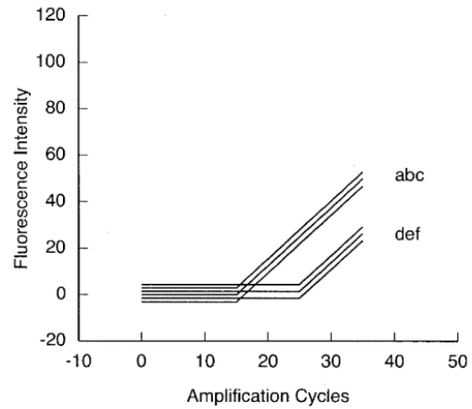
Appendix C

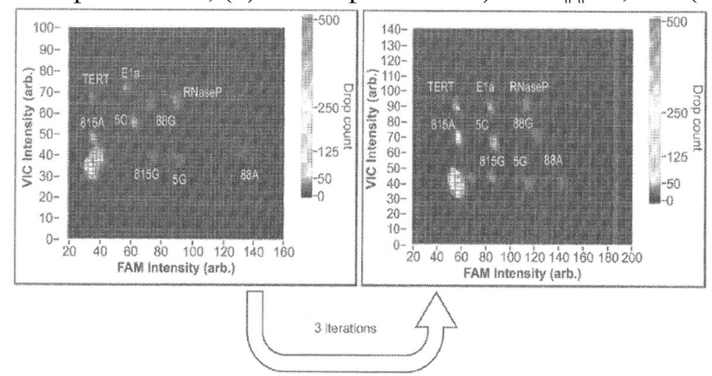
Invalidity of U.S. Patent No. 10,068,051

by U.S. Patent Publication 2008/0124705A1 ("Kramer") and U.S. Patent Publication 2011/0250597A1 ("Larson")

Based upon the claim interpretations Plaintiffs appear to be asserting and the applications of those interpretations to Bio-Rad's products in Plaintiffs' Patent Local Rule infringement contentions, the combination of Kramer and Larson renders obvious, alone or in combination with other prior art identified in Bio-Rad's Patent Local Rule invalidity contentions, the Asserted Claims at least as described by illustrative examples, below. These invalidity contentions are not an admission by Bio-Rad that the Accused Products, including any current or past versions of such products are covered by, or infringe these claims, particularly when they are properly construed. Nothing in these contentions should be interpreted as acquiescence to an assertion of a particular claim construction by Plaintiffs.

Claim	Invalidity Analysis
1. A method of detecting the presence or absence of at least seven polynucleotide analytes, in any combination of presence or absence, in a single sample solution volume, the method comprising:	Kramer and Larson teach detecting the presence or absence of multiple analytes in a single sample solution, including detecting multiple analytes in a single optical channel: Kramer teaches an "invention [that] relates to homogenous in vitro multiplexed assays, including particularly homogeneous amplification assays, for screening biological samples for the presence of any of a large number of nucleic acid sequences." Kramer ¶ 1, *see also* Fig. 3 (depicting results from an exemplary assay for multiplex detection).

Claim	Invalidity Analysis
	 FIGURE 3 Kramer teaches exemplary "panels" of possible probes in "codebooks" that may be employed to correspond to individual target analytes based on a number of fluorophores each probe will be labeled with. Kramer ¶ 32, Fig. 1. The number of probes in a given codebook can be expanded by using probes that have different numbers of fluorophores (optimally one to four) in a single assay and such probes may be coded by "ratio coding" i.e., coding targets with more than one identical fluorophore to differentiate with other targets by intensity. *See id.* Larson similarly teaches methods using labeled probes comprising fluorophores to detect multiple polynucleotide analytes. *See, e.g.*, Larson ¶ ¶ 34, 35, 150, 156, Figs. 14, 15, 17. Larson Fig. 15 depicts a 9-plex dPCR assay for spinal muscular atrophy with only two fluorophores, showing the process of optimizing droplet intensities. Figs. 15a and 15b show 2-D histograms of droplet fluorescence intensity,

Claim	Invalidity Analysis
	shown as heat maps with hotter colors representing higher droplet counts, for the 9-plex assay against the synthetic model chromosome ((a)=Before optimization; (b)=after optimization). *see* ¶¶ 35, 150 (describing Fig. 15]  FIG. 15 To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
a) providing a sample solution volume	Kramer and Larson teach providing a sample solution volume: "Assays according to this invention are homogeneous nucleic acid in vitro assays fluorescently labeled utilizing hybridization probes. By "homogeneous'. I mean that nucleic acid targets are detected in solution without segregating targets spatially and without washing away unbound hybridization probes." Kramer ¶ 9. That is to say, the sample is in a solution volume.

Claim	Invalidity Analysis
	Additionally, "[k]its may include additional assay reagents such as enzymes, amplification buffer and, if desired, sample preparation reagents for isolation of nucleic acids; that is, up to all reagents needed for performing the assay, from sample preparation through detection." Kramer ¶ 19. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
comprising or potentially comprising, at least one of at least seven polynucleotide analytes, and	Kramer and Larson teach a sample solution volume comprising or potentially comprising at least one of at least seven polynucleotide analytes: Kramer teaches assays according to the invention that are "capable of detecting any of at least six, preferably at least 10, and in certain embodiments 30-60 and even more possible target sequences." Kramer ¶ 8. For example, using four fluorophores and only probes that comprise two fluorophores per probe, without ratio coding, Kramer disclose six unique probe combinations representative of target analytes that may be detected (ab, ac, ad, bc, bd, and cd, each of a, b, c, and d representing a unique fluorophore). Kramer ¶ 22, 30-32, Fig. 1. Kramer further teaches that single-labeled probes may be used, such as a, b, c, and d, which would equal a total of ten unique probes before addition of ratio coding or coding with three fluorophores per probe (which would add another four unique probe combinations without ratio coding). *See id.* A POSA would have understood Kramer teaching using multiple colors and intensities, providing for distinctly identifying more polynucleotide analytes than colors, to teach or suggest an assay including up to at least seven polynucleotide analytes. Larson illustrates, as was known in the art, higher-plex assays for seven or more polynucleotide analytes. For example, Larson teaches a "9-plex assay for certain SMA related targets was also demonstrated with just two colors (probes containing FAM and VIC fluorophores)." Larson ¶ 150, Fig. 15. Thus, Larson would enable a POSA to generate even more unique probes than based solely on combinatorial signals as described in the "code books" in Kramer by allowing a POSA to differentiate between targets using the same fluorophore(s) as a code.

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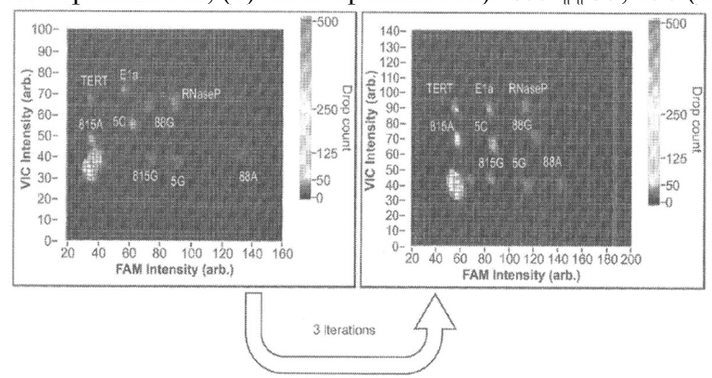
	Larson similarly teaches methods using labeled probes comprising fluorophores to detect multiple polynucleotide analytes. *See, e.g.*, Larson ¶ ¶ 34, 35, 150, 156, Figs. 14, 15, 17. Larson Fig. 15 depicts a 9-plex dPCR assay for spinal muscular atrophy with only two fluorophores, showing the process of optimizing droplet intensities. Figs. 15a and 15b show 2-D histograms of droplet fluorescence intensity, shown as heat maps with hotter colors representing higher droplet counts, for the 9-plex assay against the synthetic model chromosome ((a)=Before optimization; (b)=after optimization). *see* ¶¶ 35, 150 (describing Fig. 15]  FIG. 15 To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
comprising at least seven hybridization probes, each hybridization probe corresponding to one of the at least seven polynucleotide analytes,	Kramer and Larson teach using at least seven hybridization probes that each correspond to one of the polynucleotide analytes:

Claim	Invalidity Analysis
	Kramer teaches assays according to the invention wherein "[e]ach probe is specific to one target among the multitude of possible targets being screened." Kramer ¶ 10. These probes may be "fluorescently labeled hybridization probes." *Id.* ¶ 5, *see also* ¶¶ 9-10, 15, 16. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
wherein each hybridization probe comprises at least one fluorophore selected from four fluorophores, and	Kramer and Larson teach the use of multiple fluorophores in an assay: Kramer recites that the code possibilities for the assays described by the invention "include up to four different fluorophore per code element. The different fluorophores are from a panel of at least four distinguishable fluorophores." Kramer ¶ 11. Further Kramer discloses that the probes may be labeled with between one to four unique or identical fluorophores in varying combinations "[t]he combinatorial code may be duplex coding in which the code elements comprise two colors, optionally enlarged by additional code elements of one color. The combinatorial code may by triplex coding in which the code elements comprise three colors, optionally enlarged by additional code elements of two colors (triplex code combined with a duplex code), and optionally enlarged by code elements of one color. The combinatorial code may be quadraplex coding in which the code elements comprise four colors, optionally enlarged by additional code elements of three colors, two colors or one color, or some combination thereof." *Id.* To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
wherein each hybridization probe, when excited and when contacted with its corresponding polynucleotide analyte, generates a cumulative intensity signal,	Kramer and Larson teach the use of hybridization probes that when contacted with their corresponding polynucleotide analyte generate a cumulative intensity signal:

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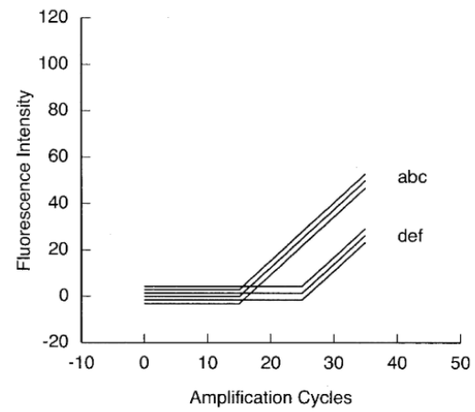
	Kramer discloses generating cumulative intensity signals from labeled probes when they are hybridized to their corresponding polynucleotide targets. Kramer ¶¶ 24-26, Figs. 2-4. Specifically, for example, Figure 3 shows two targets present at different concentrations (as one probe appears after more amplification cycles), one detected by a probe labeled with "abc" the other with "def" fluorophores, the signal of each probe being the cumulative signal representative of each target, "abc" for a first target and "def" for target two. *See id.*  FIGURE 3 To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.

Claim	Invalidity Analysis
further wherein each generated cumulative intensity signal comprises at least one signal generated by excitement of at least one of the four fluorophores;	Kramer and Larson teach cumulative intensity signals comprising at least one signal generated by excitement of at least one of the four fluorophores: Kramer discloses, as described above, the use of one to four fluorophores per probe and per polynucleotide target. *See supra*. Further, Kramer discloses that the signal may be generated by excitation of at least one fluorophore: "[a]mplification assays with real-time detection can be performed on a variety of instruments that utilize different techniques for exciting fluorophores and detecting emissions. Excitation can be by lasers, white light coupled with filters, or light-emitting diodes." Kramer ¶ 38. Kramer Figures 2-5 also illustrate fluorescence emissions of fluorophores from probes, with each probe, i.e., each cumulative intensity signal generator, comprising excitement of at least one fluorophore. Kramer ¶¶ 23-26, Figs. 2-5. For example, Figure 3 shows a cumulative intensity signal "abc" that is generated by excitement of fluorophores a, b, and c.

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	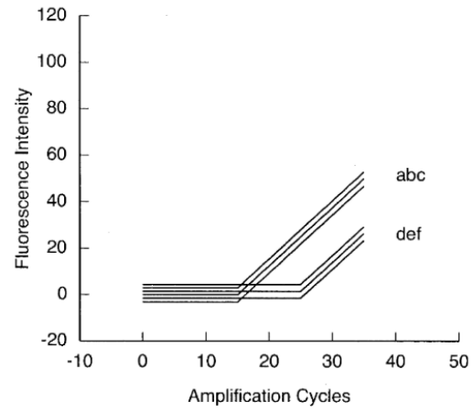 FIGURE 3 To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
b) contacting said sample solution volume with the plurality of hybridization probes and	Kramer and Larson teach contacting the sample solution volume with the plurality of hybridization probes: Kramer discloses the use of oligonucleotide probes that may be "species-specific." Kramer ¶ 43, 47. These probes may be "nucleic acid hybridization probes," i.e. probes that require contact to bind to their corresponding target and emit a fluorescence. Kramer ¶¶ 10.

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	When a single target sequence is present, Kramer teaches an exemplary assay wherein "one probe (labeled with three different colors of equal fluorescence intensity) among the many different probes in the assay mixture binds to the amplified target sequence." Kramer ¶ 23. To the extent it is argued that Kramer does not teach this limitation, a POSA would have understood it to be known in the art to do so, as evidenced by Larson. Larson discloses solutions comprising target-specific probes that hybridize to target sequences, and merging these solutions with sample fluid droplets, containing the target polynucleotide(s). Larson ¶¶ 68 ("A [first sample fluid] droplet containing the nucleic acid is then caused to merge with the PCR reagents in the second [sample] fluid as described above, producing a droplet that includes Taq polymerase, deoxynucleotides of type A, C, G and T, magnesium chloride, forward and reverse primers, detectably labeled probes, and the target nucleic acid."), 74 ("a first droplet formation module produces the sample droplets consistent with limiting or terminal dilution of target nucleic acid….The second droplet also includes detectably labeled probes for detection of the amplified target nucleic acid."). To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
exciting the 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	Kramer and Larson teach exciting hybridization probes to generate cumulative intensity signals to show the presence of polynucleotide analytes: Kramer discloses, as described above, exciting fluorophores to generate a cumulative intensity signal, wherein the fluorophores are located on hybridization probes. *See supra*. For example, Kramer Figures 2-5 illustrate fluorescence emissions of fluorophores from probes that have been excited, with each probe, i.e., each cumulative intensity signal generator, comprising excitement of at least one fluorophore. Kramer ¶¶ 23-26, Figs. 2-5. For example, Figure 3 shows a cumulative intensity signal "abc" that is generated by excitement of fluorophores a, b, and c.

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	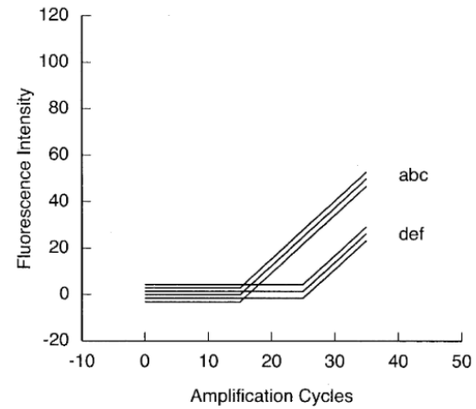 FIGURE 3 Further, Kramer discloses that the signal may be generated by excitation of at least one fluorophore, which, again, is located on the hybridization probes: "[a]mplification assays with real-time detection can be performed on a variety of instruments that utilize different techniques for exciting fluorophores and detecting emissions. Excitation can be by lasers, white light coupled with filters, or light-emitting diodes." Kramer ¶ 38. To the extent it is argued that Kramer does not teach this limitation, a POSA would have understood it to be known in the art to do so, as evidenced by Larson. Larson teaches the excitation of hybridization probes comprising fluorophores using a laser. Larson ¶¶ 156 ("As before with the 5- and 9-plex assays for SMA, TaqMan assays were used with FAM and VIC fluorophores (excited by a 488 nm laser). The fluorescence from the FAM and VIC fluorophores were recorded simultaneously with the fluorescence from the optical labels, requiring modifications to

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	the optical layout of the instrumentation described for the SMA assay (the optical schematic for two-laser excitation and 4-color detection is shown in entirety in FIG. 16"), 195, Fig. 16. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
c) measuring the cumulative intensity signal(s), thereby generating a cumulative signal measurement,	Kramer and Larson teach measuring cumulative intensity signals: Kramer discloses, as described above, generating cumulative intensity signals. *See supra*. Kramer, in describing Figure 2 recites "FIG. 2 is a plot of results that will be obtained in this assay. The 'x' axis represents the number of amplification cycles performed by the time that each measurement of fluorescence is made. This measurement is made automatically by the assay instrument in a manner that permits the fluorescence intensity of each of the differently colored fluorophores that are used to label the probes to be measured. The 'y' axis represents the fluorescence intensity due a particular colored fluorophore. Measurements are taken during the annealing phase of each amplification cycle. Measurements are taken in real time during each amplification cycle throughout the course of the amplification. The fluorescence intensity of each of the differently colored fluorophores used to label the probes is plotted as a function of the number of amplification cycles completed." Kramer ¶ 43, Fig. 2. Further, relating to Figure 4, Kramer describes that signal measurements in different fluorophores may be cumulative across different probes to generate a cumulative signal, even when probes comprise an identical fluorophore, as is the case in Figure 4, where the analytes present both comprise a "c" fluorophore, as is apparent by its accelerated increase in fluorescence at amplification cycle ~25 when the "cde" probe becomes detectable above noise fluorescence. Kramer ¶¶ 25, 46, Fig. 4.

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	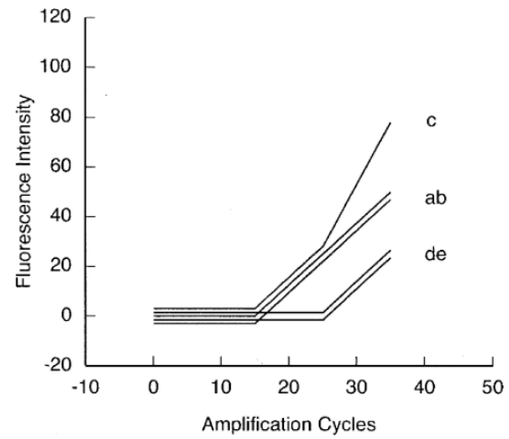 FIGURE 4 To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
wherein the cumulative signal measurement non-degenerately indicates the presence or absence of the at	Kramer and Larson teach cumulative intensity signal measurements that non-degenerately represents the presence or absence of polynucleotide analytes in any combination of presence or absence:

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least seven polynucleotide analytes, in any combination of presence or absence,	Kramer teaches assays and methods of designing assays to generate non-degenerate results in any combination of presence or absence. For example, Figure 5 depicts an unambiguous result of two targets in presence in combination. Kramer ¶¶ 26 Fig. 5. Kramer further teaches methods wherein probes with different numbers of unique fluorophores are used, "[the] combinatorial code may be quadraplex coding in which the code elements comprise four colors, optionally enlarged by additional code elements of three colors, two colors or one color, or some combination thereof," Kramer ¶ 11, and further methods wherein the targets are labeled with differing amounts of common fluorophores to differentiate between targets, "[i]n ratio coding differing amounts of the same label are used for differentiation. Combinatorial codes according to this invention may be augmented with ratio coding, preferably integral ratio coding, that is, ratios of whole numbers such as 2:1, 3:1, 4:1 or 5:1, and vice versa." Kramer 14. Each of these methods can be used to increase the "spatial segregation" between the targets and combinations thereof. Kramer ¶ 3. Further, to the extent it is argued Kramer does not teach the measurement of cumulative intensity signal measurements that non-degenerately represent the presence of polynucleotide analytes, Larson teaches non-degenerate detection of nine polynucleotide analytes. FIG. 15 depicts non-degenerately indication of nine (9) polynucleotide analytes using two colors. Larson ¶¶ 35, 150, Fig. 15. Larson further teaches that "adding extra colors increase the capability [of the assay]," Larson ¶ 153, and would do so "geometrically," Larson ¶ 47, i.e., would allow resolution in greater "spatial segregation" of the targets. Kramer ¶ 3. Larson teaches that "multiplexing capacity exceeding 50x can be envisioned" using well-known methods to overcome the difficulties associated with the use of more colors. Larson ¶ 153. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
wherein said method non-degenerately detects the presence or absence of the at least seven polynucleotide	Kramer and Larson teach the non-degenerate detection of the presence or absence of polynucleotide analytes in a sample solution volume, in any combination of presence or absence:

Claim	Invalidity Analysis
analytes in said single sample solution volume, in any combination of presence or absence,	*See supra*, generally; *see also supra*, preamble. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
without requiring any step of immobilization of said polynucleotide analytes, physical separation of said polynucleotide analytes, or mass spectrometry.	Kramer and Larson teach the performance of the described assays without immobilization, physical separation or mass spectrometry: Kramer recites "[a]ssays according to this invention are homogeneous nucleic acid in vitro assays fluorescently labeled utilizing hybridization probes. By "homogeneous'. I mean that nucleic acid targets are detected in solution without segregating targets spatially and without washing away unbound hybridization probes." Kramer ¶ 9. Kramer further describes the detection of multiple polynucleotide analytes in a single sample solution, thus not requiring physical separation. *See, e.g.*, Kramer ¶¶ 5, 25, 46, Fig. 4. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
2. The method of claim 1, wherein said hybridization probes comprise an identical fluorophore, and wherein said plurality of hybridization probes are specific for different polynucleotide analytes.	Kramer and Larson teach the use of hybridization probes that each include an identical fluorophore and are specific for different polynucleotide analytes: Kramer teaches a method for performing an assay wherein a common fluorophore is used on each probe to optimize probe fluorescence emissions: "one option is to utilize a common short-wavelength fluorophore (which I call the 'harvester' fluorophore), vary the long wavelength fluorophores (which I call the 'emitter' fluorophores), and detect the signal change in the latter. In that case, each portion will emit a signal in a different color. Another option is the reverse, namely, to use a common emitter fluorophore, vary the harvester fluorophores, and detect the signal change in the latter." Kramer ¶ 13.

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	To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
3. The method of claim 1, wherein said detecting is performed with a plurality of hybridization probes comprising different fluorophores, wherein said plurality of hybridization probes are specific for different analytes	Kramer and Larson teaches the use of hybridization probes that comprise different fluorophores that are specific to different analytes: *See supra* Claim 1, describing hybridization probes. *See supra* Claim 2, describing the six exemplary hybridization probes each specific for different analytes comprising between one to four unique and total fluorophores. *See* Kramer Figs. 1-8 (depicting various combinations of multiply-labeled fluorophores and results of assays wherein such fluorophores are employed). Kramer further recites that the use of probes comprising different fluorophores (colors) "'[c]odebooks' useful in this invention utilize four colors per probe, three colors per probe, two colors per probe, or combinations of four, three or two colors per probe, with or without single-color probes." Kramer ¶ 32. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
4. The method of claim 1, wherein said cumulative intensity signal(s) are generated during a polymerase chain reaction.	Kramer and Larson teaches cumulative intensity signals that are generated during a polymerase chain reaction: Kramer discloses that "measurements are taken during the annealing phase of each amplification cycle." Kramer ¶ 43. It is further apparent from, for example, Figure 2, that measurements of cumulative intensity signals are taken during "amplification cycles."

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	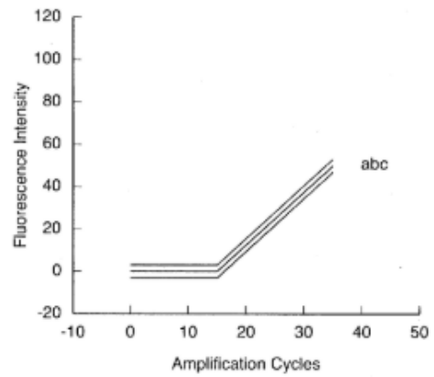 FIGURE 2 Kramer also recites that "amplification of target sequences [may be performed] by any of several amplification techniques, for example, PCR." Kramer ¶ 2, *see also* Kramer ¶ 9, 16. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
5. The method of claim 1, further comprising transmitting information concerning the presence or	Kramer and Larson teach transmitting information concerning the presence or absence of polynucleotide analytes through a computer network:

Claim	Invalidity Analysis
absence of said polynucleotide analytes through a computer network.	Kramer depicts a number of images that would require a computer to generate. *See e.*g., Kramer Figs. 2-5, 7-8. Further, Kramer explicitly teaches that "results of these assays can be automatically decoded and interpreted by computer programs in real time, enabling the assays to be highly accurate, and to be carried out in an automated, high-throughput fashion in clinical diagnostic settings." Kramer ¶ 20. Work in a clinical diagnostic setting would require transmission of data among different doctors, labs, etc. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
6. The method of claim 1, further comprising providing information concerning the presence or absence of said polynucleotide analytes to a health care professional, wherein the health care professional makes a clinical decision based on said information.	Kramer and Larson teach providing information concerning the presence or absence of polynucleotide analytes to a healthcare professional to make a clinical decision: As discussed above, Kramer and Larson teach transmitting information concerning the presence or absence of polynucleotide analytes through a computer network and that it may be done in "clinical diagnostic settings." *See supra* Claim 5. Larson specifically discloses that "methods of the invention may be used to monitor a patient for recurrence of a cancer." Larson ¶ 177. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
7. The method of claim 1, wherein at least one step of said method is performed using a computer.	Kramer and Larson teach performing at least one step of said method using a computer: Kramer depicts a number of images that would require a computer to generate. *See e.*g., Kramer Figs. 2-5, 7-8. Further, Kramer explicitly teaches that "results of these assays can be automatically decoded and interpreted by

Claim	Invalidity Analysis
	computer programs in real time, enabling the assays to be highly accurate, and to be carried out in an automated, high-throughput fashion in clinical diagnostic settings." Kramer ¶ 20. Larson similarly discloses that a computer is used for droplet detection, stating that "suitable detection apparatuses include … processors (e.g., computers and software)." Larson ¶ 89. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
8. The method of claim 7, wherein said computer is located on a remote server.	Kramer and Larson teach performing at least one step of said method using a computer located on a remote server: Kramer depicts a number of images that would require a computer to generate. *See e.*g., Kramer Figs. 2-5, 7-8. Further, Kramer explicitly teaches that "results of these assays can be automatically decoded and interpreted by computer programs in real time, enabling the assays to be highly accurate, and to be carried out in an automated, high-throughput fashion in clinical diagnostic settings." Kramer ¶ 20. A POSA would understand that a computer to be used in a clinical diagnostic setting may be connected to a remote server, such as a hospital server. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.
9. The method of claim 7, wherein said computer is located on a thermal cycler.	Kramer and Larson teach performing at least one step of said method using a computer located on a thermal cycler: Kramer discloses an exemplary method for performing the assay that includes the use of "thermal cycling." Kramer ¶¶ 16, 20. In addition, Kramer teaches explicitly that "results of these assays can be automatically decoded and

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	interpreted by computer programs in real time, enabling the assays to be highly accurate, and to be carried out in an automated, high-throughput fashion in clinical diagnostic settings." Kramer ¶ 20. To the extent Kramer and Larson is argued by Plaintiffs or found by the Court to not explicitly teach certain limitations in the asserted claims, such limitations would have been inherent and/or obvious as described in Bio-Rad's invalidity contentions.