IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF DELAWARE

AGILENT TECHNOLOGIES, INC.,	)	
	)	
Plaintiff,	)	
	)	
v.	)	C.A. No. _____
	)	
AXION BIOSYSTEMS, INC.,	)	**DEMAND FOR JURY TRIAL**
	)	
Defendant.	)	

COMPLAINT

Plaintiff, Agilent Technologies, Inc. ("Agilent"), for its Complaint against defendant, Axion BioSystems, Inc. ("Axion" or "Defendant"), requests a trial by jury and alleges as follows:

1. This is an action for patent infringement, as well as for unfair competition under the Lanham Act.

2. Agilent alleges that Axion infringes U.S. Patent Nos. 7,192,752 ("the '752 Patent") (Exhibit A), 7,468,255 ("the '255 Patent") (Exhibit B), and 8,026,080 ("the '080 Patent") (Exhibit C) (collectively, "the Asserted Patents").

3. The '752 Patent, entitled "Real Time Electronic Cell Sensing Systems and Applications for Cell-Based Assays," is directed to the invention of researchers Xiao Xu, Yama Abassi, Xiaobo Wang, and Jiangbo Gan, each of whom is listed as a named inventor.

4. The '255 Patent, entitled "Method for Assaying for Natural Killer, Cytotoxic T-Lymphocyte and Neutrophil-Mediated Killing of Target Cells Using Real-Time Microelectronic Cell Sensing Technology," is directed to the invention of researchers Xiao Xu, Yama Abassi, and Xiaobo Wang, each of whom is listed as a named inventor.

5. The '080 Patent, entitled "Real Time Electronic Cell Sensing System and Applications for Cell-Based Assays," is directed to the invention of researchers Xiaobo Wang, Yama Abassi, Xiao Xu, and Jiangbo Gan, each of whom is listed as a named inventor.

6. Agilent alleges that Axion: (1) directly infringes one or more method claims of the Asserted Patents by performing infringing methods for impedance-based cell analysis; (2) induces at least its customers to infringe one or more method claims of the Asserted Patents by its acts, including its instructions in combination with sale, offer for sale, and/or importation of at least the Maestro platforms, and CytoView-Z Plates, and AxIS Z software to perform impedance-based analysis; and (3) contributes to infringement of one more method claims of the Asserted Patents by its sale, offer for sale, and/or importation of at least the CytoView-Z Plates for use in such patented methods for impedance-based analysis. Agilent seeks damages and other relief for Axion's infringement of the Asserted Patents.

7. ACEA Biosciences, Inc. ("ACEA"), where the named inventors were employed at the time of the invention, invested substantial effort to invent methods for measuring and analyzing impedance of cells distributed in wells of a multi-well plate to improve researchers' ability to analyze cell behavior such as cancer cell death in response to cytotoxic immune cells and/or therapies in real-time. Agilent acquired ACEA in 2018 and has continued to invest substantial resources in developing this technology. Over the years, around 4,500 papers have cited Agilent's impedance technology, with 690 references cited in 2021 alone. The Asserted Patents are just three of Agilent's patents in this innovative area. Axion performs infringing methods, and induces and contributes to infringement of method claims of the Asserted Patents by at least Axion's customers.

8. This is also an action, in part, for unfair competition under the Lanham Act, 15 U.S.C. § 1125(a), arising out of Axion's false and misleading advertising appearing at least on

Axion's website and, upon information and belief, that Axion has presented elsewhere to audiences including, but not limited to, prospective customers. Axion's website and materials made available on its website and, upon information and belief, to prospective customers and other audiences, falsely and misleadingly state that Axion's Maestro platform combined with CytoView-Z plates can make accurate measurements of the impedance of three-dimensional (3D) balls or structures of cells known as "spheroids." Axion's statements are false and misleading because Axion's products cannot accurately measure the impedance of spheroids and, upon information and belief, the impedance measured by Axion's products reflects the impedance of cells attached to a substrate, not a 3D spheroid.

9. Axion's statements are false and misleading to customers looking to purchase systems that can provide real-time high throughput impedance measurement. Axion's false and misleading statements that its products can accurately measure impedance of 3D spheroids deceives customers and creates confusion in the marketplace about the performance, capabilities, and appropriate use of these products and has harmed and will continue to harm Agilent.

THE PARTIES

10. Agilent is a corporation organized and existing under the laws of the State of Delaware with its principal place of business at 5301 Stevens Creek Boulevard, Santa Clara, California 95051.

11. Agilent is a world-leading supplier in life sciences, diagnostics and applied chemical markets. Agilent advances quality of life with a broad range of high-quality solutions to customers in 110 countries. For example, Agilent provides laboratories with instruments, services, consumables, applications, and expertise, enabling customers to achieve their research, production, therapeutic, and discovery goals. Agilent instruments, software, and sample preparation solutions help scientists at top-tier universities conduct faster, more accurate research

to learn more about cancer, cardiovascular diseases, diabetes, Alzheimer's, Parkinson's, autism, and other ailments. Agilent solutions further help pathology laboratories deliver fast, accurate information to the physicians, hospitals, and medical centers they serve. Agilent solutions also provide precise answers for every segment of the pharmaceutical industry, from disease research and drug discovery to drug development, manufacturing, and quality control.

12. Agilent is the owner by assignment of the Asserted Patents and holds all rights necessary to bring this action.

13. On information and belief, Axion is a corporation organized under the laws of the State of Delaware with a principal place of business at 1819 Peachtree Road Northeast, Suite 350, Atlanta, Georgia, 30309-1855. Axion has committed and continues to commit acts of infringement throughout the United States, including, on information and belief, in the District of Delaware, including but not limited to the sales of products in this judicial district and active steps to induce the infringement of its customers in this district.

14. Axion resides in the District of Delaware at least because it is incorporated in Delaware.

JURISDICTION AND VENUE

15. This is an action arising under the patent laws of the United States, 35 U.S.C. §§ 271, *et seq*. and under the Lanham Act, 15 U.S.C. § 1125(a). Accordingly, this Court has subject matter jurisdiction pursuant to 28 U.S.C. §§ 1331 and 1338(a).

16. This Court has personal jurisdiction over Axion due, *inter alia*, to its incorporation in Delaware, and its continuous presence in, and systematic contact with, Delaware. Axion is further subject to this Court's jurisdiction, upon information and belief, at least because of Axion's substantial business in Delaware, including at least part of its past infringing activities and false advertising at issue in this action, regularly doing or soliciting business in Delaware, and engaging

in persistent conduct and/or deriving substantial revenue from goods and services provided in Delaware. Upon information and belief, Axion, directly and/or through intermediaries, has committed and continues to commit acts of infringement in Delaware by, among other things, performing and inducing performance of, and contributing to performance of methods that infringe one or more method claims of the Asserted Patents.

17. Venue is proper in Delaware pursuant to 28 U.S.C. §§ 1391(b) and (c), and 1400(b), at least because Axion is incorporated in the State of Delaware and, upon information and belief, has committed acts of infringement and false advertising in Delaware.

FACTUAL ALLEGATIONS

Technology Underlying Patent Infringement Claims

18. Bioelectronics is an interdisciplinary field that involves the integration of biomaterials with electronic devices. Bioelectronic methods can be used to analyze cells and assaying biological molecules and cells. In one application, cells can be cultured on microelectrodes, and cell-electrode impedance can be measured to monitor cellular changes.

19. Bioelectronics provide benefits in several types of scientific studies, including but not limited to studies of immune-mediated cell activation and/or cytotoxicity, anticancer drug screening and discovery, and excitable cells such as cardiomyocytes in response to drugs and/or other environmental manipulation.

20. ACEA sought and obtained patent protection for its inventions in the field of bioelectronics.

The '752 Patent

21. The United States Patent and Trademark Office ("USPTO") duly and legally issued the '752 Patent, after a full and fair examination, on March 20, 2007.

22. The '752 Patent claims inventions that provide high-throughput methods for monitoring cell-substrate impedance. Claim 11 of the '752 Patent is directed to a method of performing an assay that monitors cell-substrate impedance, including the steps of providing a system for monitoring cell-substrate impedance that comprises a multi-well device for monitoring impedance, wherein each well has an electrode array at the bottom of the well and the electrode resistances between two locations do not differ by more than 30%; an impedance analyzer; a device station for connecting the electrode arrays to the impedance analyzer; and software to control and record data; introducing cells into wells of the multi-well plate; and monitoring cell-substrate impedance. Exhibit A at Claim 11.

23. At the time of the invention of the '752 Patent, conventional methods for measuring immunoglobulin ("Ig") E-mediated signaling were based on taking destructive endpoint assays of the IgE-mediators in a particular well. *See id.* at 3:14–21. Similarly, conventional methods for determination of time dependent IC50 values for potential anticancer drugs also were based on taking endpoint assays. *Id.* at 3:34–39. This dependence on endpoint assays significantly limited the ability of conventional methods to screen large chemical libraries, or to provide increased time and dosing resolution. *Id.* at 3:17–21; 38–42. Thus, conventional methods did not provide for a method of measuring either IgE-mediated signaling or cytolytic activity in real-time.

24. The claims of the '752 Patent recite inventive concepts that were not routine or conventional use of computer components, but, instead, provided a novel solution to these discrete, technological problems by providing the patented inventions for performing non-destructive assays utilizing measurements of electrical impedance in separated wells of a multi-well plate,

allowing for label-free monitoring the desired parameters (such as IgE-mediated signaling or cancer cell cytolysis) on a real-time basis.

25. Claim 11 of the '752 Patent is directed to a method of performing an assay, the requirements of which are reproduced below:

> A method of performing an assay that monitors cell-substrate impedance, comprising:
>
> providing a system for monitoring cell-substrate impedance, comprising:
>
> a) one or more multiple well cell-substrate impedance monitoring devices, wherein at least two of the multiple wells of said device comprise an electrode array at the bottom of the well, wherein said electrode array is individually addressed, further wherein said device can be used to measure differences in impedance values that relate to cell behavior;
>
> b) an impedance analyzer;
>
> c) a device station comprising electronic circuitry that can engage said device and selectively connect said two or more electrode arrays of said device to said impedance analyzer; and
>
> d) a software program that can control said device station and record and analyze data obtained from said impedance analyzer;
>
> wherein said electrode array has an approximately uniform electrode resistance distribution across said electrode array so that the electrode resistances between two locations on said array do not differ by more than 30%;
>
> introducing cells into at least one well of said system;
>
> monitoring cell-substrate impedance of said at least one well.

26. Claim 11 and the other method claims of the '752 Patent are directed to particular methods for solving this technological problem that conventional assays could only provide endpoint analysis and not provide information on a real-time basis, by using the non-conventional technique of monitoring the cell-substrate impedance in a well by using an electrode array with an approximately uniform electrode resistance distribution. The method claims of the '752 Patent are not directed to an abstract idea or law of nature, do not preempt natural laws, and otherwise satisfy all requirements of 35 U.S.C. § 101.

The ’255 Patent

27. The USPTO duly and legally issued the ’255 Patent, after a full and fair examination, on December 23, 2008.

28. The ’255 Patent claims inventions that provide high-throughput methods for measuring cytolytic activity of effector cells (e.g., immune cells such as T-cells and Natural Killer T cells) on target cells in real time. The claimed methods involve adding target cells (e.g., cancer cells) and effector cells (e.g., immune cells with cytolytic activity) to test wells on a multi-well plate and measuring impedance. *See* Exhibit B at Claim 9. The impedance measured in test wells is compared to the impedance of control wells, which only contain target cells. *Id.* Viability of the target cells, i.e., the cytolytic activity of the effector cells, is then determined at a given time point. *Id.*

29. At the time of the invention of the ’255 Patent, conventional methods for measurement of cytolytic activity of effector cells were based on taking destructive “snapshots” of the cytolytic activity in a particular well. *Id.* at 3:50–4:10. Further, the most popular prior art method involved the use of radioactive chromium-51 labeling, which was both cumbersome due to the radioactivity, and limited to analysis of approximately four hours after labeling. *Id.* Thus, prior art methods did not provide for a method of measuring cytolytic activity in real-time, or through an extended duration of more than four hours.

30. The claims of the ’255 Patent solved these discrete, technological problems by providing the claimed apparatus and method for performing real-time label-free measurements of electrical impedance in each well, and describing methods of correlating the impedance measurements to the cytolytic activity for natural killer, cytotoxic T-lymphocyte and neutrophil mediated killing of target cells. *See id.* at 5:6–13; claim 9.

31. Claim 9 of the ’255 Patent is directed to a method of performing an assay, the requirements of which are reproduced below:

> A method of measuring cytolytic activity comprising:
>
> a) providing a device capable of monitoring cell-substrate impedance operably connected to an impedance analyzer, wherein said device comprises two or more wells for receiving cells;
>
> b) adding target cells to at least two wells, wherein at least one well is a control well and at least one well is a test well;
>
> c) adding effector cells to said test well;
>
> d) monitoring impedance of said control and said test wells before and after adding said effector cells and optionally determining a cell index from said impedance, wherein said monitoring said impedance comprises measuring said impedance during at least two time points; and
>
> e) determining viability of said target cells in said test well at a given time point after said adding effector cells by comparing said impedance or optionally said cell index of said test well to said control well at said given time point.

32. Claim 9 and the other method claims of the ’255 Patent are directed to a particular solution to the technological problem of determining cytolytic activity on a real-time basis, by using the non-conventional technique of performing non-destructive impedance measurements on at least one control and one test well for at least two time points, and determining the viability of the target well by comparing the measurements to the control well. The method claims of the ’255 Patent are not directed to an abstract idea or law of nature, and they satisfy the requirements of 35 U.S.C. § 101.

The ’080 Patent

33. The USPTO duly and legally issued the ’080 Patent, after a full and fair examination, on September 27, 2011.

34. The ’080 Patent claims inventions that provide high-throughput methods for monitoring cell-substrate impedance. Claim 1 of the ’080 Patent is directed to a method of

performing an assay that monitors cell-substrate impedance, including the steps of providing a system for monitoring cell-substrate impedance that comprises a multi-well device for monitoring impedance, wherein at least two of the wells have an individually addressed electrode array at the bottom of the well and each electrode array comprises two electrode structures of multiple electrode elements, an impedance analyzer, a device station for connecting the electrode arrays to the impedance analyzer, and software to control the device station and acquire and analyze data from the impedance analyzer; introducing cells into wells of the system; adding at least one test compound to the wells; monitoring cell-substrate impedance before and after adding the test compound(s); and analyzing impedance values and calculating cell index values before and after adding the test compound(s). Exhibit C at Claim 1.

35. At the time of the invention of the ’080 Patent, conventional methods for measuring immunoglobulin (“Ig”) E-mediated signaling were based on taking destructive endpoint assays of the IgE-mediators in a particular well. *See id.* at 3:21–28. Similarly, conventional methods for determination of time dependent IC50 values for potential anticancer drugs also were based on taking endpoint assays. *Id.* at 3:39–45. This dependence on endpoint assays significantly limited the ability of conventional methods to screen large chemical libraries, or to provide increased time and dosing resolution. *Id.* at 3:23–28; 43–47. Thus, conventional methods did not provide for a method of measuring either IgE-mediated signaling or cytolytic activity in real-time.

36. The claims of the ’080 Patent recite inventive concepts that were not routine or conventional use of computer components, but, instead, provided a novel solution to these discrete, technological problems by providing the patented inventions for performing non-destructive assays utilizing measurements of electrical impedance in separated wells of a multi-well plate,

allowing for label-free monitoring the desired parameters (such as IgE-mediated signaling or cancer cell cytolysis) on a real-time basis.

37. Claim 1 of the ’080 Patent is directed to a method of performing an assay, the requirements of which are reproduced below:

> A method of performing a cell-based assay that monitors cell-substrate impedance in response to one or more test compounds, comprising:
>
> (a) providing a cell-substrate impedance monitoring system, comprising:
>
> (i) at least one multiple-well cell-substrate impedance measuring device, wherein at least two of the multiple wells comprise an electrode array at the bottom of the well, wherein each electrode array comprises two electrode structures and each electrode structure comprises multiple electrode elements, further wherein each electrode array is individually addressed;
>
> (ii) an impedance analyzer;
>
> (iii) a device station comprising electronic circuitry capable of engaging said device and selecting and connecting electrode arrays within any of the multiple wells to the impedance analyzer;
>
> (iv) a software program capable of controlling the device station and performing data acquisition and data analysis from said impedance analyzer;
>
> (b) introducing cells into one or more wells of said system that comprise electrode arrays;
>
> (c) adding at least one test compound to said one or more wells;
>
> (d) monitoring cell-substrate impedance of said one or more wells before and after adding said at least one test compound; and
>
> (e) analyzing impedance values and calculating cell index values before and after adding said at least one test compound and providing information about cell responses to said at least one test compound.

38. Claim 1 and the other method claims of the ’080 Patent are directed to particular methods for solving this technological problem that conventional assays could only provide endpoint analysis and not provide information on a real-time basis, by using the non-conventional technique of monitoring the cell-substrate impedance in a well by using an electrode array with an approximately uniform electrode resistance distribution. The method claims of the ’080 Patent are

not directed to an abstract idea or law of nature, do not preempt natural laws, and otherwise satisfy all requirements of 35 U.S.C. § 101.

Axion's Infringing Use of the Patented Technology

39. Beginning at least as early as 2019, Axion began using, marketing, and instructing customers to use infringing methods using the Maestro platform, which includes, at a minimum, the following products, consumables, and software: Maestro Edge, Maestro Pro, Maestro Z, Maestro ZHT, Maestro TrayZ, AxIS Impedance Module/AxIS Z software (whether included with a Maestro device or added in combination), and Cytoview-Z Plates. Upon information and belief, Axion performed infringing methods before releasing these instrumentalities.

40. For example, Axion's Maestro Z and ZHT platforms "offer[] continuous, label-free, impedance-based monitoring of [] cells." Exhibit D (Maestro Z Brochure) at 2; Exhibit E (Maestro ZHT Brochure) at 2. Per Axion, the Maestro Z platform works as follows:

a. "Axion's 384-well and 96-well CytoView-Z plates have a recording electrode embedded in the culture surface of each well (1)."

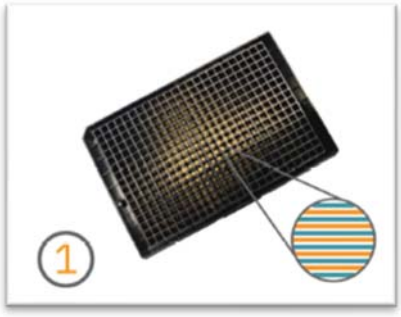
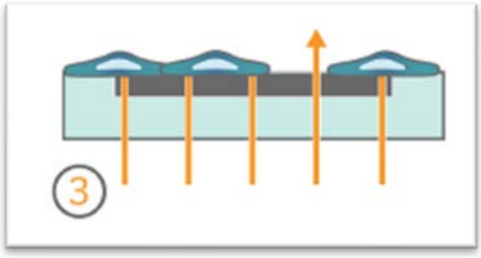


Exhibit E at 2.

b. "The Maestro Z platform uses impedance measurements (ohms, Ω) to quantify the presence of cells on the electrode (2)."

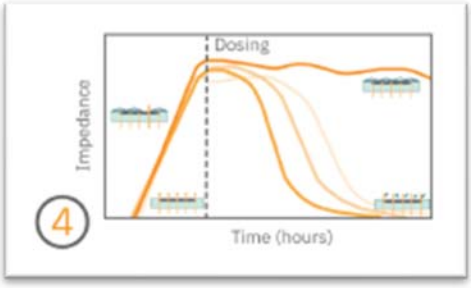
Id.

c. "Impedance measures how much electrical signal (orange arrows) is blocked by the electrode-cell interface (3)."



Id.

d. "When the electrode is uncovered, electrical signal easily passes and the impedance is low. When cells cover the electrode, less electrical signal passes and impedance is high. When cells die or detach, the impedance decreases back toward baseline (4)."



Id.

41. Axion's AxIS Z software provides for "[a]naly[zing] changes in cell proliferation, morphology, and viability in the CytoView-Z plate label-free and in real time." *Id.*

42. Axion touts the Maestro Z and ZHT systems as "the world's most advanced electrode-based real-time cell analysis system," referring to high-throughput plates, continuous cell monitoring, and powerful data analysis. *Id.* at 5; Exhibit D at 5.

Axion's Knowledge of the Asserted Patents

43. Upon information and belief, since at least October 21, 2015, Axion has had specific knowledge of the Asserted Patents as well as other Agilent patents related to the Asserted Patents:

a. Axion cited the '752 Patent and patents related to the '255 Patent and '080 Patent during prosecution of its own patents related to impedance technology. For example, during prosecution of the application that ultimately issued as U.S. Patent No. 9,279,801, entitled "Devices, systems and methods for high-throughput electrophysiology," Axion filed an Information Disclosure Statement with the United States Patent and Trademark Office on October 21, 2015, that identified the '752 Patent and U.S. Patent No. 7,470,533 (the "'533 Patent"). Exhibit F at 1–2. The '255 Patent is a continuation-in-part of the '752 Patent, and the '752 Patent is a continuation-in-part of the '533 Patent. *Id.*; Exhibits A, B. The '080 Patent is a divisional of the '752 Patent and a continuation-in-part of the '533 Patent. Exhibit C.

b. Even before developing the Maestro platform, Axion knew about the technology patented in the Asserted Patents. For example, representatives of Axion attended the Society of Toxicology's 52 Annual Meeting, March 10–14, 2013 in San Antonio, where ACEA presented "the use of the xCELLigence Cardio System to evaluate iCell Cardiomyocytes for sensitivity to compounds with broad mechanisms of action." Exhibit G. Additionally, later in 2013, the American College of Toxicology 34th Annual Meeting in San, Antonio, Texas from November 3–6, 2013 Genentech published an abstract "Comparison of *In Vitro* Cardiac Electrophysiological Assessments on the ACEA xCELLigence and Axion Maestro Platforms." Exhibit H at 59.

Axion and Agilent are direct competitors for the sale of impedance-based cell analysis systems. *See, e.g.*, Exhibit I (website printout of https://www.axionbiosystems.com/resources/news/axion-biosystems-bioelectronic-assays-aid-development-cancer-immunotherapies) (last visited November 17, 2022) (news release in 2021 on Axion's website acknowledging the introduction of the Maestro platform allows Axion to join the "other players in the real-time, live-cell assay space like Sartorius ***and Agilent***,"); Exhibit J (available at https://www.axionbiosystems.com/sites/default/files/2019_callaghan_et_al_modeling_cardiac_complexity.pdf) (last visited November 17, 2022) (third party 2019 article comparing Axion's Maestro system to ACEA Biosciences' (now Agilent's) competing product, the xCELLigence); Exhibit K (available at https://www.axionbiosystems.com/sites/default/files/titmarsh_microfluidics_2014.pdf) (last visited November 17, 2022) (third party 2014 article identifying commercially developed impedance-sensing systems, including Axion and ACEA (later acquired by Agilent)). Upon information and belief, Axion was aware of ACEA's technologies far earlier, as Axion undertook to launch its offerings in the limited market in which Axion and ACEA (now Agilent) competed and continue to compete for sales of products.

c. Moreover, Axion engaged in a course of acquiring personnel from Agilent or its acquired companies in the technology space at issue in this case, to place them in various roles at Axion, ranging from sales to management. Upon information and belief, these personnel acquisitions facilitated the flow of knowledge from Agilent to Axion. For example, In January 2022, Axion introduced David Ferrick as Axion's new Chief Scientific Officer. Exhibit L (website printout of https://www.axionbiosystems.com/resources/news/david-ferrick-announced-new-axion-chief-scientific-officer) (last visited November 17, 2022). Immediately before Dr. Ferrick's

move to Axion, he held the role of Associate Vice President of New Market Development at Agilent. Exhibit M (Ferrick LinkedIn profile). Prior to that role, he was Senior Director of Marketing and Applications at Agilent. *Id.* In each of these roles, on information and belief, Dr. Ferrick obtained knowledge of Agilent's patent portfolio, including the Asserted Patents.

44. Thus, on information and belief, Axion had knowledge of the Asserted Patents, and knew that Axion's use and provision of instructions to use its impedance-monitoring systems infringed one or more claims, including at least claim 11 of the '752 Patent, claim 9 of the '255 Patent, and claim 1 of the '080 Patent, or Axion was willfully blind to such infringement.

Technology Underlying Lanham Act False Advertising Claim

45. Impedance-based analysis of cells involves measuring the change of electrical current flow from one electrode to another. According to Axion, "[t]o measure impedance, small electrical currents are delivered to electrodes embedded in a cell culture substrate. The opposition to current flow from one electrode to another defines the impedance of the cell-electrode interface. When cells are present and attached to the substrate, they block these electrical currents and are detected as an increase in impedance." Exhibit N (website printout of https://www.axionbiosystems.com/technology/impedance-general)(last visited January 24, 2023).

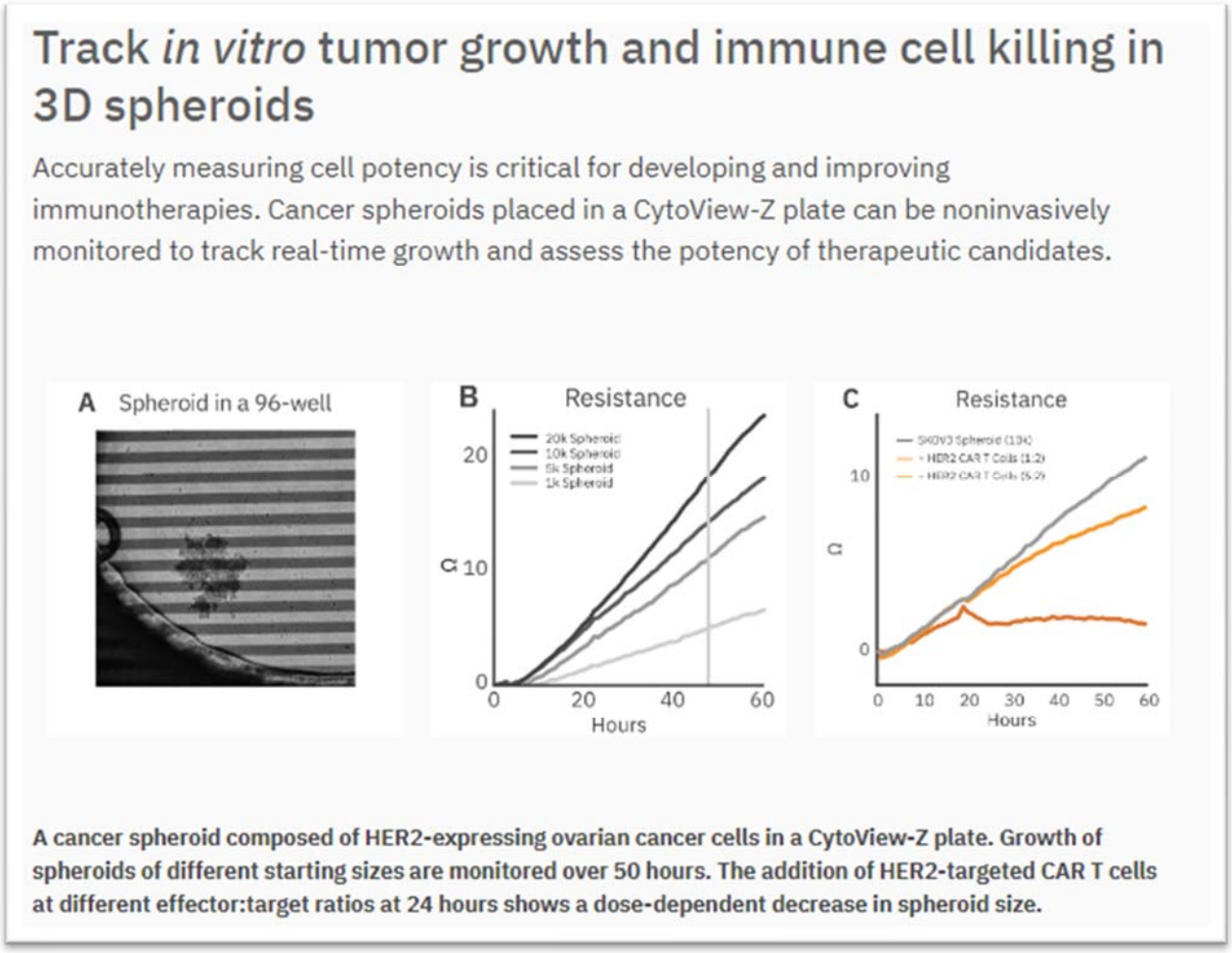
46. Thus, impedance analysis requires "cells [be] present and ***attached to the substrate***." *Id.* (emphasis added). Accordingly, systems for monitoring impedance, including Axion's Maestro platform, generally comprise a surface coated with a substrate such as extracellular matrix that promotes cell attachment and two-dimensional ("2D") monolayer growth of cells. *See, e.g.*, Exhibit O at 1–2 (available at https://www.axionbiosystems.com/sites/default/files/resources/Axion%20Bio%20-%20Cancer%20Spheroids%20-%20Cell%20Culture%20Protocol.pdf) (last visited January 24, 2023).

47. In contrast to 2D growth of cells, cancer cell lines grown in a contact-free or ultra-low attachment environment can produce a 3D cancer spheroid. *See, e.g.*, *id.* at 1 (using "ultra-low attachment (ULA) U-bottom plates" to culture spheroids). Researchers believe that 3D cancer spheroids more closely mimic the complex environment of a solid tumor compared to 2D culture. However, analytical methods that depend on cell-substrate attachment to characterize 2D cell cultures, such as impedance-based analysis, are not suitable for 3D models.

Axion's False Advertising Promoting its Maestro Platform

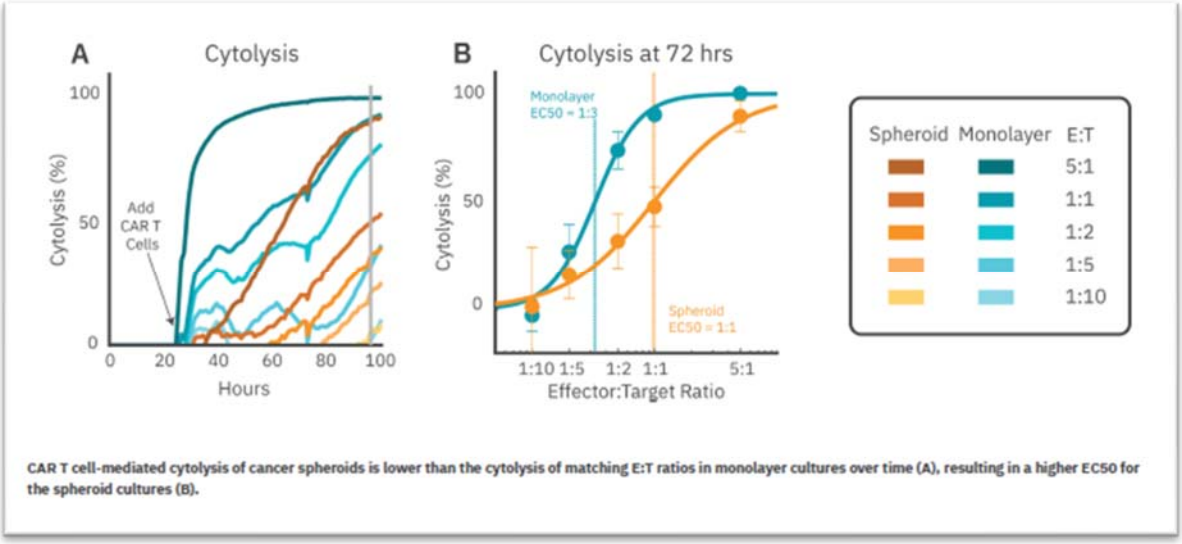
48. Irrespective of the fact that impedance-based analysis requires cells "attached to the substrate," and 3D spheroids are grown in conditions prohibiting attachment, Axion falsely and misleadingly has stated that its impedance platforms can measure impedance of 3D cancer spheroids accurately though its website, presentations, and other marketing activities. *See* Exhibit N; Exhibit P (website printout of https://axionbiosystems.com/applications/oncology/cancer-spheroid) (last visited January 23, 2023); Exhibit O; Exhibit Q (available at https://axionbiosystems.com/sites/default/files/resources/AppNote_CAR%20T%20in%203D%20Cancer%20Spheroids.pdf) (last visited January 23, 2023).

49. Axion's website touts the Maestro Z platform's ability to "accurately measure tumor grown and immune cell killing of 3D cancer spheroid models." Exhibit P at 1. In the screenshot below from Axion's website, Axion purports to identify cancer spheroids plated in a well of a CytoView-Z plate and purports to demonstrate measurement of impedance of these "3D spheroids."



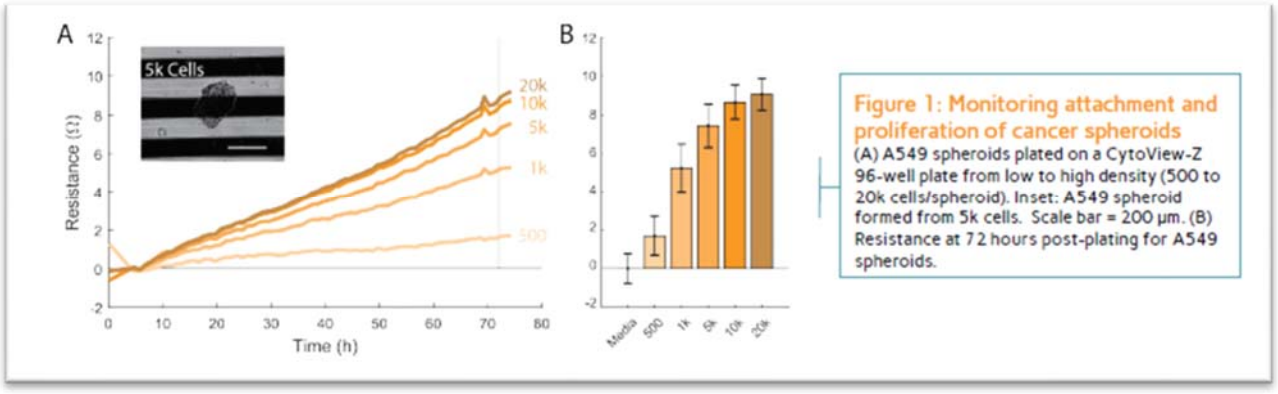
Id.

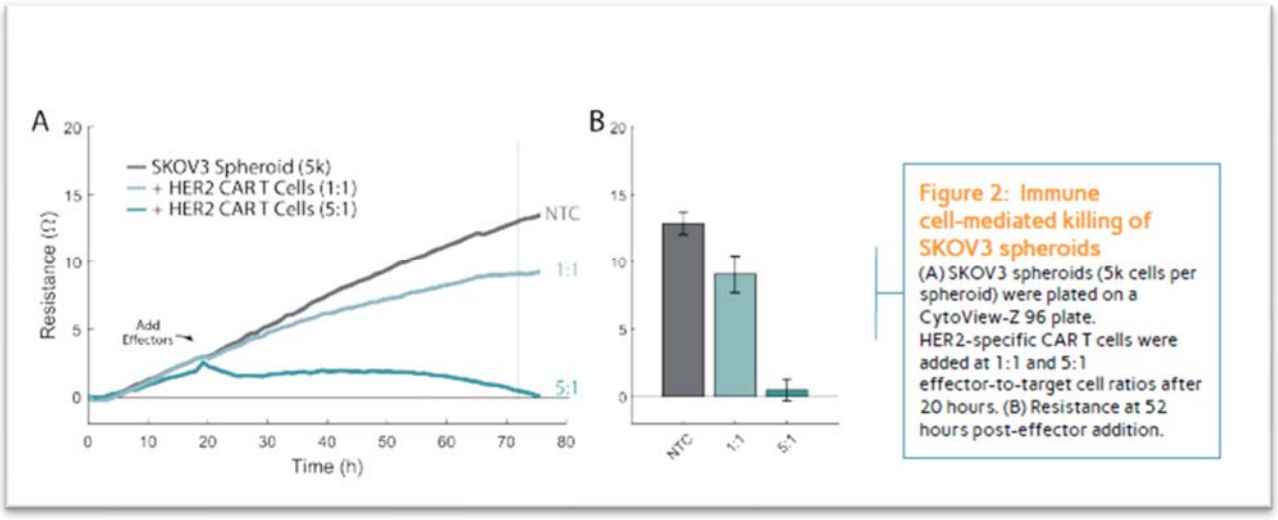
50. Axion further touts this purported ability to measure impedance of 3D cancer spheroids as "closer to complex tumor biology" when compared to 2D monolayer cell cultures, providing the following data purportedly showing the differences in impedance between 3D spheroid and 2D monolayer cell cultures:



Id. at 2.

51. In its cell culture protocol entitled "Cancer Spheroids for the Maestro Z" (hereinafter, "Spheroid Cell Culture Protocol")), Axion purports to instruct customers how to measure impedance of cancer spheroids in CytoView-Z plates on the Maestro Edge, Pro, Z, or ZHT platforms. Exhibit O. Axion's Spheroid Cell Culture Protocol instructs customers to culture spheroids in an "ultra-low attachment (ULA) U-bottom plate," prepare the CytoView-Z plate by adding extracellular matrix to the CytoView-Z plate, "transfer the media with the spheroid into the well of the CytoView-Z plate," and then "[d]ock the plate into the Maestro platform." *Id.* at 1–2. Axion provides figures purporting to demonstrate successful impedance measurement of spheroids on CytoView-Z plates following this Spheroid Cell Culture Protocol:





Id. at 2.

52. Axion's website also features an "Application Note" entitled "CAR T Cell Potency Assessment with 3D Cancer Spheroid Models" (hereinafter, "3D Spheroid Application Note") regarding the Maestro Z platform's purported ability to track growth and cytolysis of cancer spheroids in real time using impedance technology. Exhibit Q. Figure 2 of the 3D Spheroid Application Note purports to demonstrate the ability to "track the size and growth of cancer spheroids" using the Maestro Z platform with CytoView-Z plate, concluding that "[a]s the spheroids attached and grew, resistance increased (Fig. 2B and E), with larger spheroids correlating to higher resistance (Fig. 2C and F)." *Id.*

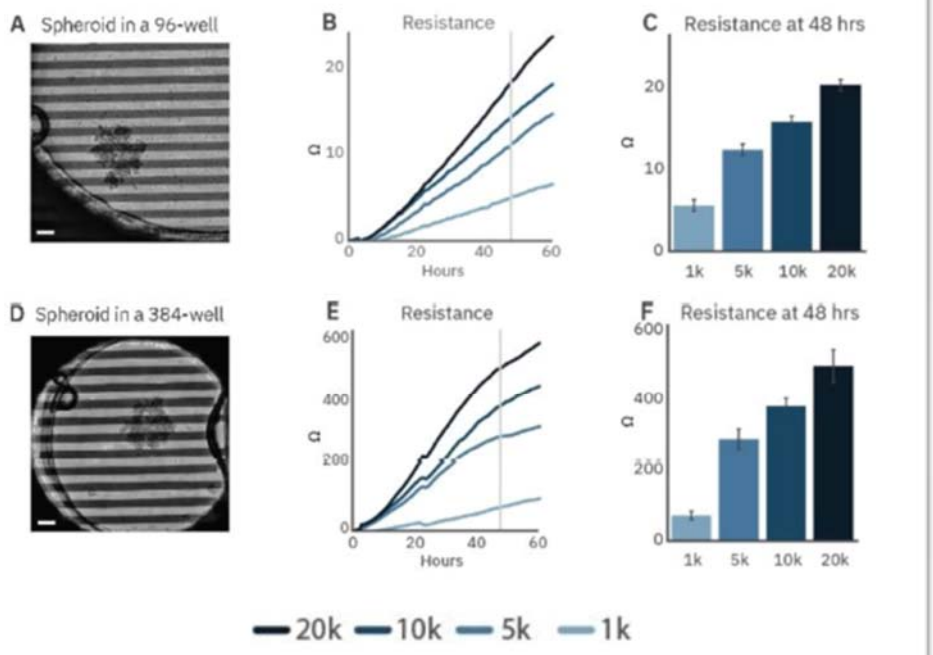


Figure 2: Cancer spheroid growth tracked over time. Spheroids are labeled according to the initial seeding density during formation. Images of 5k SKOV3 spheroids plated on a CytoView-Z 96-well plate (A) and a CytoView-Z 384-well plate (D) immediately after plating. Scale bar is 200 µm. Time course of growth for spheroid of different initial sizes on CytoView-Z 96 (B) and CytoView-Z 384 (E) plates as measured by resistance. At 48 hours post-plating, spheroid size was positively correlated with resistance.

53. The 3D Spheroid Application Note concludes, "The Maestro Z allows for a simple evaluation of *in vitro* tumor growth and death in cancer spheroids. CAR T cell-mediated killing was demonstrated across different effector-target ratios, illustrating the ability of the Maestro Z to evaluate and characterize immunotherapies against 3D cancer models *in vitro*." *Id.* at 6. Upon information and belief, Axion made similar statements in additional settings and contexts with prospective customers.

54. Axion's statements that its Maestro platform combined with the CytoView-Z plate can accurately measure impedance of 3D cancer spheroids is false and misleading. Contrary to Axion's statements, impedance measured on Axion's Maestro platforms combined with the CytoView-Z plate reflect the presence of cells attached to a substrate, not the presence of a 3D cancer spheroid.

Axion's False Advertising is Material

55. Axion's false and misleading statements are material to customers.

56. Because 3D cancer spheroids more closely mimic the complex environment of a tumor compared to 2D culture, and because impedance-based analysis has the benefits of real-time, high throughput analysis, customers consider Axion's false and misleading statements material in that they are likely to influence, and, in some cases, do influence customers' decisions as to whether to purchase an Axion Maestro platform or a competing Agilent xCELLigence platform.

Axion's False Advertising Causes Injury to Agilent

57. Agilent's own impedance system, the xCELLigence platform, directly competes with Axion's Maestro platform, because both systems provide real-time, high throughput impedance measurements.

58. As a direct competitor of Axion with respect to the sale of real-time, high throughput impedance systems, Agilent is within the class that may invoke claims of a violation of the Lanham Act because it has suffered and likely will continue to suffer injury to a commercial interest in sales or business reputation proximately caused by Axion's false and misleading statements.

59. Axion's false and misleading statements that its Maestro platforms combined with the CytoView-Z plate can accurately measure impedance of 3D cancer spheroids have resulted in

injury to Agilent, including but not limited to damages from lost sales. As one example, Axion's false and misleading statements have caused Agilent to lose sales of its xCELLigence platform. Specifically, upon information and belief prospective customers common to Agilent and Axion purchased an Axion Maestro platform over Agilent's xCELLigence platform based upon Axion's false and misleading statements that its Maestro platform could measure impedance of 3D cancer spheroids.

60. Axion's false and misleading statements that its Maestro platforms combined with, for example, the CytoView-Z plate can accurately measure impedance of 3D cancer spheroids have caused and continue to cause irreparable harm to Agilent.

61. Axion's false and misleading statements have caused and continue to cause harm to Agilent's position in the marketplace because Axion's claim is likely to deceive customers about the performance and utility of Axion's Maestro platform and Agilent's xCELLigence platform.

62. Axion's false and misleading statements have diminished and continue to diminish Agilent's goodwill and the value of Agilent's xCELLigence platform in the minds of customers.

63. Axion's false and misleading statements have caused and will continue to cause diversion of present and future sales from Agilent to Axion.

FIRST COUNT
(INFRINGEMENT OF U.S. PATENT NO. 7,192,752)

64. Agilent incorporates by reference the allegations set forth in the foregoing paragraphs of this Complaint as though fully set forth herein.

65. Axion has directly infringed and continues to infringe one or more method claims, including at least claim 11, of the '752 Patent, in the United States by performing infringing methods for impedance-based cell analysis using at least the Maestro platforms, CytoView-Z Plates, and AxIS Z software ("the '752 Patent Accused Instrumentalities") in violation of 35

U.S.C. § 271(a). Axion has induced infringement of one or more method claims, including at least claim 11, of the '752 Patent, in the United States by providing instructions to at least Axion's customers to performing infringing methods for impedance-based cell analysis using at least the '752 Patent Accused Instrumentalities (whether initially included with the Maestro or added as a module thereafter) in violation of 35 U.S.C. § 271(b). Axion has contributorily infringed one or more method claims, of the '752 Patent, including at least claim 11, in the United States and, on information and belief, in this judicial district, by offering for sale, selling, and/or importing into the United States, at least Axion's CytoView-Z Plates, which are especially made or adapted for use for use with Axion's Maestro's Platforms and AxIS Z software for infringing one or more method claims, including at least claim 11, of the '752 Patent, and constitute a material part of the claimed methods performed with at least Axion's Maestro platform and AxIS Z software, such that the CytoView-Z Plates are not a staple article or commodity of commerce suitable for substantial non-infringing use, in violation of 35 U.S.C. § 271(c).

66. As a non-limiting example, Axion's Maestro Z in combination with the Cytoview-Z Plate and AxIS Z Impedance Module (upon information and belief, included with the Maestro Z) is a system used for performing a method of monitoring cell-substrate impedance. Exhibit D at 2 (Maestro Z Brochure) ("Axion BioSystems' Maestro Z platform offers continuous, label-free, impedance-based monitoring of your cells.").

67. Axion's Cytoview-Z 96-well and 384-well Plates, depicted below, comprises one or more multiple well cell-substrate impedance monitoring devices.

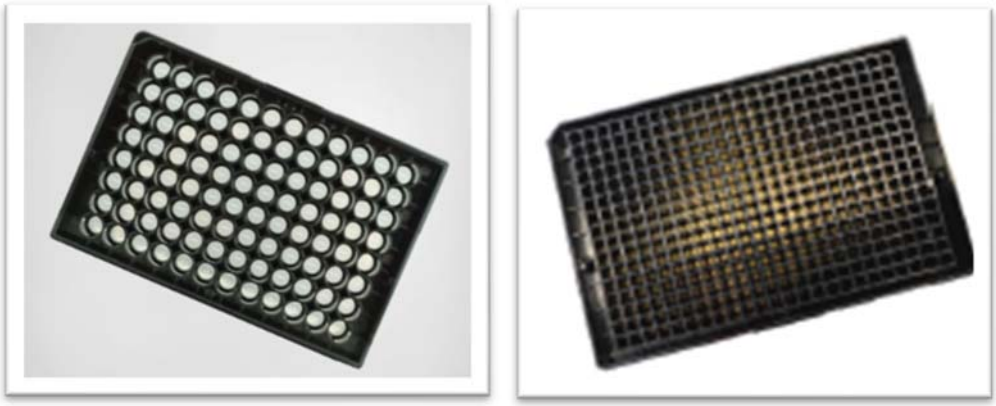


Exhibit R (website printout of https://www.axionbiosystems.com/products/consumables/cytoview-z-plate) (last visited November 9, 2022); Exhibit E at 2.

68. As depicted below, at least two of the multiple wells of the Cytoview-Z 96-well and 384-well Plates comprise an electrode array at the bottom of the well:

Exhibit S (CytoView-Z Plate Brochure).

CytoView-Z 96	Z96-IMP-96B	96	1 Gold		Transparent	Black
CytoView-Z 384	Z384-IMP-384B	384	1 Gold		Transparent	Black

***Schematic of well illustrating the recording electrode (blue) and the ground (orange).**

Exhibit R ("CytoView-Z plates have a recording electrode embedded in the culture surface of each well" and noting that the figure is a "[s]chematic of [a] well illustrating the recording electrode (blue) and the ground (orange)").

69. The electrode array is individually addressed. *See* Exhibit D at 2 (Maestro Z Brochure) ("To measure impedance, small electrical signals are delivered to the electrodes.") Exhibit E at 2 (same as to Maestro ZHT); *see also* https://youtu.be/Hz1HAZnfhbs?t=125 (showing voltage applied across array by using electronic switches).

70. The Cytoview-Z Plate can be used to measure differences in impedance values that relate to cell behavior. Exhibit D at 2 (Maestro Z Brochure) ("Culture your cells in an Axion multiwell CytoView-Z plate. Load this plate into the Maestro Z system and allow the environmental chamber to automatically equilibrate. Analyze changes in cell proliferation, morphology, and viability in the CytoView-Z plate label-free and in real time with AxIS Z software."); Exhibit E at 2 (same as to Maestro ZHT). Axion's product materials indicate that the CytoView-Z Plate, used with the Maestro Z or ZHT and AxIS Z software, can measure differences in cell behavior. *Id.* The CytoView-Z Plates are especially adapted for infringing use with Axion's Maestro platform, as shown on Axion's website, with the CytoView-Z 96 Plate adapted for use in the Maestro Edge, Pro, Z, and ZHT, and the CytoView-Z 384 Plate is adapted for use with the Maestro Pro and Maestro ZHT, and neither the CytoView-Z 96 Plate nor the CytoView-Z 384 Plate is a staple article of commerce or commodity:

CytoView-Z

The CytoView-Z plates combine robust impedance data collected with a transparent well bottom for cell visualization and assay multiplexing

Plate	Cat No.	Wells	Electrode/ well	Electrode layout*	Bottom	Walls	Maestro Edge	Maestro Pro	Maestro Z	Maestro ZHT	Maestro Original
CytoView-Z 96	Z96-IMP-96B	96	1 Gold		Transparent	Black	•	•	•	•	
CytoView-Z 384	Z384-IMP-384B	384	1 Gold		Transparent	Black		•		•	

Exhibit R.

71. The Maestro Z and Maestro ZHT comprise an impedance analyzer because they have electronic circuitry that engages with the Cytoview-Z Plate to measure impedance. Exhibit D at 2 ("The Maestro Z platform uses impedance measurements (ohms, Ω) to quantify the presence of cells on the electrode (2)."); Exhibit E at 2 (same as to Maestro ZHT).

72. The Maestro Z and Maestro ZHT comprise a device station having electronic circuitry that can engage the Cytoview-Z Plate and selectively connect said two or more electrode arrays of the Cytoview-Z Plate to said impedance analyzer. Exhibit D at 2 ("To measure impedance, small electrical signals are delivered to the electrodes."); Exhibit E at 2 (same as to Maestro ZHT).

73. The Maestro Z and Maestro ZHT platforms comprise a software program (AxIS Z) that can control said device station and record and analyze data obtained from said impedance analyzer. Exhibit D at 2; Exhibit E at 2.

See also Exhibit T (website printout of https://www.axionbiosystems.com/products/software/impedance-module) (last visited November 9, 2022) ("The Impedance Module with AxIS Z makes impedance-based assays easy. Take control of experimental settings, view real-time cellular profiles, extract straightforward endpoints, or perform in-depth analysis of cytolysis or barrier function with ease.").

74. Upon information and belief, each well of the Cytoview-Z 96-well and 384-well Plates has approximately uniform electrode resistance distribution across the electrode array so that the electrode resistances between two locations on said array do not differ by more than 30%. *See, e.g.*, Exhibit U (Application Note entitled "Validation of an Impedance-based Cytotoxicity Assay for High Throughput Screening") (characterizing the "high sensitivity and repeatability across plates" and "assay performance was characterized spatially across the plate, with no evidence of drift or edge effects.").

75. Axion uses the Maestro Z system to monitor impedance by introducing cells into at least one well of the system and monitoring cell-substrate impedance of said at least one well. *See* Exhibit V at 2 (Application Note entitled "Quantifying Dynamic Cellular Profiles of Human Cancer Cell lines using the Maestro Z Impedance Assay") ("HeLa cells were seeded into the CytoView-Z [96-well] plate at varying densities and monitored on the Maestro Z system during the attachment, spreading, and proliferation phases. After 16 hours, the highest cell densities had

the largest impedance, whereas lower densities had lower impedance as they continued to grow and spread.").

76. By performing the above-described infringing methods for impedance-based cell analysis, Axion has injured Agilent and is liable to Agilent for directly infringing one or more method claims of the '752 Patent, including without limitation claim 11, pursuant to 35 U.S.C. § 271(a).

77. For example, the Maestro Z and ZHT Brochures tout that "Axion BioSystems' Maestro Z [and ZHT] platform offers continuous, label-free, impedance-based monitoring of your cells. Reveal the detailed kinetics of cell-signaling interactions, cytotoxicity, and a host of drug responses for a better biological understanding without the time- and cost-intensive process of repeating multiple endpoint assays." Exhibit D at 2; Exhibit E at 2.

78. Axion has induced and continues to induce infringement of one or more method claims of the '752 Patent, including at least claim 11, as a result of, among other activities, instructing, encouraging, recommending, and directing its customers on the use of '752 Patent Accused Instrumentalities in an infringing manner in violation of 35 U.S.C. § 271(b). Through its website, product brochures, product videos, technical datasheets, white papers, publications, culture protocols, webinars, flyers, and application notes, Axion provides its customers with detailed explanations, instructions, and information on how to use and implement the '752 Patent Accused Instrumentalities, which demonstrate active steps taken to encourage direct infringement. *See, e.g.*, Exhibit D at 2 ("Culture your cells in an Axion multiwell CytoView-Z plate. . . . Analyze changes in cell proliferation, morphology, and viability in the CytoView-Z plate label-free and in real time with AxIS Z software."); Exhibit E at 2 (same as for Maestro ZHT); Exhibit W (Application Note entitled "Monitoring Migration of Breast Cancer Cells using Maestro Z Real-

Time Impedance Assay"); *see also* Exhibit X (Culture Protocol entitled "Impedance – Non-Adherent Cell Lines"). In these materials, Axion provides detailed instructions to customers of how to culture cells in Cytoview-Z plates and record impedance measurements, including a listing of required consumables and equipment from Axion.

79. Axion has contributorily infringed and continues to contributorily infringe one or more method claims of the '752 Patent, including at least claim 11, in violation of 35 U.S.C. § 271(c) as a result of Axion's offer for sale, sale, and/or importation of at least the CytoView-Z Plates for use in the processes performed with the Maestro platform and AxIS software described above and, further, because at least the CytoView-Z Plates are a material part of the claimed invention, are especially made or adapted for use to perform infringing processes with the Maestro Platform and AxIS software, and are not a staple article or commodity of commerce suitable for substantial noninfringing use, such as use in machines other than the Maestro platform.

80. Axion has had actual knowledge of the '752 Patent at least as early as October 21, 2015, and in no event later than the date of this Complaint and has known of or was willfully blind to its infringement of the '752 Patent at least as early as its development of the Maestro platform during or before 2019. Despite this knowledge of the '752 Patent, Axion has continued to engage in activities to: (1) encourage and assist its customers in the use of Axion-suppled technology to perform infringing methods; and (2) offer for sale, sell, and/or import Axion's CytoView-Z Plates for use in infringing processes. Thus, on information and belief, Axion (1) had actual knowledge of the '752 Patent; (2) knowingly induced its customers to infringe one or more method claims of the '752 Patent, including at least claim 11 or was willfully blind to such infringement; (3) knowingly contributed to the infringement of one or more method claims of the '752 Patent,

including at least claim 11; and (4) had specific intent to induce and contribute to the patent infringement.

81. On information and belief, by using the Axion-supplied instrumentalities identified above, as encouraged, recommended and assisted by Axion, Axion has induced its customers to directly infringe and continue to directly infringe one or more claims of the '752 Patent, including at least claim 11. Exhibit Y at 23–24 (Y Chen et al., "A Versatile Polypharmacology Platform Promotes Cryoprotection and Viability of Human Pluripotent and Differentiated Cells," Nat Methods. 2021 May; 18(5): 528–541, doi:10.1038/s41592-021-01126-2).

82. Thus, Axion indirectly infringes one or more method claims of the '752 Patent, including at least claim 11, within the United States by inducing infringement under 35 U.S.C. § 271(b). For example, since learning of the '752 Patent and by failing to cease offering the '752 Patent Accused Instrumentalities for sale, Axion has knowingly and intentionally induced users of the '752 Patent Accused Instrumentalities to directly infringe one or more claims of the '752 Patent, *inter alia*, by (1) instructing users on how to use the '752 Patent Accused Instrumentalities in a manner than infringes the '752 Patent as described in the foregoing paragraphs; (2) providing customer support and training through its technical documentation; and (3) providing video guides on publicly accessible platforms such as YouTube that provide information and/or instructions on how to perform its infringing method using Axion-supplied instrumentalities. Axion performs, and instructs its customers to perform, its infringing method of using the system to monitor impedance. Additionally, Axion indirectly infringes one or more method claims of the '752 Patent, including at least claim 11, within the United States, by contributing to infringement under 35 U.S.C. § 271(c) by the offer for sale, sale, and/or importation of at least CytoView-Z Plates with knowledge that they are used to perform an infringing process.

83. Axion's infringement of the '752 Patent has been and continues to be deliberate and willful, and this is, therefore, an exceptional case warranting an award of enhanced damages and attorneys' fees and costs pursuant to 35 U.S.C. §§ 284–285.

84. On information and belief, Axion will continue to infringe the '752 Patent unless enjoined by this Court.

85. As a result of Axion's infringement of the '752 Patent, Agilent has suffered monetary damages, and seeks recovery, in an amount to be proven at trial, adequate to compensate for Axion's infringement, but, in no event, less than a reasonable royalty with interest and costs. Axion's infringement of Agilent's rights under the '752 Patent will continue to damage Agilent, causing irreparable harm for which there is no adequate remedy at law, unless enjoined by this Court.

SECOND COUNT
(INFRINGEMENT OF U.S. PATENT NO. 7,468,255)

86. Agilent incorporates by reference the allegations set forth in the foregoing paragraphs of this Complaint as though fully set forth herein.

87. Axion has directly infringed and continues to directly infringe one or more method claims of the '255 Patent, including at least claim 9 of the '255 Patent, in the United States by, among other things, performing infringing methods for impedance-based analysis using at least the Maestro platforms, CytoView Z Plates, and AxIS Z Software ("the '255 Patent Accused Instrumentalities") in violation of 35 U.S.C. § 271(a). Axion has induced infringement of one or more method claims, including at least claim 9, of the '255 Patent, in the United States by providing instructions to at least Axion's customers to perform infringing methods for impedance-based cell analysis using at least the '255 Patent Accused Instrumentalities (whether initially included with the Maestro platforms or added as a module thereafter) in violation of 35 U.S.C.

§ 271(b). Axion has contributorily infringed one or more method claims, including at least claim 9, of the '255 Patent, in the United States by offering for sale, selling, and/or importing into the United States at least Axion's CytoView-Z Plates, which are especially made or adapted for us with Axion's Maestro Platforms and AxIS Z software for infringing one or more method claims of the '255 Patent, including at least claim 9, constitute a material part of the claimed method performed with at least Axion's Maestro platform and AxIS Z software, and are not a staple article or commodity of commerce suitable for substantial noninfringing use, in violation of 35 U.S.C. § 271(c). The CytoView-Z Plates are especially adapted for infringing use with Axion's Maestro platform, as shown on Axion's website, with the CytoView-Z 96 Plate adapted for use in the Maestro Edge, Pro, Z, and ZHT, and the CytoView-Z 384 Plate is adapted for use with the Maestro Pro and Maestro ZHT, and neither the CytoView-Z 96 Plate nor the CytoView-Z 384 Plate is a staple article of commerce or commodity:

CytoView-Z

The CytoView-Z plates combine robust impedance data collected with a transparent well bottom for cell visualization and assay multiplexing

Plate	Cat No.	Wells	Electrode/ well	Electrode layout*	Bottom	Walls	Maestro Edge	Maestro Pro	Maestro Z	Maestro ZHT	Maestro Original
CytoView-Z 96	Z96-IMP-96B	96	1 Gold		Transparent	Black	•	•	•	•	
CytoView-Z 384	Z384-IMP-384B	384	1 Gold		Transparent	Black		•		•	

Exhibit R.

88. As a non-limiting example, Axion's Maestro Z and ZHT in combination with the Cytoview-Z Plate and AxIS Z Impedance Module provides a method of measuring cytolytic activity. Exhibit D at 3 ("With non-invasive, continuous monitoring, the Maestro Z captures the

entire time course of cell death, revealing not only the degree, but the kinetics of the response."); *id.* (". . . the percent cytolysis was tracked . . ."); Exhibit E at 3 (same as to Maestro ZHT).

89. Axion's Cytoview-Z 96-well and 384-well Plates are devices capable of use for monitoring cell-substrate impedance. Exhibit R. The Cytoview-Z Plate is operably connected to an impedance analyzer (the Maestro Z or ZHT), which comprises electronic circuitry that engages with the Cytoview-Z Plate to measure impedance. Exhibit D at 2 ("The Maestro Z platform uses impedance measurements (ohms, Ω) to quantify the presence of cells on the electrode (2)."); Exhibit E at 2 (same as to Maestro ZHT). The Cytoview-Z 96-well and 384-well Plates offered and sold by Axion, depicted below, comprise two or more wells for receiving cells.

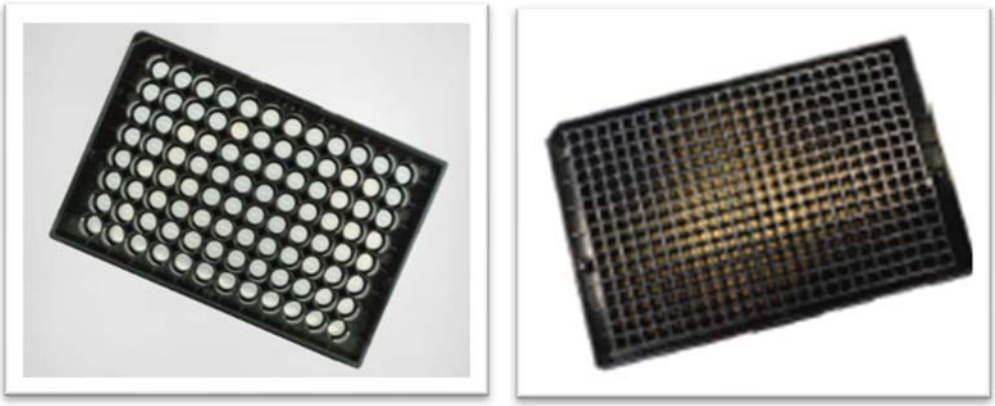


Exhibit R ("A number of different cell types perform well on the CytoView-Z plates"); Exhibit E at 2.

90. Axion's Application Note entitled "T Cell-Mediated Cytolysis of Glioblastoma using Maestro Z Real-Time Impedance Assay" is a non-limiting example of Axion's direct infringement of the method claimed in claim 9 of the '255 Patent. *See* Exhibit Z (Application Note entitled, "T Cell-Mediated Cytolysis of Glioblastoma using Maestro Z Real-Time Impedance Assay"). In this application, Axion adds target cells (U87MG cells) to at least two wells of the CytoView-Z Plate. *Id.* at 2 ("[U87MG c]ells were seeded into the CytoView-Z plate using a

100 µL addition per well"). The figure below illustrates that Axion plated the target U87MG cells in control wells (U87MG cells alone) and test wells (U87MG cells plus T-cells).

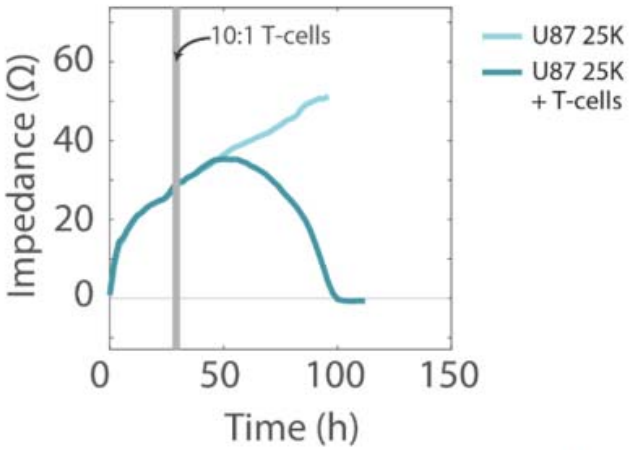


Figure 4: Time course of impedance measurement for 25K U87 – cells treated with naïve-activated T cells show a decrease in impedance, while untreated cells continue increasing in impedance. The gray vertical bar indicates the time of T cell addition.

Id. at 3; *see also id.* ("T cells were added in a 10:1 ratio (T cells:U87 cells) to 4 wells per U87 cell density. Media for untreated U87 cells and media reference wells was replaced . . . ."). The T-cells in Axion's experiment comprise effector cells. *Id.* at 1 ("Immune system effector T cells . . . .").

91. Axion monitored impedance of the control and test wells before and after adding the effector T-cells, as depicted in Figure 4 above, showing impedance measurements before and after addition of T-cells around the 40-hour time point. *Id.* at Figure 4. Also apparent from Figure 4 is that Axion monitored impedance during at least two time points. *Id.* The impedance measurements depicted in Figure 4 represent a a cell index, i.e., a parameter value that is derived from raw, measured impedance. *See* Exhibit B at 22:27–29. As another example of determining a cell index, as shown in Figure 5 below, Axion determined a cell index from the measured impedance by calculating the percent cytolysis of U87MG target cells after addition of the effector T-cells.

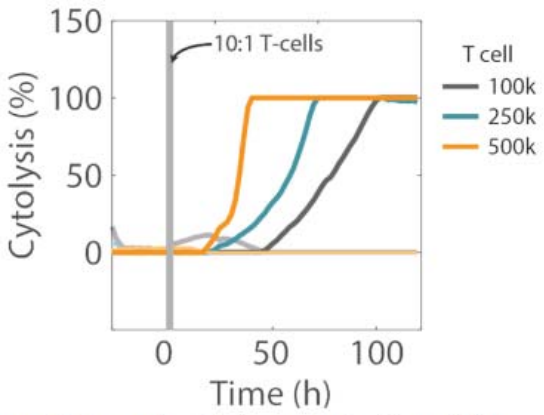


Figure 5: Percent cytolysis was tracked in real-time. Wells with a higher density of T cells showed an increase in cytolysis earlier than wells with a lower density of T cells. The figure legend indicates number of T-cells added to the U87 cultures.

Exhibit Z at 3; *see also id.* at 1 ("The addition of activated human T-cells resulted in a decrease of the impedance signal consistent with T-cell-mediated lysis of the glioma cells.").[1] Axion's calculation of the percent cytolysis of U87MG target cells after addition of the effector T-cells comprises determining viability of the target cells in said test well at a given time point after said adding effector cells by comparing said impedance (*see* Figure 4 above) or optionally said cell index (*see* Figures 4 and 5 above) of said test well to said control well at said given time point. *Id.*

92. Axion performs and instructs its customers to perform its infringing method of measuring cytolytic activity to customers. For example, the Maestro Z Brochure touts that "Axion

1 On information and belief, other graphs in Axion's materials depicting a change in impedance comprise determining a cell index because the graphs depict values derived from raw, measured impedance. *See, e.g.*, Exhibit U at 2 ("The Media control group was used as the background control, such that the average impedance of the media group was subtracted from all wells at each time point."); Exhibit W at 3 ("The raw impedance data was normalized to the impedance just prior to the scratch in each well, and then corrected for the untreated, unscratched wells."); Exhibit DD (Application Note entitled "Quantifying Proliferation and Cytotoxicity of Suspension Human Cancer Cell Lines Using the Maestro Z") at 3 ("All impedance graphs are displayed as the change in impedance from baseline and media-corrected (i.e. average impedance of media-only control wells were subtracted."); Exhibit EE (Application Note entitled "Quantifying Cellular Profiles of Non-Adherent Human Cancer Cell lines using the Maestro Z") at 3 (same).

BioSystems' Maestro Z platform offers continuous, label-free, impedance-based monitoring of your cells. Reveal the detailed kinetics of cell-signaling interactions, cytotoxicity, and a host of drug responses for a better biological understanding without the time- and cost-intensive process of repeating multiple endpoint assays." Exhibit D at 2 (Maestro Z Brochure). Additionally, the Maestro Z Brochure advertises the Maestro Z impedance assay as a "method to continuously monitor cancer cell proliferation and immune cell-mediated cytotoxicity, providing a powerful means of assessing immune cell potency." *Id.* at 3.

93. By performing the above-described infringing methods, Axion has injured Agilent and is liable to Agilent for directly infringing one or more claims of the '255 Patent, including without limitation claim 9, pursuant to 35 U.S.C. § 271(a).

94. In addition, Axion has induced infringement of one or more method claims of the '255 Patent, including at least claim 9, as a result of, among other activities, instructing, encouraging, recommending, and directing its customers on the use of the '255 Patent Accused Instrumentalities in an infringing manner in violation of 35 U.S.C. § 271(b). Through its website, product brochures, product videos, technical datasheets, white papers, publications, culture protocols, webinars, flyers, and application notes, Axion provides its customers with detailed explanations, instructions, and information on how to use and implement the '255 Patent Accused Instrumentalities which demonstrate active steps taken to encourage direct infringement. *See, e.g.,* Exhibit D at 2 ("Culture your cells in an Axion multiwell CytoView-Z plate. . . . Analyze changes in cell proliferation, morphology, and viability in the CytoView-Z plate label-free and in real time with AxIS Z software."); Exhibit E at 2 (same as to Maestro ZHT); Exhibit Z.

95. Axion has contributorily infringed and continues to contributorily infringe one or more method claims of the '255 Patent, including at least claim 9, in violation of 35 U.S.C.

§ 271(c) as a result of Axion's offer for sale, sale, and/or importation of at least the CytoView-Z Plates for use in the processes performed with the Maestro platform and AxIS software described above and, further because at least the CytoView-Z Plates are a material part of the claimed invention, are especially made or adapted for use to perform infringing processes with the Maestro Platform and AxIS software, and are not a staple article or commodity of commerce suitable for noninfringing use, such as in machines other than the Maestro platform.

96. Axion has had actual knowledge of the '255 Patent at least as early as October 21, 2015, and in no event later than the date of this Complaint and has known of or was willfully blind to its infringement of the '255 Patent at least as early as its development of the Maestro platform during or before 2019. Despite this knowledge of the '255 Patent, Axion has continued to engage in activities: (1) to encourage and assist its customers in the use of Axion-supplied technology to perform infringing methods; (2) knowingly induced its customers to infringe one or more method claims of the '255 Patent, including at least claim 9, or was willfully blind to such infringement; (3) knowingly contributed to the infringement of one or more method claims of the '255 Patent , including at least claim 9; and (4) had specific intent to induce and contribute to the patent infringement.

97. On information and belief, by using the Axion-supplied instrumentalities identified above, as encouraged, recommended and assisted by Axion, Axion has induced its customers to directly infringe and continue to directly infringe one or more claims of the '255 Patent, including at least claim 9. Exhibit AA (Y Yin et al., "Locally secreted BiTEs complement CAR T cells by enhancing killing of antigen heterogeneous solid tumors," Mol. Therapy, 2022 30(7): 2537–2533.

98. Thus, Axion indirectly infringes one or more method claims of the '255 Patent, including at least claim 9, within the United States by inducing infringement under 35 U.S.C.

§ 271(b). For example, since learning of the ’255 Patent and by continuing to engage in the acts described above, Axion has knowingly and intentionally induced users of the ’255 Patent Accused Instrumentalities to directly infringe one or more claims of the ’255 Patent, *inter alia*, by (1) instructing users on how to use the ’255 Patent Accused Instrumentalities in a manner than infringes the ’255 Patent as described in the foregoing paragraphs; (2) providing customer support and training through its technical documentation; and (3) providing video guides on publicly accessible platforms such as YouTube that provide information and/or instructions on how to use Axion-supplied instrumentalities to monitor impedance. Additionally, Axion indirectly infringes one or more method claims of the ’255 Patent, including at least claim 9, within the United States, by contributing to infringement under 35 U.S.C. § 271(c) by the offer for sale, sale, and or importation of at least CytoView-Z Plates with knowledge that they are used to perform an infringing process.

99. Axion’s infringement of the ’255 Patent has been and continues to be deliberate and willful, and this is therefore an exceptional case warranting an award of enhanced damages and attorneys’ fees and costs pursuant to 35 U.S.C. §§ 284–285.

100. On information and belief, Axion will continue to infringe the ’255 Patent unless enjoined by this Court.

101. As a result of Axion’s infringement of the ’255 Patent, Agilent has suffered monetary damages and seeks recovery, in an amount to be proven at trial, adequate to compensate for Axion’s infringement, but, in no event, less than a reasonable royalty with interest and costs. Axion’s infringement of Agilent’s rights under the ’255 Patent will continue to damage Agilent, causing irreparable harm for which there is no adequate remedy at law, unless enjoined by this Court.

THIRD COUNT
(INFRINGEMENT OF U.S. PATENT NO. 8,026,080)

102. Agilent incorporates by reference the allegations set forth in the foregoing paragraphs of this Complaint as though fully set forth herein.

103. Axion has directly infringed and continues to infringe one or more method claims, including at least claim 1, of the '080 Patent, in the United States by performing infringing methods for impedance-based cell analysis using at least the Maestro platforms, CytoView-Z Plates, and AxIS Z software ("the '080 Patent Accused Instrumentalities") in violation of 35 U.S.C. § 271(a). Axion has induced infringement of one or more method claims, including at least claim 1, of the '080 Patent, in the United States by providing instructions to at least Axion's customers to performing infringing methods for impedance-based cell analysis using at least the '080 Patent Accused Instrumentalities (whether initially included with the Maestro or added as a module thereafter) in violation of 35 U.S.C. § 271(b). Axion has contributorily infringed one or more method claims, of the '080 Patent, including at least claim 1, in the United States by offering for sale, selling, and/or importing into the United States, at least Axion's CytoView-Z Plates, which are especially made or adapted for use for use with Axion's Maestro's Platforms and AxIS Z software for infringing one or more method claims, including at least claim 1, of the '080 Patent, and constitute a material part of the claimed methods performed with at least Axion's Maestro platform and AxIS Z software, such that the CytoView-Z Plates are not a staple article or commodity of commerce suitable for substantial non-infringing use, in violation of 35 U.S.C. § 271(c).

104. As a non-limiting example, Axion's Maestro Z or ZHT in combination with the Cytoview-Z Plate and AxIS Z Impedance Module (upon information and belief, included with the Maestro Z and ZHT) is a cell-substrate impedance monitoring system for monitoring cell-substrate

impedance in response to one or more test compounds. Exhibit D at 2 ("Axion BioSystems' Maestro Z platform offers continuous, label-free, impedance-based monitoring of your cells. Reveal . . . a host of drug responses"); Exhibit E at 2 (same as to Maestro ZHT).

105. Axion's Cytoview-Z 96-well and 384-well Plates, depicted below, comprise at least one multiple-well cell-substrate impedance measuring devices.

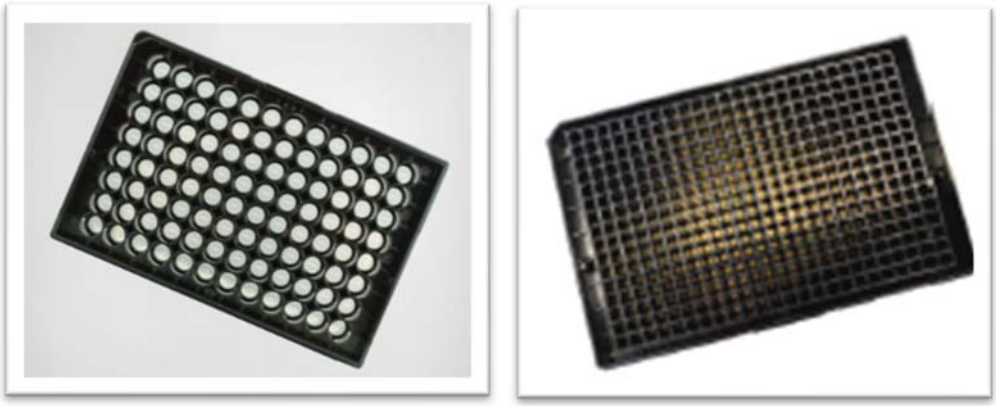


Exhibit R; Exhibit E at 2.

106. As depicted below, at least two of the multiple wells of the Cytoview-Z Plate comprise an electrode array at the bottom of the well:

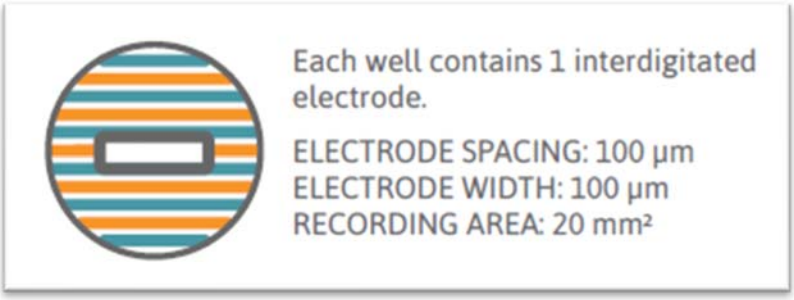


Exhibit S. Each electrode array comprises two electrode structures—a recording electrode depicted in blue and a ground electrode depicted in orange:

CytoView-Z 96	Z96-IMP-96B	96	1 Gold		Transparent	Black
CytoView-Z 384	Z384-IMP-384B	384	1 Gold		Transparent	Black

***Schematic of well illustrating the recording electrode (blue) and the ground (orange).**

Exhibit R ("CytoView-Z plates have a recording electrode embedded in the culture surface of each well" and noting that the figure is a "[s]chematic of [a] well illustrating the recording electrode (blue) and the ground (orange)").

107. Each electrode structure comprises multiple electrode elements because each well of the CytoView-Z plate has "an interdigitated electrode" with fingerlike projections. *See* Exhibit S.

108. The electrode array is individually addressed. *See* Exhibit D at 2 (Maestro Z Brochure) ("To measure impedance, small electrical signals are delivered to the electrodes."); Exhibit E at 2 (same as to Maestro ZHT); *see also* https://youtu.be/Hz1HAZnfhbs?t=125 (showing voltage applied across array by using electronic switches).

109. The Maestro Z and ZHT comprise an impedance analyzer because they have electronic circuitry that engages with the Cytoview-Z Plate to measure impedance. Exhibit D at 2 ("The Maestro Z platform uses impedance measurements (ohms, Ω) to quantify the presence of cells on the electrode (2)."); Exhibit E at 2 (same as to Maestro ZHT).

110. The Maestro Z and ZHT comprise a device station comprising electronic circuitry that can engage the Cytoview-Z Plate and select and connect said electrode arrays within any of

the multiple wells of the Cytoview-Z Plate to said impedance analyzer. Exhibit D at 2 ("To measure impedance, small electrical signals are delivered to the electrodes."); Exhibit E at 2 (same as to Maestro ZHT).

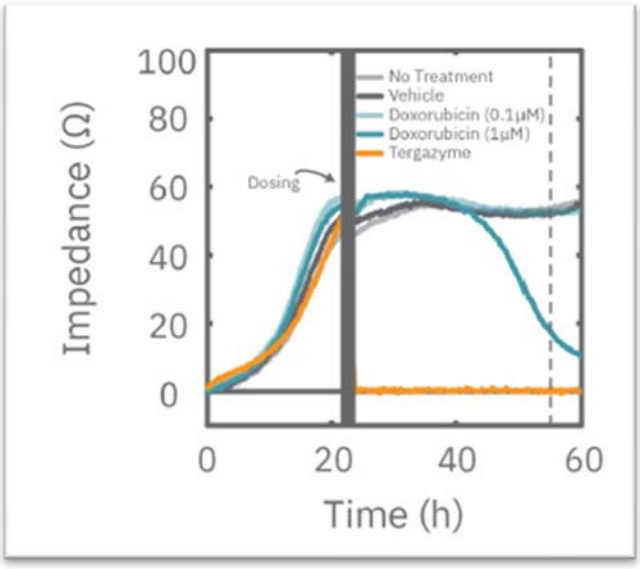
111. The Maestro Z and ZHT platforms comprise a software program (AxIS Z) that can control said device station and perform data acquisition and data analysis from said impedance analyzer. *Id.*

See also Exhibit T ("The Impedance Module with AxIS Z makes impedance-based assays easy. Take control of experimental settings, view real-time cellular profiles, extract straightforward endpoints, or perform in-depth analysis of cytolysis or barrier function with ease.").

112. Axion uses the Maestro Z system to monitor impedance by introducing cells into one or more wells of the CytoView-Z plate. *See* Exhibit BB at 2 (website printout of https://www.axionbiosystems.com/applications/oncology/cytotoxicity-and-cell-viability) (last visited February 5, 2023) ("SKOV cancer cells were cultured at 5k cells per well in a CytoView-Z 96-well plate.").

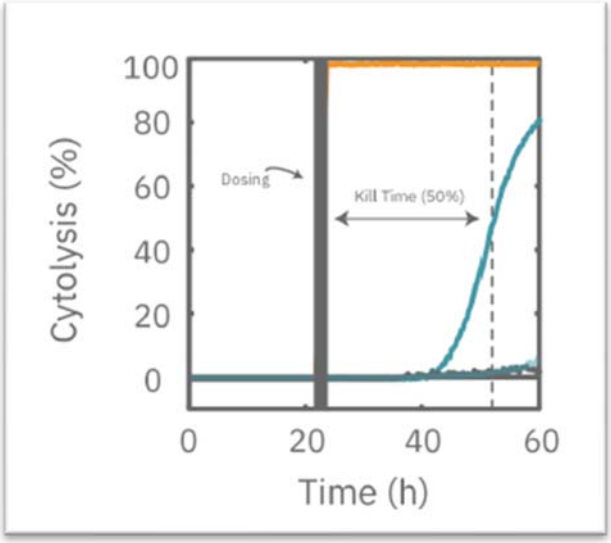
113. Axion adds at least one test compound to said one or more wells. *Id.* ("After 24 hours of culture, the SKOV3 cells were dosed with doxorubicin . . . .").

114. As depicted below, Axion monitors cell-substrate impedance of said one or more wells before and after adding said at least one test compound:



Id. (depicting impedance measured before and after doxorubicin dosing at the 24 hour time point).

115. The figure above illustrates that the Maestro Z system analyzes impedance values and calculates cell index values—i.e., a parameter derived from measured impedance values—before and after adding said at least one test compound and provides information about cell response to said at least one test compound. *Id.* As another example of the Maestro Z system analyzing impedance values and calculating cell index values, the figure below depicts percent cytolysis of cells based on impedance measurements before and after doxorubicin dosing at the 24-hour time point:



Id..[2]

116. By performing the above-described infringing methods for impedance-based cell analysis, Axion has injured Agilent and is liable to Agilent for directly infringing one or more method claims of the '080 Patent, including without limitation claim 1, pursuant to 35 U.S.C. § 271(a).

117. For example, the Maestro Z and ZHT Brochures tout that "Axion BioSystems' Maestro Z platform offers continuous, label-free, impedance-based monitoring of your cells. Reveal the detailed kinetics of cell-signaling interactions, cytotoxicity, and a host of drug

2 On information and belief, other graphs in Axion's materials depicting a change in impedance comprise determining a cell index because the graphs depict values derived from raw, measured impedance. *See, e.g.*, Exhibit U at 2 ("The Media control group was used as the background control, such that the average impedance of the media group was subtracted from all wells at each time point."); Exhibit W at 3 ("The raw impedance data was normalized to the impedance just prior to the scratch in each well, and then corrected for the untreated, unscratched wells."); Exhibit DD (Application Note entitled "Quantifying Proliferation and Cytotoxicity of Suspension Human Cancer Cell Lines Using the Maestro Z") at 3 ("All impedance graphs are displayed as the change in impedance from baseline and media-corrected (i.e. average impedance of media-only control wells were subtracted."); Exhibit EE (Application Note entitled "Quantifying Cellular Profiles of Non-Adherent Human Cancer Cell lines using the Maestro Z") at 3 (same).

responses for a better biological understanding without the time- and cost-intensive process of repeating multiple endpoint assays." Exhibit D at 2; Exhibit E at 2 (same as to Maestro ZHT).

118. Axion has induced and continues to induce infringement of one or more method claims of the '080 Patent, including at least claim 1, as a result of, among other activities, instructing, encouraging, recommending, and directing its customers on the use of '080 Patent Accused Instrumentalities in an infringing manner in violation of 35 U.S.C. § 271(b). Through its website, product brochures, product videos, technical datasheets, white papers, publications, culture protocols, webinars, flyers, and application notes, Axion provides its customers with detailed explanations, instructions, and information on how to use and implement the '080 Patent Accused Instrumentalities, which demonstrate active steps taken to encourage direct infringement. *See, e.g.*, Exhibit D at 2 ("Culture your cells in an Axion multiwell CytoView-Z plate. . . . Analyze changes in cell proliferation, morphology, and viability in the CytoView-Z plate label-free and in real time with AxIS Z software."); Exhibit E at 2 (same as to Maestro ZHT); Exhibit W; *see also* Exhibit CC (Application Note entitled "Tracking the Dynamics of Cytotoxicity in Real-Time with the Maestro Z Impedance Assay"). In these materials, Axion provides detailed instructions to customers of how to culture cells in CytoView-Z plates and record impedance measurements before and after adding one or more test compounds, including a listing of required consumables and equipment from Axion.

119. Axion has contributorily infringed and continues to contributorily infringe one or more method claims of the '080 Patent, including at least claim 11, in violation of 35 U.S.C. § 271(c) as a result of Axion's offer for sale, sale, and/or importation of at least the CytoView-Z Plates for use in the processes performed with the Maestro platform and AxIS software described above and, further, because at least the CytoView-Z Plates are a material part of the claimed

invention, are especially made or adapted for use to perform infringing processes with the Maestro Platform and AxIS software, and are not a staple article or commodity of commerce suitable for substantial noninfringing use, such as use in machines other than the Maestro platform.

120. Axion has had actual knowledge of the ’080 Patent at least as early as October 21, 2015, and in no event later than the date of this Complaint and has known of or was willfully blind to its infringement of the ’080 Patent at least as early as its development of the Maestro platform during or before 2019. Despite this knowledge of the ’080 Patent, Axion has continued to engage in activities to: (1) encourage and assist its customers in the use of Axion-suppled technology to perform infringing methods; and (2) offer for sale, sell, and/or import Axion’s CytoView-Z Plates for use in infringing processes. Thus, on information and belief, Axion (1) had actual knowledge of the ’080 Patent; (2) knowingly induced its customers to infringe one or more method claims of the ’080 Patent, including at least claim 1 or was willfully blind to such infringement; (3) knowingly contributed to the infringement of one or more method claims of the ’080 Patent, including at least claim 1; and (4) had specific intent to induce and contribute to the patent infringement.

121. On information and belief, by using the Axion-supplied instrumentalities identified above, as encouraged, recommended and assisted by Axion, Axion has induced its customers to directly infringe and continue to directly infringe one or more claims of the ’080 Patent, including at least claim 1. Exhibit Y at 23–24, Figure 3d (“A versatile polypharmacology platform promotes cytoprotection and viability of human pluripotent and differentiated cells”).

122. Thus, Axion indirectly infringes one or more method claims of the ’080 Patent, including at least claim 1, within the United States by inducing infringement under 35 U.S.C. § 271(b). For example, since learning of the ’080 Patent and by failing to cease offering the ’080

Patent Accused Instrumentalities for sale, Axion has knowingly and intentionally induced users of the ’080 Patent Accused Instrumentalities to directly infringe one or more claims of the ’080 Patent, *inter alia*, by (1) instructing users on how to use the ’080 Patent Accused Instrumentalities in a manner than infringes the ’080 Patent as described in the foregoing paragraphs; (2) providing customer support and training through its technical documentation; and (3) providing video guides on publicly accessible platforms such as YouTube that provide information and/or instructions on how to perform its infringing method using Axion-supplied instrumentalities. Axion performs, and instructs its customers to perform, its infringing method of using the system to monitor impedance. Additionally, Axion indirectly infringes one or more method claims of the ’080 Patent, including at least claim 1, within the United States, by contributing to infringement under 35 U.S.C. § 271(c) by the offer for sale, sale, and/or importation of at least CytoView-Z Plates with knowledge that they are used to perform an infringing process.

123. Axion’s infringement of the ’080 Patent has been and continues to be deliberate and willful, and this is, therefore, an exceptional case warranting an award of enhanced damages and attorneys’ fees and costs pursuant to 35 U.S.C. §§ 284–285.

124. On information and belief, Axion will continue to infringe the ’080 Patent unless enjoined by this Court.

125. As a result of Axion’s infringement of the ’080 Patent, Agilent has suffered monetary damages, and seeks recovery, in an amount to be proven at trial, adequate to compensate for Axion’s infringement, but, in no event, less than a reasonable royalty with interest and costs. Axion’s infringement of Agilent’s rights under the ’080 Patent will continue to damage Agilent, causing irreparable harm for which there is no adequate remedy at law, unless enjoined by this Court.

FOURTH COUNT
(FALSE ADVERTISING UNDER THE LANHAM ACT)

126. Agilent incorporates by reference the allegations set forth in the foregoing paragraphs of this Complaint as though fully set forth herein

127. Axion's advertising described herein is false and misleading in violation of Section 43(a) of the Lanham Act, 15 U.S.C. § 1125(a).

128. Axion's false and misleading statements that its Maestro platform combined with, for example, the CytoView-Z plate can accurately measure impedance of 3D cancer spheroids are a false and misleading descriptions and representations of fact because impedance cannot be used to accurately measure anything other than what is attached to a surface.

129. Axion's false and misleading statements have a tendency to deceive a substantial portion of customers and potential customers of both Axion's Maestro platform and Agilent's xCELLigence platform, and, on information and belief, Axion's false and misleading statements actually deceived and will continue to deceive customers and potential customers of the Maestro and xCELLigence platforms.

130. Axion's false and misleading statements are willfully deceptive, at least as of the date that this Complaint is filed.

131. Axion's false and misleading statements are material in that they are likely to influence and, on information and belief, actually have influenced the purchasing decisions of the customers to which they are directed.

132. By selling its Maestro and CytoView-Z products to customers in various states of the United States, as well as internationally, Axion has caused its Maestro and CytoView-Z products to enter interstate commerce. Additionally, Axion's false and misleading statements are posted on its website, which reaches across state lines to national and international audiences.

133. As a direct and proximate result of Axion's false and misleading statements, Agilent has suffered, is suffering, and will continue to suffer immediate and continuing irreparable injury for which there is no adequate remedy at law.

134. By making these false and misleading statements in the marketplace, Axion caused injury to Agilent.

135. As a direct and proximate result of Axion's false and misleading statements, Agilent has suffered and will continue to suffer injury to its reputation by a loss of goodwill associated with Agilent's xCELLigence platform and brand.

136. On information and belief, Agilent has suffered and will continue to suffer injury in the form of monetary damages by the diversion of sales from Agilent to Axion.

137. On information and belief, Axion's false and misleading statements are knowing and willful and/or with intentional disregard as to the true nature of the product it offers. Agilent is entitled to injunctive relief and to the recovery of all available damages, interest, attorneys' fees, costs, and Axion's profits.

138. This is an exceptional case within the meaning of Section 35 of the Lanham Act, 15 U.S.C. § 1117.

PRAYER FOR RELIEF

WHEREFORE, Agilent prays for judgment and seeks relief against Axion as follows:

A. for judgment that Axion has infringed and continues to infringe one or more method claims of the '752 Patent, '255 Patent, and '080 Patent, directly, and indirectly by both inducement of infringement and contributory infringement;

B. for a preliminary and permanent injunction against Axion, enjoining it from direct infringement, inducement of infringement, and contributory infringement of the '752 Patent, '255 Patent, and '080 Patent;

C. for judgment awarding Agilent damages adequate to compensate it for Axion's infringement of the '752 Patent, '255 Patent, and '080 Patent, including all pre-judgment and post-judgment interest;

D. for judgment that Axion has willfully infringed and continues to willfully infringe one or more claims of the ’752 Patent, ’255 Patent, and ’080 Patent;

E. for judgment awarding enhanced damages pursuant to 35 U.S.C. § 284;

F. in the absence of a permanent injunction, for judgment imposing a mandatory future royalty payable on each and every act of infringement by Axion in the future that infringes the ’752 Patent, ’255 Patent, ’080 Patent and on all future acts that are not colorably different from acts that infringe;

G. for judgment awarding attorneys’ fees pursuant to 35 U.S.C. § 285 or otherwise permitted by law;

H. for judgment awarding to Agilent all gains, profits, and advantages derived by Axion from its false and misleading statements;

I. for judgment awarding monetary damages sustained by Agilent as a result of its false and misleading statements;

J. for judgment awarding monetary damages in the amount necessary for corrective advertising that dispels Axion’s false and misleading statements;

K. for a judgment awarding enhanced damages and/or attorneys’ fees pursuant to 15 U.S.C. § 1117;

L. for a permanent injunction that: (a) enjoins Axion, its officers, agents, servants, and employees, and all persons in active concert and participation with them, including their affiliates, from further disseminating the false and misleading advertising claims in any form or medium; and (b) requires Axion to withdraw and/or retrieve all offending advertising materials from the marketplace;

M. for judgment awarding costs of suit; and

N. for judgment awarding Agilent such other and further relief as the Court may deem just and proper.

DEMAND FOR JURY TRIAL

Pursuant to Rule 38(b) of the Federal Rules of Civil Procedure, Agilent hereby demands a trial by jury of this action.

MORRIS, NICHOLS, ARSHT & TUNNELL LLP

/s/ Brian P. Egan

Jack B. Blumenfeld (#1014)
Brian P. Egan (#6227))
1201 North Market Street
P.O. Box 1347
Wilmington, DE 19899-1347
(302) 658-9200
jblumenfeld@morrisnichols.com
began@morrisnichols.com

Attorneys for Plaintiff Agilent Technologies, Inc.

OF COUNSEL:

Peter J. Chassman
Hallie H. Wimberly
Michael J. Forbes
REED SMITH LLP
801 Main Street, Suite 1700
Houston, TX 77002
(713) 469-3800

February 23, 2023