LAW OFFICE OF T. SPENCE CHUBB
1025 CONNECTICUT AVENUE, N.W., SUITE 1000
WASHINGTON, DC 20036
(703) 623-7739
TSCHUBB@TSPENCECHUBB.COM

The Honorable Lisa R. Barton
Secretary to the Commission
U.S. International Trade Commission
500 E Street, SW
Washington, DC 20436

March 8, 2016

Re: *Certain Nanopores and Products Containing Same*; Docket No. 3123 – Public Interest Comments

Dear Secretary Barton:

Proposed respondents Oxford Nanopore Technologies Ltd. and Oxford Nanopore Technologies, Inc. (collectively, "Oxford Nanopore") respectfully submit the following comments in response to the Commission's Notice of Receipt of Complaint; Solicitation of Comments Relating to the Public Interest (81 Fed. Reg. 10278 (February 29, 2016)).

Oxford Nanopore categorically denies that it is liable for infringing the asserted patents. The allegations of Complainant Illumina, Inc. ("Illumina") are based on nothing more than unsubstantiated speculation, with no proof that the current version of Oxford Nanopore's MinION device has any relationship to the technology claimed in the asserted patents.[1]

The relief requested by Complainants raises substantial public interest concerns because an exclusion order against Oxford Nanopore's devices would be detrimental to consumers, to competitive conditions in the United States, and to the public health, safety and welfare. The exclusion of the MinION would interfere with important on-going medical, scientific and industrial research because neither Illumina nor any other supplier can fill the resulting void.[2]

[1] Without limiting Oxford Nanopore's assertion that it is not liable for infringement, Oxford Nanopore's products, the MinION and PromethION, are comprised of much more than a nanopore. Each device includes proprietary chemical, fluidics, semiconductor, software control, signal analysis, and reporting technologies. The asserted patents, even if valid and construed in extremis, only cover the single-use disposable nanopore flowcell used with the device and not the device itself. Moreover, the asserted patents relate to a single, specific type of nanopore comprised of *Mycobacterium smegmatis* (Msp) porin. Oxford Nanopore's devices can be configured to work with any pore. Moreover, despite Illumina' assertions, the MspA pore is not particularly special nor is it the best pore for use in DNA sequencing. Oxford Nanopore continuously explores a range of nanopore designs and develops "wild-type" nanopores into more efficacious structures. Indeed, Oxford Nanopore, together with scientists at Vrje Universiteit Brussel and the University of London, has developed a proprietary nanopore based upon a non-Msp protein. *See* "Structural and mechanistic insights into the bacterial amyloid secretion channel CsgG," Goyal et al., Nature, 516, 250-253 (Dec. 11, 2014), http://www.nature.com/nature/journal/v516/n7530/full/nature13768.html.

[2] Although a proto-type of a PromethION (without nanopores) was shown at a conference in the United States, Oxford Nanopore's PromethION has never been imported into the United States; the only Oxford Nanopore device that could be at issue in this proceeding is the MinION.

Moreover, nanopore technology, a field in which Oxford Nanopore is the world leader, is a revolutionary and disruptive technology[3] that represents a significant competitive threat to Illumina's monopolistic hold on the U.S. sequencing market. Nanopore technology has the potential to replace traditional Sequencing-by-Synthesis (SBS) technology on which Illumina's instruments are based and to greatly expand the base of potential users and applications. Illumina acquired the asserted patents, and has filed this ITC action, to stifle competition.

A. The Relief Sought Would Harm Public Health, Safety and Welfare.

Weighing in at less than 100 grams, Oxford Nanopore's pocket-sized MinION is the world's first portable, real-time DNA sequencing device and the only such device currently available. It's so small scientists can easily take it out into the field, like they did during the Ebola outbreak. In contrast, Illumina's typical machine is the size of a refrigerator and desktop copier. The MinION also is the only sequencer that costs less than $1,000. Other sequencers cost from several tens of thousands of dollars to several million dollars for Illumina's most powerful system.

The MinION is a research tool currently used in biological research, environmental science, pathogen analysis, cancer research, and an increasing number of other fields. This broad base of research using Oxford Nanopore technology is starting to translate to actual and potential real-world, field-based applications in public health (e.g. surveillance of Ebola, Zika, salmonella, and flu viruses), environmental safety (e.g. rapid identification of species in water or other samples), healthcare (e.g. rapid detection of cancer and genetic abnormalities), and security (e.g. development of bioterrorism countermeasures). The MinION is being used by dozens of leading U.S. universities (often funded by the National Science Foundation or the National Institutes of Health), as well as 68 U.S. agencies and departments, including the Centers for Disease Control, Defense Forensic Science Center, NASA Johnson Space Center, U.S. Army, U.S. Air Force, Los Alamos National Lab, U.S. Department of Agriculture, and the Smithsonian Institution.

The MinION is being used to conduct ground-breaking field research aimed at breaking the chain of transmission of viruses such as Ebola and Zika, research that could not be completed as rapidly and in the field without MiniONs. Traditional sequencing technology often requires time to ship blood samples from the field back to a sophisticated laboratory for analysis, and then ship results from the laboratory to the field. In contrast, the field deployable MinION device can identify viruses and mutations in viruses in real time—researchers battling the Zika virus have reported detection in as little as four minutes from starting a MinION experiment. Surveillance data shows that this allows health workers combating emergencies in the field to quickly identify signatures of host adaptation, identify and monitor diagnostic targets, and characterize responses to vaccines and treatments. In the U.S., blood samples must be sent to the Centers for Disease Control, and it can take up to three weeks from the onset of infection for the test results to arrive.[4] Scientists hope and believe the MinION will eventually be "...a device that can detect all pathogens—virus, bacteria, fungus, parasite known or

[3] A disruptive innovation is an innovation with new properties when compared to the incumbent that creates a new market and value network and eventually disrupts an existing market and value network, displacing established market leaders and alliances and having significant societal impact.

[4] *See* "New Rapid Zika Test Could Contain Spread of Disease," KQED SCIENCE, Sheraz Sadiq (February 4, 2016).

unknown—in a single test."[5] Beyond the initial test, collecting DNA information allows broad genomic surveillance of an infectious disease and the MinION can allow rapid deployment and turnaround of results in remote or diverse locations for this purpose.[6]

Unlike Illumina's machines, which break DNA into small fragments and use software to align fragments after sequencing, Oxford Nanopore's technology sequences very long DNA fragments, that has implications across a variety of processes and applications. Scientists increasingly agree that understanding the complexity of cancer requires identification of structural variants in DNA sequencing. According to Scientists at Johns Hopkins, structural variants remain difficult to reliably detect with short-read technology (such as Illumina's SBS-based technology). Their research, summarized in the article, states that the MinION, because of its ability to sense long DNA fragments, may improve detection of structural variants. "Given the speed, small footprint, and low capital cost, nanopore sequencing could become the ideal tool for the low-level detection of cancer-associated structural variants needed for molecular relapse, early detection, or therapeutic monitoring."[7]

Illumina's assertion that "competing products are otherwise available from Illumina and other sources" is completely specious—a statement analogous to arguing for restricting the trade of smartphones because mainframe and desktop computers are available. The technologies are not interchangeable, and neither Illumina nor any other provider offers a sequencer comparable to the MinION that includes all the properties of portability, real-time data streaming, direct electronic sensing, and long read lengths.

Indeed, Illumina has not published any data proving that it has ever successfully and accurately sequenced DNA using nanopore technology, even in the laboratory much less in the field. Nor has Illumina demonstrated any ability to embody nanopore technology in a practical commercial format. And even if Illumina could somehow get a nanopore sequencer ready for market, it would have issues commercializing it. Oxford Nanopore believes it would be difficult for Illumina to offer a competing nanopore product in light of patents owned by Oxford Nanopore, Harvard University and University of California.

Excluding Oxford Nanopore's devices would harm the public interest. Interruption of the availability of MinION devices would interfere with research vital to the public interest. Researchers and industry in the United States would be denied the portable, real-time sequencing capabilities that only the MinION can offer. U.S. security, U.S. public health, and U.S. research, including more than 800 U.S. researchers, would be placed at a significant disadvantage compared to their colleagues and

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[5] *See* "Ebola, Zika and More: Designing One Test to Catch Them All" www.UCSF.edu, Jyoti Madhusoodanan (February 11, 2016)(quoting Dr. Charles Chiu, an associate professor of Laboratory Medicine and director of the UCSF-Abbott Viral Diagnostics and Discovery Center).

[6] *See*, "Real-time, portable genome sequencing for Ebola surveillance," Nature, 530, 228-232, Quick et al (Feb. 11, 2016), available at http://www.nature.com/nature/journal/v530/n7589/full/nature16996.html; "Real-time digital pathogen surveillance—the time is now," Genome Biology 15:155, Gardy et al (July 30, 2015), available at http://genomebiology.biomedcentral.com/articles/10.1186/s13059-015-0726-x .

[7] "Hopkins Team Assesses Oxford Nanopore MinION for Cancer Structural Variant Detection," Julia Karow (Oct 5, 2015), available at https://www.genomeweb.com/sequencing-technology/hopkins-team-assesses-oxford-nanopore-minion-cancer-structural-variant.

competitors throughout the rest of the world who will have continued access to Oxford Nanopore's unique devices.

B. Illumina Seeks To Stifle Emerging Competition and To Enhance Its Monopoly In The Conventional DNA Sequencing Market.

Illumina is a $23 billion company that for many years controlled an ever-increasing majority of the DNA sequencing market. With upwards of 75% market share, "owing to the company's essential monopoly of the high-throughput portion of the market, over 90% of sequenced genetic material likely comes off an Illumina machine."[8] Until recently, the DNA sequencing market consisted entirely of complex, non-portable and expensive devices capable of sequencing only small fragments of DNA; Illumina dominates that market. Nanopore technology is a revolutionary sequencing technology, and while Oxford Nanopore is small emerging company, it is the only competitor with a commercial product utilizing nanopore technology. Indeed, Oxford Nanopore's MinION device has been described as "a radical step in the evolution of reading DNA, a smartphone in a world of supercomputers."[9]

Illumina paints Oxford Nanopore as unfairly competing in the market for nanopore sequencing, but the facts do not support its allegations. For a decade, Oxford Nanopore has been collaborating with and supporting research at Harvard, University of California Santa Cruz, and Oxford and has collaborations with approximately 30 institutions around the world, complemented by substantial investment in internal research and development. It is the only company to successfully develop a nanopore-based sequencer. Oxford Nanopore has a broad patent portfolio, through in-house development and licensing agreements with third parties.

In its quest to monopolize the market for conventional DNA sequencing devices, Illumina historically has paid scant attention to and made minimal investments in nanopore technology. Contrary to the picture that Illumina tries to paint in its Complaint, Illumina holds very little IP in the nanopore space and, to date, has not shown any related innovation or that it has been successful in exploiting the little nanopore IP that it does own. Indeed, all of Illumina's nanopore-specific IP was filed or acquired by Illumina subsequent to 2008 when Oxford Nanopore gave Illumina confidential presentations of its nanopore technology prior to the two parties entering into a Commercialization Agreement. Shortly after the Commercialization Agreement was consummated, Illumina performed a freedom to operate exercise purportedly on Oxford Nanopore's behalf and after representing that it did not intend to develop its own nanopore product. The freedom to operate exercise did not reveal any IP held by Illumina relating to nanopore technology.

Illumina's Statement on the Public Interest indicates a strong public interest in protecting intellectual property rights, but the public interest does not favor protecting intellectual property rights acquired by unclean hands. Illumina's hands are unclean here as it violated a position of trust when it acquired the license for the asserted patents that are the basis for this ITC action. The CEO of

[8] "Illumina hopes to sustain growth by investing in clinical adoption of genome sequencing," Morningstar, Michael Waterhouse (Feb. 3, 2016), available at http://analysisreport.morningstar.com/stock/research/c-report?t=XNAS:ILMN&region=usa&culture=en-US&productcode=MLE&cur

[9] "Nanopore Sequencing is Here to Stay," Bio IT World, Aaron Krol (Dec. 22, 2014), available at http://www.bio-itworld.com/2014/12/22/nanopore-sequencing-here-stay.html

Illumina, Jay Flatley, participated as an observer on Oxford Nanopore's Board of Directors from March 2009 to September 2013 where regular updates were given regarding Oxford Nanopore's effort to license the asserted patents from the University of Washington. Despite denying any conflicts of interest when asked and despite having signed a nondisclosure agreement, Illumina secretly entered into negotiations with the University of Washington and Jens Gundlach which eventually resulted in Illumina procuring a license to the asserted patents. Indeed, even after the license agreement was finalized in December 2012, Mr. Flatley continued to attend Oxford Nanopore's Board meetings as an observer while denying that he had any conflicts of interest and refusing to respond to direct questions regarding whether Illumina was negotiating a license agreement with the University of Washington.

Despite Illumina's anticompetitive conduct, Oxford Nanopore continued to progress toward commercialization of its nanopore products, and Illumina had to change its tactics. In September 2013, in a blatant attempt to disrupt one of Oxford Nanopore's fund raising programs, Illumina without any notice or forewarning put its entire 15% shareholding in Oxford Nanopore up for sale in the middle of the fund raising. Illumina offered its shares for sale at a 20% discount to the fund raising price. Oxford Nanopore was forced to raise an additional £56 million ($92 million) on top of its own fundraising to buy Illumina out. It was only due to strong investor confidence in the potential future of the nanopore technology that Illumina's disruptive and anti-competitive tactics did not succeed.

Illumina has filed this action admitting that it does not really know what nanopore Oxford Nanopore is actually using in its devices. Before filing this action, Illumina did not ask Oxford Nanopore what nanopore it uses, give any notice, or demand that Oxford Nanopore stop the infringing activity that Illumina alleges Oxford Nanopore is committing. Instead, Illumina seeks to use this ITC action as yet another weapon in its long-running campaign to thwart Oxford Nanopore's research and commercialization efforts. Illumina hopes to use this proceeding to block the commercialization of Oxford Nanopore's products, all with the ultimate intent of expanding its already overwhelming monopoly power into the nanopore space, which would be extremely detrimental to competition in the DNA sequencing market in the United States.

C. Conclusion: Exclusion of Oxford Nanopore's Technology Stymies Research

The Commission has long recognized that "basic scientific research...is precisely the kind of activity intended by Congress to be included when it required the Commission to consider the effect of a remedy on the public health and welfare." In the Matter of Certain Inclined-Field Acceleration Tubes and Components Thereof, Inv. No. 337-TA-67, Comm'n Op. Dec 1980. Illumina here seek to exclude devices that are of great and irreplaceable public value. Because the relief Illumina seeks would adversely impact the public health, safety and welfare and competitive conditions in the United States, the Commission should permit the Administrative Law Judge to conduct fact-finding on these public interest issues during the investigation.

Respectfully submitted,

/s/ T. Spence Chubb
T. Spence Chubb

cc: Certificate of Service
David Wille, Baker Botts

***Certain Nanopores and Products Containing Same*, Inv. No. 337-TA-3123**

CERTIFICATE OF SERVICE

I, T. Spence Chubb, hereby certify that true and correct copies of the foregoing PUBLIC INTEREST LETTER were filed and served on this 8th day of March, 2016 by the indicated means on the following:

Via Electronic Filing (EDIS) and Hand Delivery (8 copies):
The Honorable Lisa R. Barton
Secretary to the Commission
U.S. International Trade Commission
500 E. Street, S.W., Room 112A
Washington, DC 20436

Counsel for Complainants Illumina, Inc., the University of Washington, and the UAB Research Foundation: *Via Email: fusco@fr.com:*
Michael J. McKeon
Christian A. Chu
Thomas S. Fusco
FISH & RICHARDSON P.C.
1425 K Street NW, 1lth Floor
Washington, DC 20005
Tel: (202) 783-5070
Facsimile: (202) 783-2331

Craig E. Countryman
FISH & RICHARDSON P.C.
12390 El Camino Real
San Diego, CA 92130
Tel: (858) 678-5070
Facsimile: (858) 678-5099

/s/ *T. Spence Chubb*
T. Spence Chubb
Law Office of T. Spence Chubb
1025 Connecticut Avenue, N.W.
Suite 1000
Washington, DC 20036
(703) 623-7739
(703) 563-6055 (fax)
tschubb@tspencechubb.com
Counsel for Respondents Oxford Nanopore Technologies Ltd. and Oxford Nanopore Technologies, Inc.