio-Rad's Quality Systems Development Division is based in Irvine,  
11 California.

#### 12 **JURISDICTION AND VENUE**

13 7. This Court has subject matter jurisdiction over this patent  
14 infringement action pursuant to 28 U.S.C. §§ 1331 and 1338(a).

15 8. This Court has personal jurisdiction over Bio-Rad because of Bio-  
16 Rad's purposeful, systematic, and continuous contacts with California, and  
17 particularly the Central District of California. Bio-Rad maintains regular and  
18 established places of business in this District at least at the following addresses:  
19 9500 Jeronimo Road, Irvine, California 92618; 21 Technology Drive, Irvine,  
20 California 92618; and 9 Holland Drive, Irvine, California 92618. Bio-Rad's  
21 headquarters are located in Hercules, California. Bio-Rad is therefore physically  
22 located in the State of California. Bio-Rad conducts design, development,  
23 manufacturing, and distribution of software/informatics products and *in vitro*  
24 diagnostic medical devices for clinical laboratory quality control programs in  
25 Irvine, California (*i.e.*, in this District). Bio-Rad also sells products, including the  
26 Infringing Products (defined below), in Irvine, California, and elsewhere in the  
27 Central District of California.

28 9. Venue is proper in the Central District pursuant to 28 U.S.C. § 1400.

1 The facts establishing this are included throughout this Amended Complaint. Bio-  
2 Rad maintains regular and established places of business in this District, as  
3 identified above, and offers for sale and sells its infringing products in this District.

#### 4 **BACKGROUND**

5 10. The patented technology at issue in this case concerns the ability to  
6 detect, unambiguously, multiple targets in a single sample without having to label  
7 every target with a different color. This novel approach offers a fast and  
8 inexpensive alternative to researchers and clinicians who need unambiguous  
9 identification of multiple targets in a single sample.

##### 10 **A. Traditional Methods of Identifying Multiple Targets in One** 11 **Sample**

12 11. For years, researchers invested substantial resources and time to  
13 overcome the single-target limitations of then-existing target identification  
14 systems. In an early improvement, researchers were able to modestly increase the  
15 number of targets unambiguously identified in a single sample by expanding the  
16 variety of colors used to tag targets. Probes designed to bind to particular targets  
17 were labeled with fluorophores which, when excited, emit light at different  
18 wavelengths (each of which correspond to a color range), and sensors tuned to  
19 detect those different wavelengths could then identify the presence or absence of  
20 each respective target. The probes were designed such that they would only emit  
21 light when a particular target was amplified. In other words, if a blue light probe  
22 designed to target A emits blue light, that means A is present in the sample. If no  
23 blue light is emitted, that means A is not present in the sample. If, in the same  
24 sample, a red light probe designed to target B emits red light, that means B is  
25 present in the sample. If no red light is emitted, that means B is not present in the  
26 sample. And so on. For every target, a different color could indicate its presence  
27 or absence.

28 12. Theoretically, with a one-target-one-color approach, one could

unambiguously identify a nearly infinite number of targets in a single sample. For example, consider a target identification approach as indicated in the table below:

| Target | Assigned Shades of Blue |
|--------|-------------------------|
| A      |                         |
| B      |                         |
| C      |                         |

13. This table includes just three shades of blue for each target. The average human eye can detect up to around 10 million shades of different colors.<sup>1</sup> Unfortunately, fluorescent probes cannot be relied upon to emit light in any one particular shade with anywhere near this level of precision. Each fluorophore has a wide emission spectra, meaning they emit light in various shades of each color. Accordingly, in our example, rather than unambiguously identifying A from B from C, each shade of blue could correspond to each target, as shown below.

| Target      | Assigned Shades of Blue |
|-------------|-------------------------|
| A or B or C |                         |
| A or B or C |                         |
| A or B or C |                         |

14. For this reason, to avoid what is called spectral overlap (bleeding colors) and preserve spectral resolution (the ability to detect different colors), only a relatively small number of colors (*e.g.*, 4 to 6) are typically used simultaneously in multiplexed fluorescent assays.

15. To overcome this limitation, researchers combined additional labor-intensive processing steps along with fluorescence to identify more targets from a single sample, including aliquoting, spatial arraying, and sequential processing.

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<sup>1</sup> See <https://www.aao.org/eye-health/tips-prevention/how-humans-see-in-color>.

1 These additional processing steps are labor-intensive and frequently require  
2 relatively expensive and complex optical and mechanical systems. Although these  
3 tools offered some ability to increase the number of targets detected in a sample,  
4 there remained a significant need for inexpensive multiplexed encoding and  
5 decoding methods that could identify unambiguously a significantly higher number  
6 of targets.

7 **B. ChromaCode Broke the One-Target-One-Color Barrier**

8 16. Researchers continued to investigate a solution to the one-target-one-  
9 color approach. Then, in 2011, a team of researchers from Caltech, comprised of  
10 Drs. Emil Kartalov, Aditya Rajagopal, and Axel Scherer, conceived of a solution  
11 that enabled high definition multiplexing—specifically, the unambiguous  
12 identification of multiple targets for each color.

13 17. Dr. Emil Kartalov earned his B.S. in Physics (1998), M.S. in Applied  
14 Physics (2004), and Ph.D. in Applied Physics (2004), all from Caltech. His  
15 doctoral thesis focuses on single-molecule fluorescence microscopy, single-  
16 molecule DNA sequencing, and microfluidic DNA sequencing by synthesis. The  
17 first two developed techniques resulted in the founding of Helicos Biosciences in  
18 Boston, MA. For his postdoctoral work, Dr. Kartalov moved to the Biochemistry  
19 Dept and later the Pathology Department at the Keck School of Medicine at the  
20 University of Southern California (“USC”), where the focus shifted to fundamental  
21 microfluidics and biomedical applications of microfluidic devices. Dr. Kartalov  
22 invented microfluidic vias and resultant autoregulatory devices, and built multi-  
23 analyte microfluidic immunoassay chip for protein diagnostics in fingerprick  
24 amounts of human serum and plasma. In 2006, Dr. Kartalov won the NIH  
25 K99/R00 Career Award and became tenure-track faculty in Pathology at USC in  
26 2008. His group focuses on microfluidic point-of-care diagnostics and techniques  
27 for high-throughput analysis of pathology tissue slices. Dr. Kartalov has over 33  
28

1 peer-reviewed publications and 32 issued patents.<sup>2</sup>

2 18. Dr. Aditya Rajagopal earned his B.S. (2008), M.S. (2010), and Ph.D.  
3 (2014) in Electrical Engineering, all from Caltech. He is a Visiting Associate in  
4 Electrical Engineering at Caltech. Dr. Rajagopal's research in medical  
5 engineering, microfluidics, nanotechnology and bioengineering has resulted in  
6 numerous innovative technological developments. He is the inventor of core  
7 technologies related to not only multiplexed PCR assay design, but also  
8 combinatorics for biochemical labeling and algorithms for data processing. In the  
9 aggregate, Dr. Rajagopal has authored over 45 patents and patent publications. He  
10 is the recipient of numerous honors including the Caltech Grubstake Award in  
11 2017, the Caltech Innovation Initiative (CI2) in 2014 and 2015, the Demitriadis-  
12 Kafka-Kokallis Thesis Prize in January 2013, and various fellowships and  
13 scholarships sponsored by the National Science Foundation and Carnation  
14 Foundation from 2006 to 2013. In addition to co-founding ChromaCode, Dr.  
15 Rajagopal co-founded a healthcare company called Esperto Medical—a venture-  
16 backed Caltech spin-out utilizing compressed sensing methods with ultrasound to  
17 continuously and non-invasively measure patient blood pressure.

18 19. Dr. Axel Scherer is the Bernard Neches Professor of Electrical  
19 Engineering, Physics, and Applied Physics at Caltech, where his research focuses  
20 on the design and microfabrication of optical, magnetic and fluidic devices. He is  
21 also a distinguished visiting professor at Thayer School of Engineering at  
22 Dartmouth College. He is known for fabricating the world's first semiconducting  
23 vertical-cavity surface-emitting laser ("VCSEL") at Bell Labs, now widely used in  
24 data communications systems. More recently, his group developed  
25 electromagnetic design tools and fabrication techniques for the definition of

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26 <sup>2</sup> See, e.g., <https://nps.edu/web/physics/nps-physics-research-kartalov>; see also,  
27 e.g., [https://presentations.akamaized.net/Shows/UBM/Standalone/IVDT/9-7-  
28 11/EmilBio.html](https://presentations.akamaized.net/Shows/UBM/Standalone/IVDT/9-7-11/EmilBio.html); <https://nps.edu/faculty-profiles/-/cv/epkartal>.

1 lithographically integrated optical devices. This led to pioneering work in  
 2 photonic bandgap lasers, silicon photonic circuits, as well as tunable microfluidic  
 3 dye lasers, leading to new classes of integrated optics. The first demonstration of  
 4 strong coupling between single quantum dots and optical nanocavities recently  
 5 emerged from a collaboration between Dr. Scherer and Hyatt Gibbs.  
 6 Collaborations with Larry Dalton (University of Washington) resulted in some of  
 7 the world's smallest and fastest light modulators. Dr. Scherer also fabricated some  
 8 of the first surface plasmon enhanced high brightness light emitting diodes. His  
 9 group miniaturized fluidic systems and demonstrated the first multi-layer  
 10 replication molded fluidic chips, with thousands of valves creating microfluidic  
 11 "laboratories" and single cell analysis systems. He leads a group focused on the  
 12 miniaturization and integration of fluidic, optical, electronic and magnetic devices  
 13 for applications in biotechnology. Scherer has co-authored over 300 publications  
 14 and holds over 100 patents on the area of microfabrication and design of devices.<sup>3</sup>

15 20. As a result of continued diligent research efforts, the Caltech  
 16 researchers' high definition multiplexing solution was reduced to practice by at  
 17 least February 3, 2012, when Caltech filed U.S. Provisional Patent Application No.  
 18 61/594,480, to which the '051 and '170 Patents claim priority.

19 21. The Caltech researchers' innovative approach to high definition  
 20 multiplexing, referred to as high-definition PCR<sup>4</sup> ("HDPCR"), involves using

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22 <sup>3</sup> See, e.g., <https://www.eas.caltech.edu/people/etcher#profile-d0b3cee6-tab>; see  
 23 also, e.g., <https://www.eas.caltech.edu/people/etcher#publications-d0b3cee6-tab>;  
 24 <https://feeds.library.caltech.edu/people/Scherer-A/>.

25 <sup>4</sup> "PCR" stands for the Polymerase Chain Reaction, which is a method of  
 26 exponential amplification of specific target DNA in a reaction mix with a DNA  
 27 polymerase and primers. Primers are short single-stranded DNA oligonucleotides,  
 28 which bind to particular regions of a target sequence. The reaction mixture is  
 cycled in heating and cooling steps. The heating cycle denatures or splits the  
 double-stranded DNA target into single-stranded templates. In the cooling cycle,  
 (continued...)

1 multiple fluorescent probes in a single reaction, each probe corresponding to a  
2 different target but not necessarily a different color, and distinguishing targets  
3 unambiguously based on cumulative signal intensities from each fluorophore.  
4 HDPCR is the subject of multiple U.S. patents assigned to Caltech, including the  
5 '051 and '170 Patents (collectively, the "HDPCR Patents").

6 **C. The Founding and Mission of ChromaCode**

7 22. In 2012, Dr. Aditya Rajagopal teamed up with Dr. Alex Dickinson to  
8 found ChromaCode in order to bring the patented HDPCR technology to the  
9 market. Drs. Rajagopal and Dickinson understood that the commercialization of  
10 multiplexing technologies, like HDPCR, was critical to the creation of widely-  
11 available, efficient and affordable PCR assays able to detect various diseases and  
12 medical conditions. ChromaCode obtained an exclusive license to the HDPCR  
13 Patents from Caltech for the purpose of developing and delivering commercial  
14 embodiments of the HDPCR technology to the market. ChromaCode sought to  
15 bridge the gap where one-target-one-color multiplexing falls short because it is not  
16 comprehensive enough and next generation sequencing ("NGS") falls short  
17 because it can be too slow, costly, and require too much tissue. ChromaCode knew  
18 that its HDPCR multiplexing technology could deliver results to patients faster,  
19 require less painful procedures, and cost significantly less.

20 23. ChromaCode's market strategy was to be first-to-market with its  
21 groundbreaking HDPCR technology, either through its own commercialization  
22 efforts or a partnership with an existing multi-color digital PCR ("dPCR")  
23 company. Because ChromaCode's first-to-market strategy was protected by its  
24 exclusive patent rights, several third parties invested millions of dollars in

25 \_\_\_\_\_  
26 the primers bind to the target. After the template is primed, the DNA polymerase  
27 creates a copy of the original template. Repeated cycling exponentially amplifies  
28 the target 2 fold with each cycle leading to approximately a billion-fold increase of  
the target sequence in 30 cycles.

1 ChromaCode. Indeed, ChromaCode's value is inextricably tied to its ability to  
2 execute on its first-to-market strategy.

3 24. ChromaCode's exclusive intellectual property rights in the HDPCR  
4 Patents provide ChromaCode with a valuable competitive shield against much  
5 larger multi-billion-dollar competitors like Bio-Rad. Bio-Rad's infringement of  
6 the HDPCR Patents has eroded that shield and severely diminished ChromaCode's  
7 economic advantage.

8 25. The global PCR market is immense. In the United States alone, the  
9 PCR market was estimated to be \$7.10 billion in 2020.<sup>5</sup> The market only continues  
10 to grow. The increase in PCR research and forensic laboratories and increasing  
11 demand for advanced diagnostics, which depend on the ability to detect multiple  
12 target sequences in single PCR reactions, are expected to drive market growth.  
13 Among other things, the increase in the prevalence of chronic and infectious  
14 diseases and genetic disorders is expected to boost PCR demand.

15 26. Thus, ChromaCode's market value will be irreparably harmed if Bio-  
16 Rad is not enjoined from selling its infringing products. ChromaCode's primary  
17 asset is its intellectual property. If Bio-Rad is allowed to infringe the HDPCR  
18 Patents, ChromaCode's market value will be irreparably reduced. Even if  
19 ChromaCode recovers money damages from Bio-Rad, its market value will not be  
20 repaired.

## 21 **THE ASSERTED PATENTS**

### 22 **A. The HDPCR Patents**

23 27. On September 4, 2018, the USPTO issued the '051 Patent, entitled  
24 "Signal Encoding and Decoding in Multiplexed Biochemical Assays," to Drs. Emil  
25 Kartalov, Aditya Rajagopal and Axel Scherer. Caltech is the assignee of the '051  
26

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27 <sup>5</sup> See [https://www.fortunebusinessinsights.com/polymerase-chain-reaction-pcr-](https://www.fortunebusinessinsights.com/polymerase-chain-reaction-pcr-market-102528)  
28 [market-102528](https://www.fortunebusinessinsights.com/polymerase-chain-reaction-pcr-market-102528).

1 Patent. ChromaCode is the exclusive licensee of the '051 Patent pursuant to a  
2 license agreement with Caltech dated June 8, 2015. A true and correct copy of the  
3 '051 Patent is attached hereto as **Exhibit A**.

4 28. The '051 Patent claims priority to U.S. Provisional Application No.  
5 61/594,480, filed on February 3, 2012. Independent claim 1 of the '051 Patent  
6 recites:

- 7
- 8 1. A method of detecting the presence or absence of at  
9 least seven polynucleotide analytes, in any combination  
10 of presence or absence, in a single sample solution  
11 volume, the method comprising:
- 12 a) providing a sample solution volume comprising or  
13 potentially comprising, at least one of at least seven  
14 polynucleotide analytes, and comprising at least seven  
15 hybridization probes, each hybridization probe  
16 corresponding to one of the at least seven  
17 polynucleotide analytes, wherein each hybridization  
18 probe comprises at least one fluorophore selected from  
19 four fluorophores, and wherein each hybridization  
20 probe, when excited and when contacted with its  
21 corresponding polynucleotide analyte, generates a  
22 cumulative intensity signal, further wherein each  
23 generated cumulative intensity signal comprises at least  
24 one signal generated by excitement of at least one of the  
25 four fluorophores;
- 26 b) contacting said sample solution volume with the  
27 plurality of hybridization probes and exciting the  
28 hybridization probes to generate the cumulative  
intensity signal(s) if one or more of the at least seven  
polynucleotide analytes is present in the sample  
volume; and
- c) measuring the cumulative intensity signal(s), thereby  
generating a cumulative signal measurement, wherein  
the cumulative signal measurement non-degenerately  
indicates the presence or absence of the at least seven

1 polynucleotide analytes, in any combination of presence  
2 or absence,

3 wherein said method non-degenerately detects the  
4 presence or absence of the at least seven polynucleotide  
5 analytes in said single sample solution volume, in any  
6 combination of presence or absence, without requiring  
7 any step of immobilization of said polynucleotide  
analytes, physical separation of said polynucleotide  
analytes, or mass spectrometry.

8 29. On September 4, 2018, the USPTO issued the '170 Patent, entitled  
9 "Signal Encoding and Decoding in Multiplexed Biochemical Assays," to Drs. Emil  
10 Kartalov, Aditya Rajagopal and Axel Scherer. Caltech is the assignee of the '170  
11 Patent. ChromaCode is the exclusive licensee of the '170 Patent pursuant to a  
12 license agreement with Caltech dated June 8, 2015. A true and correct copy of the  
13 '170 Patent is attached hereto as **Exhibit B**.

14 30. The '170 Patent shares the same specification as the '051 Patent and  
15 claims priority to U.S. Provisional Application No. 61/594,480, filed on February  
16 3, 2012. Independent claim 1 of the '170 Patent recites:

- 17 1. A method of unambiguously detecting any unique  
18 combination of presence or absence of at least five  
19 polynucleotide analytes in a plurality of droplets, the  
20 method comprising:
  - 21 a) providing a sample comprising, or potentially  
22 comprising, at least one of said at least five  
polynucleotide analytes;
  - 23 b) forming a mixture of said sample and at least five  
24 hybridization probes, wherein each of said at least five  
25 hybridization probes further comprises at least one  
fluorophore and at most four fluorophores;
  - 26 c) partitioning said mixture into said plurality of droplets;
  - 27 d) exciting said at least one fluorophore to generate one or  
28 more signals if one or more of said at least five

polynucleotide analytes is present in said plurality of droplets, wherein said one or more signals comprise at least one signal generated by excitement of said at least one fluorophore;

e) measuring said one or more signals to generate a cumulative intensity measurement, wherein said cumulative intensity measurement corresponds to the presence of a unique combination of presence or absence of said at least five polynucleotide analytes in said sample; and

f) determining whether each of said least five polynucleotide analytes is present, in any unique combination of presence or absence, based on said cumulative intensity measurement,

wherein the method does not require any step of immobilization of said at least five polynucleotide analytes or mass spectrometry.

31. The HDPCR Patents describe a method of unambiguously identifying more than one target per color by using a cumulative signal from all fluorescent probes in a reaction. By designing the assay so that each cumulative signal can **only** belong to one target—notwithstanding the fact that multiple targets may be assigned the same color—the HDPCR Patents describe a method of doing what others could not: unambiguously identifying multiple targets in a single sample by using less colors than targets.

32. The HDPCR Patents provide solutions to the long-existing problem of how to unambiguously identify multiple targets without expanding the colors used, and in some cases, how to unambiguously identify at least five or more targets in less than the same number of colors (*e.g.*, five targets with four colors or less). ChromaCode's exclusively licensed and patented multiplexing solution dramatically improved on existing dPCR technology and opened the door to providing usable and commercially viable advanced PCR detection assays that

1 could aid in the fight against difficult diseases like cancer.

## 2 **THE INFRINGING PRODUCTS**

### 3 **A. Bio-Rad Launches its Infringing QX600 Droplet Digital PCR** 4 **System**

5 33. Upon information and belief, Bio-Rad also had been trying to develop  
6 an advanced multiplexing technology of its own. In 2011, Bio-Rad researchers  
7 allegedly figured out a process of identifying more targets than colors in a single  
8 sample and filed for patent protection of their process. *See* U.S. Provisional Patent  
9 Application No. 61/454,373, filed on March 18, 2011. Although Bio-Rad received  
10 patents on their approach to multiplexing, *see* U.S. Patent Nos. 9,222,128 and  
11 9,921,154, Bio-Rad was unable to unambiguously detect multiple targets per color  
12 or unambiguously detect more than four targets with two colors. Despite many  
13 years trying to make its own inferior multiplexing technology work, this limitation  
14 rendered Bio-Rad's approach commercially unviable.

15 34. Bio-Rad knew, however, that ChromaCode had been able to develop  
16 an elegant, functional multiplexing solution to unambiguously detect multiple  
17 targets per color. ChromaCode shared an overview of its patented, proprietary  
18 technology with Bio-Rad during fundraising discussions in 2014. These  
19 fundraising discussions included an overview of ChromaCode's intellectual  
20 property portfolio, including then-pending Caltech patent applications covering the  
21 HDPCR multiplexing technology. ChromaCode shared with Bio-Rad that it was  
22 the exclusive licensee to these patents.

23 35. The application that became the '051 Patent published on February  
24 26, 2015. The '051 Patent issued on September 4, 2018. Around this period,  
25 discussions with Bio-Rad continued. In those discussions with Bio-Rad,  
26 ChromaCode reiterated that it had the exclusive rights to patented HDPCR  
27 multiplexing technology. Indeed, in 2017 and 2018, ChromaCode shared slides  
28 with Bio-Rad stating that, in its multiplexing assay, "[t]argets are amplitude

1 multiplexed using ChromaCode’s patented and proprietary methods.” The slides  
 2 ChromaCode shared with Bio-Rad also referred to ChromaCode’s “[p]atented  
 3 multiplex coding methods,” and stated that ChromaCode had “[e]xclusive rights to  
 4 patented HDPCR™ from Caltech.” On information and belief, armed with this  
 5 knowledge, a sophisticated legal department, and significant prior experience with  
 6 patent disputes and patent litigation, Bio-Rad should have investigated the scope of  
 7 ChromaCode’s patent rights, including the ’051 and ’170 Patents.

8 36. Unable to make its own approach commercially viable, Bio-Rad  
 9 decided instead to copy ChromaCode’s multiplexing solution and willfully infringe  
 10 the HDPCR Patents. In late 2022, Bio-Rad announced its new QX600 Droplet  
 11 Digital PCR System (the “QX600 System”).<sup>6</sup> For example, in an April 5, 2023  
 12 press release, Bio-Rad touted that its QX600 System is capable of unambiguously  
 13 identifying 12 targets in its 6 color instrument:

14 Bio-Rad Laboratories, Inc. (NYSE: BIO and BIOb), a  
 15 global leader in life science research and clinical  
 16 diagnostic products, is accelerating measurable residual  
 17 disease (MRD) research through more than a half dozen  
 18 collaborations with institutions and companies leveraging  
 19 its new QX600™ Droplet Digital™ PCR System.

20 ***Launched late last year, it boasts six color detection***  
 21 ***capable of quantifying 12 targets per well***, a simple user  
 22 workflow, and powerful data analysis. Maintaining Bio-  
 23 Rad's best-in-class ddPCR™ technology, this platform  
 24 utilizes the same droplet generation and processing  
 25 protocols as the QX200™ system, enabling thousands of  
 26 current customers to easily adopt its advanced  
 27 multiplexing capabilities.<sup>7</sup>

---

28 <sup>6</sup> As used herein, the term “QX600 System” includes Bio-Rad’s QX600 Droplet  
 Digital PCR System and related systems, components and assays, such as Bio-  
 Rad’s QX600 Auto DG Droplet Digital System.

<sup>7</sup> Emphasis added.

1           37. A true and correct copy of Bio-Rad's April 5, 2023 press release is  
2 attached hereto as **Exhibit C**.<sup>8</sup>

3           38. Beginning at least as of December 14, 2022, Bio-Rad's website  
4 offered the QX600 System for sale, announcing: "The QX600™ Droplet Digital™  
5 PCR System enables advanced six-color multiplexing, allowing clear  
6 discrimination of multiple targets with assays that are cross-compatible with the  
7 QX200™ Droplet Digital PCR System. The QX600 System is designed for  
8 researchers who need to quantify multiple targets with high accuracy,  
9 reproducibility, and sensitivity." A true and correct copy of the product page for  
10 the QX600 system is attached hereto as **Exhibit D**.<sup>9</sup> The QX600 System product  
11 page continues in the "Description" section:

12           The QX600 Droplet Reader offers users:

- 13           • Sensitive multiplexing
  - 14           ○ Six-color detection capability (FAM, HEX, Cy5, Cy5.5, ROX,  
15           and ATTO 590)
  - 16           ○ Quantification of up to 12 targets in a single well
  - 17           ○ Absolute quantification with 0.1% or better sensitivity
  - 18           ○ Sensitive and precise gene expression multiplexing

19           39. Bio-Rad also began distributing instructions on how to use the QX600  
20 System and related assays to multiplex PCR processes to customers throughout the  
21 United States, including in this District, on its website, including the QX600  
22 Droplet Reader and QX Manager Software Standard Edition User Guide (the  
23 "QX600 System User Guide"). A true and correct copy of the QX600 System

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25           <sup>8</sup> See also [https://www.bio-rad.com/en-us/life-science-research/news/bio-rads-qx600-droplet-digital-pcr-system-advancing-measurable-residual-disease-research?ID=Bio-Rad-s-QX600-Drop\\_1680646933](https://www.bio-rad.com/en-us/life-science-research/news/bio-rads-qx600-droplet-digital-pcr-system-advancing-measurable-residual-disease-research?ID=Bio-Rad-s-QX600-Drop_1680646933).

26  
27           <sup>9</sup> See also <https://www.bio-rad.com/en-us/product/qx600-droplet-digital-pcr-system?ID=b07d12ac-0585-fc4c-a586-3ddf20d5c4a0>.

1 User Guide is attached hereto as **Exhibit E**.<sup>10</sup>

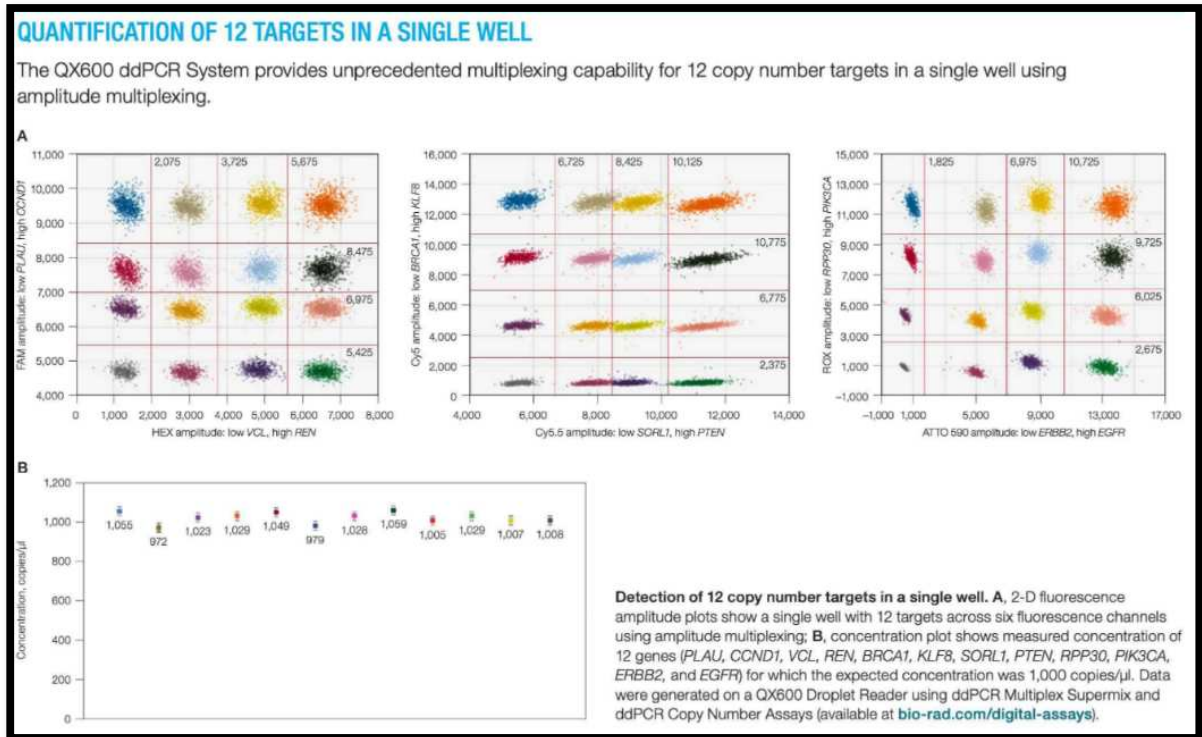
2 40. The QX600 System User Guide describes multiple assays for the  
3 QX600 that include an encoding scheme based on the cumulative signal from each  
4 fluorophore information that unambiguously identifies more targets than there are  
5 colors. For example, in Table 15 titled “Assay types,” Bio-Rad describes assay  
6 type “Amplitude multiplex” as “Method to increase multiplexing up to twelve  
7 targets per well, with one or two targets detected per [color].” Ex. E at 77. Bio-  
8 Rad also describes a “Method assuming up to six probe colors ... and up to six  
9 targets per [color].” *Id.*; *see also id.* at 79, Table 21 (describing “Fluorophore  
10 options” including “Amplitude multiplex, for 1 to 12 targets” and “Probe mix  
11 triplex, for 9 targets”).

12 41. In Bio-Rad’s “Bulletin 3557,” a true and correct copy of which is  
13 attached hereto as **Exhibit F**,<sup>11</sup> Bio-Rad provided data demonstrating their new and  
14 “unprecedented multiplexing capabilit[ies],” as reflected in the excerpt below  
15 labeled “Quantification of 12 Targets in a Single Well.”  
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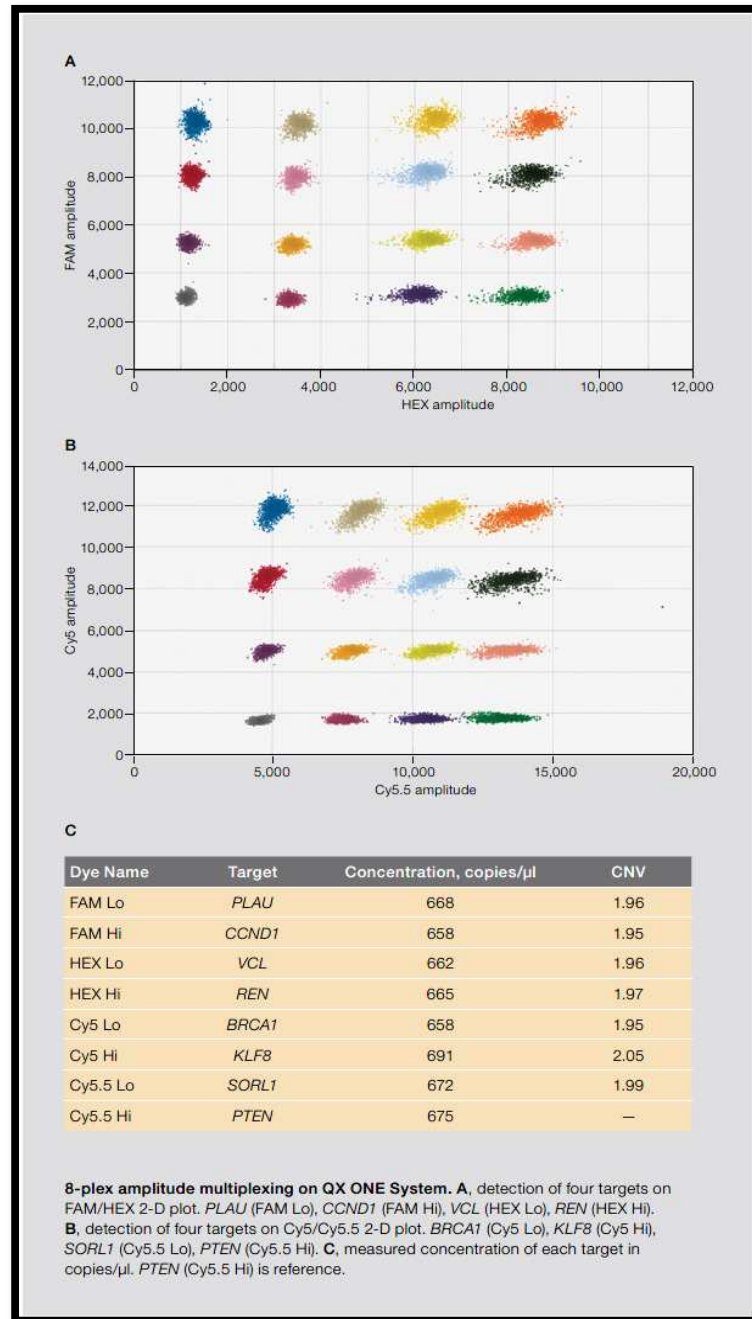
25 <sup>10</sup> See also [https://www.bio-rad.com/sites/default/files/2022-](https://www.bio-rad.com/sites/default/files/2022-12/10000153877.pdf)  
26 [12/10000153877.pdf](https://www.bio-rad.com/sites/default/files/2022-12/10000153877.pdf).

27 <sup>11</sup> See also [https://www.bio-rad.com/sites/default/files/2023-](https://www.bio-rad.com/sites/default/files/2023-08/Bulletin_3557.pdf)  
28 [08/Bulletin\\_3557.pdf](https://www.bio-rad.com/sites/default/files/2023-08/Bulletin_3557.pdf).



42. At least the QX600 System practices one or more claims of each of the HDPCR Patents. For example, the QX600 System's ability to detect multiple targets per color using cumulative signals is only possible using ChromaCode's patented approach to multiplexing recited by one or more claims of each of the HDPCR Patents. Thus, Bio-Rad's QX600 System infringes the HDPCR Patents.

43. Bio-Rad's QX ONE Droplet Digital PCR System and ddPCR Multiplex Supermix together also practice one or more claims of each of the



HDPCR Patents, as reflected in Bio-Rad's "Bulletin 6512."<sup>12</sup> A true and correct copy of Bulletin 6512 is attached hereto as **Exhibit G** and an excerpt from that

<sup>12</sup> See [https://www.bio-rad.com/webroot/web/pdf/lsr/literature/Bulletin\\_6512.pdf](https://www.bio-rad.com/webroot/web/pdf/lsr/literature/Bulletin_6512.pdf).

1 Bulletin is included above for the Court's convenience.

2 44. Bulletin 6512 states: "Bio-Rad's QX ONE Droplet Digital PCR  
3 System offers four color channels—FAM, HEX, Cy5, and Cy5.5—thereby  
4 providing additional multiplexing flexibility. By using Bio-Rad's ddPCR  
5 Multiplex Supermix on the QX ONE ddPCR System, as many as eight targets can  
6 be detected and measured in a single reaction. Such advanced multiplexing is  
7 made possible using strategies such as amplitude multiplexing in conjunction with  
8 four color channels. Extract as much information as possible with high sensitivity,  
9 using as little sample as possible in a fast, cost-effective manner." Ex. G at 9.

10 45. Bio-Rad knew or should have known about ChromaCode's exclusive  
11 rights to practice the HDPCR Patents. Despite knowledge of ChromaCode's  
12 patent rights, Bio-Rad chose not only to infringe, but to induce others to do so as  
13 well. Indeed, as described above, Bio-Rad went so far as to provide step-by-step  
14 instructions on how to use Bio-Rad's devices to infringe the HDPCR Patents. This  
15 egregious misconduct has caused Plaintiffs significant, irreparable harm that will  
16 continue unless and until Bio-Rad is enjoined from infringing the HDPCR Patents.

17 **COUNT I**

18 **INFRINGEMENT OF THE '051 PATENT**

19 46. Plaintiffs repeat and reallege each and every allegation contained in  
20 the preceding paragraphs of this Amended Complaint as if fully set forth herein.

21 47. Caltech is the assignee and owner of the '051 Patent. ChromaCode is  
22 the exclusive licensee of the '051 Patent. ChromaCode's exclusive rights include  
23 the right to enforce the '051 Patent.

24 48. Bio-Rad makes, offers to sell and/or sells its infringing products in the  
25 United States, including in this District.

26 49. For example, Bio-Rad's QX600 System practices each and every  
27 limitation, either literally or under the doctrine of equivalents, of at least claim 1 of  
28 the '051 Patent in violation of 35 U.S.C. § 271(a). For example, one or more

1 assays provided by Bio-Rad with at least the QX600 System perform amplitude-  
2 based PCR multiplexing to unambiguously identify the presence or absence of at  
3 least seven polynucleotide analytes based on cumulative signal intensity of probes  
4 that comprise at least one fluorophore selected from four fluorophores, and  
5 perform each of the other elements of claim 1. Bio-Rad's QX600 System,  
6 therefore, directly infringes the '051 Patent.

7 50. Bio-Rad also indirectly infringes the '051 Patent. Bio-Rad has  
8 knowingly induced infringement of the '051 Patent by encouraging others to  
9 infringe at least claim 1 of the '051 Patent. For example, in Bio-Rad's QX600  
10 System User Guide, Bio-Rad has induced, and will continue to induce, users to  
11 infringe the '051 Patent by expressly and intentionally instructing and encouraging  
12 users to perform each limitation of at least claim 1 of the '051 Patent in violation  
13 of 35 U.S.C. § 271(b). Bio-Rad is, therefore, liable for inducing infringement of  
14 the '051 Patent.

15 51. Bio-Rad's sale of infringing products has contributed, and will  
16 continue to contribute, to the infringement of the '051 Patent in violation of 35  
17 U.S.C. § 271(c). For example, users of the QX600 System have infringed, and will  
18 continue to infringe, at least claim 1 of the '051 Patent by performing assays in  
19 accordance with instructions set forth in the QX600 System User Guide. Bio-Rad  
20 is, therefore, liable for contributing to the infringement of the '051 Patent.

21 52. Upon information and belief, Bio-Rad had and continues to have  
22 knowledge that multiple assays it provides for the QX600 System are especially  
23 made or especially adapted for a use that infringes the '051 Patent.

24 53. Upon information and belief, Bio-Rad had actual and constructive  
25 notice of the '051 Patent prior to launching the QX600 System and knowingly or  
26 intentionally infringed the '051 Patent after acquiring that knowledge. Bio-Rad  
27 has no reasonable basis for asserting that the commercial manufacture, use, offer  
28 for sale, or sale of the QX600 System will not infringe, induce the infringement of,

1 and/or contribute to the infringement of the '051 Patent.

2 54. Bio-Rad's infringement of the '051 Patent has been, and continues to  
3 be, willful, wanton, malicious, bad faith, deliberate, consciously wrong, flagrant,  
4 and egregious, entitling Plaintiffs to an award of up to three times their actual  
5 damages pursuant to 35 U.S.C. § 284.

6 55. Bio-Rad's willful infringement of the '051 Patent further renders this  
7 an exceptional case under 35 U.S.C. § 285.

8 56. Plaintiffs have been damaged by Bio-Rad's egregious and willful  
9 infringement of the '051 Patent.

10 57. Plaintiffs will be irreparably harmed if Bio-Rad is not enjoined from  
11 infringing, and from actively inducing or contributing to the infringement of, the  
12 '051 Patent. Plaintiffs do not have an adequate remedy at law and, considering the  
13 balance of hardships between Plaintiffs and Bio-Rad, a remedy in equity is  
14 warranted. Further, the public interest would not be disserved by the entry of a  
15 permanent injunction.

## 16 **COUNT II**

### 17 **INFRINGEMENT OF THE '170 PATENT**

18 58. Plaintiffs repeat and reallege each and every allegation contained in  
19 the preceding paragraphs of this Amended Complaint as if fully set forth herein.

20 59. Caltech is the assignee and owner of the '170 Patent. ChromaCode is  
21 the exclusive licensee of the '170 Patent. ChromaCode's exclusive rights include  
22 the right to enforce the '170 Patent.

23 60. Bio-Rad makes, offers to sell and/or sells its infringing products in the  
24 United States, including in this District.

25 61. For example, Bio-Rad's QX600 System practices each and every  
26 limitation, either literally or under the doctrine of equivalents, of at least claim 1 of  
27 the '170 Patent in violation of 35 U.S.C. § 271(a). For example, one or more  
28 assays provided by Bio-Rad with at least the QX600 System perform amplitude-

1 based PCR multiplexing to unambiguously identify the presence or absence of at  
2 least five polynucleotide analytes based on cumulative signal intensity of probes  
3 that comprise between one and four fluorophores, and perform each of the other  
4 elements of claim 1. Bio-Rad's QX600 System, therefore, directly infringes the  
5 '170 Patent.

6 62. Bio-Rad also indirectly infringes the '170 Patent. Bio-Rad has  
7 knowingly induced infringement of the '170 Patent by encouraging others to  
8 infringe at least claim 1 of the '170 Patent. For example, in Bio-Rad's QX600  
9 System User Guide, Bio-Rad has induced, and will continue to induce, users to  
10 infringe the '170 Patent by expressly and intentionally instructing and encouraging  
11 users to perform each limitation of at least claim 1 of the '170 Patent in violation  
12 of 35 U.S.C. § 271(b). Bio-Rad is, therefore, liable for inducing infringement of  
13 the '170 Patent.

14 63. Bio-Rad's sale of the infringing products has contributed, and will  
15 continue to contribute, to the infringement of the '170 Patent in violation of 35  
16 U.S.C. § 271(c). For example, users of the QX600 System have infringed, and will  
17 continue to infringe, at least claim 1 of the '170 Patent by performing assays in  
18 accordance with instructions set forth in the QX600 System User Guide. Bio-Rad  
19 is, therefore, liable for contributing to the infringement of the '170 Patent.

20 64. Upon information and belief, Bio-Rad had and continues to have  
21 knowledge that multiple assays it provides for the QX600 System are especially  
22 made or especially adapted for a use that infringes the '170 Patent.

23 65. Upon information and belief, Bio-Rad had actual and constructive  
24 notice of the '170 Patent prior to launching the QX600 System and knowingly or  
25 intentionally infringed the '170 Patent after acquiring that knowledge. Bio-Rad  
26 has no reasonable basis for asserting that the commercial manufacture, use, offer  
27 for sale, or sale of the QX600 System will not infringe, contribute to the  
28 infringement of, and/or induce the infringement of the '170 Patent.



e. That an accounting be performed to determine the monetary damages to be awarded to Plaintiffs as a result of Bio-Rad's infringing activities, including an accounting for infringing conduct not presented at trial and an award of additional damages for any such infringing activities;

f. That the Court find that Bio-Rad's infringement of the HDPCR Patents was egregious and willful and award Plaintiffs three times their actual damages;

g. That the Court declare that this case is exceptional under 35 U.S.C. § 285 and award Plaintiffs their attorneys' fees, costs, and expenses incurred in this action;

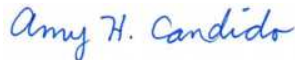
h. That the Court award Plaintiffs any further and additional relief as the Court may deem just, equitable, and proper.

### **JURY DEMAND**

Plaintiffs hereby demand a jury trial on all issues and claims so triable.

Dated: October 13, 2023

WILSON SONSINI GOODRICH & ROSATI, PC



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HAMPTON, LLP

/s/ Martin R. Bader

Martin R. Bader

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and California Institute of Technology*