Response to Referral Decision

This is Illumina's response of the CMA's Phase 1 Decision of 27 June 2019 (the Decision) in respect of the anticipated acquisition by Illumina of Pacific Biosciences (the Transaction).

1. Executive summary

Illumina is seeking to acquire PacBio because it believes that by doing so it will be in the position to:

a. Expand and accelerate uses for both short read and native long read sequencing;

b. Broaden customer access to, and improve user experience for, PacBio's systems, driving broader uptake;

c. Accelerate development and delivery of PacBio's systems for clinical customers; and

d. Accelerate introduction of future generation sequencing technologies that lead to enhanced capabilities and lower sequencing prices to expand and potentially create new end uses.

The Parties believe that there is no overlap between native long read and short read use cases, and that accurate native long reads will both address several specific stand-alone use cases and complement short read sequencing in certain other use cases. As a result, increasing availability of accurate native long reads will increase demand for both short and native long read sequencing. Illumina believes that such growth will occur in the two markets concomitantly, and not in one at the expense of the other. Short read and native long read technologies have fundamentally different characteristics that determine the use cases for which each technology is used. Short read systems are used in the large majority cases primarily because their attributes address the majority of customers' needs with substantially more favorable economics. Where a customer can use short read systems, it will do so. Only where short read systems cannot address a particular use case will a customer use a native long read system and accept the higher costs, lower output, potentially lower accuracy, and in many cases, higher amounts of DNA material needed.

After the transaction, the Parties will continue to face material (and growing) competition in short read and native long read sequencing. Today, Illumina faces material competition in the supply of short read systems and sequencing services from Beijing Genomics Institute ("BGI"), Thermo Fisher Scientific ("Thermo Fisher"), and Qiagen N.V. ("Qiagen"). Customers view the systems supplied by these companies as competitive alternatives to Illumina's systems. Consistent with developments in the last two years, Illumina expects intensified competition over the next three years from those competitors. Similarly, PacBio faces strong competition from ONT, a rapidly growing well-financed competitor whose revenues grew by 246% in its 2018 financial year.[1]. Beyond these existing competitors, the growing demand for sequencing and significant forecast future growth has attracted new entrants and has generated significant investment interest.

2. The parties and the acquisition

Illumina, Inc. ("Illumina") is a publicly traded global genomics company headquartered in San Diego, California, U.S.A. Illumina develops, manufactures and commercialises systems, consumables, bioinformatics and services used for genetic analysis. Illumina's systems include second generation, short read, DNA sequencers based on its Sequencing by Synthesis ("SBS") technology as well as DNA microarray scanners. Illumina's sequencing systems run on consumables that include library preparation kits, sequencing kits and flow cells. The sequencing data that they produce is interpreted using specific bioinformatics software and applications.

[1] https://twitter.com/nanopore/status/1148115409595449347

Illumina's systems, consumables and bioinformatics tools are used by major government and not-for-profit genomic research institutes, academic institutions, hospitals, genomics centers as well as pharmaceutical, biotechnology, agrigenomics, clinical and diagnostic laboratories, and consumer genomics companies. Since its creation in 1998, Illumina has been a major force in driving down the cost of genetic analysis, especially in the field of sequencing. Illumina also provides product support services for its systems as well as genetic analysis services powered by its sequencing and microarray technologies.

Pacific Biosciences of California, Inc. ("PacBio") is a publicly traded genomics company headquartered in Menlo Park, California, U.S.A. PacBio develops, manufactures and commercialises third generation, native long read, DNA sequencing systems based on its Single Molecule, Real Time ("SMRT®") technology. PacBio's native long read systems run on proprietary consumables that include library preparation kits, sequencing kits and SMRT Cells commercialised by PacBio. The sequencing data that they produce is interpreted with bioinformatics tools provided by PacBio and by third parties (such third parties are typically employed by or affiliated with not-for-profit genomic research institutes and genome centers). PacBio's customers include government and not-for-profit genomic research institutes, genomic centers, pharmaceutical companies and agricultural companies. PacBio also provides product support services for its native long read sequencing systems.

The transaction entails the acquisition of sole control by Illumina of PacBio. Pursuant to an executed Agreement and Plan of Merger ("Merger Agreement"), dated November 1, 2018, by and among PacBio, Illumina, and FC Ops Corp. ("Merger Subsidiary"), a wholly-owned direct subsidiary of Illumina, Illumina will acquire 100% of the voting securities of PacBio through a merger of the Merger Subsidiary with PacBio. PacBio will continue as the surviving corporation and as a wholly-owned direct subsidiary of Illumina.

3. DNA Sequencing

DNA sequencing enables the study of the genomes of numerous species, including humans, animals, plants and microbes. DNA sequencing is foundational and useful for virtually all types of biological research, in clinical settings and in various applied fields. Variations between organisms are due, in large part, to differences in their DNA sequences. Humans differ by approximately 0.5% of their genome sequence, and this relatively small amount of variation makes individuals unique.[25]

Genetic variation accounts for many of the physical differences we see (*e.g.*, height, hair, eye colour). It can also have medical consequences affecting disease susceptibility, including predisposition to genetic diseases such as cancer, diabetes, cardiovascular disease, and Alzheimer. In addition, genetic variation can affect response to certain treatments, impacting on how well they respond and adverse side effects.[2]

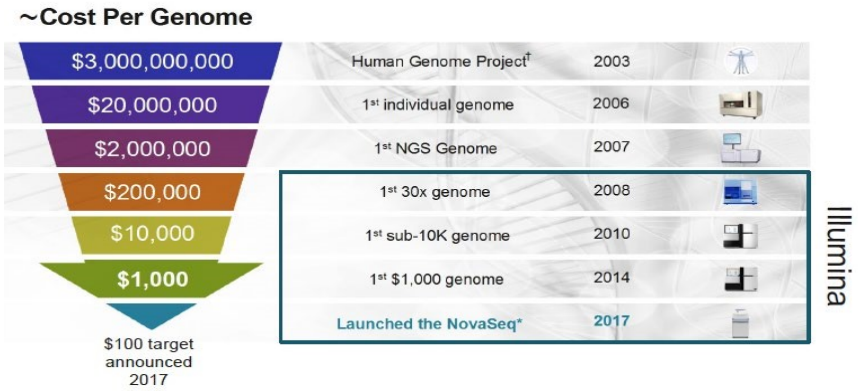
Variations in the DNA sequence can result from Single Nucleotide Polymorphism variants, insertions, deletions, inversions, translocations, or duplications of nucleotides, for example. These changes in the genetic code may cause certain genes to become overexpressed (*i.e.*, producing excessive amounts of proteins), underexpressed (*i.e.*, producing reduced amounts of proteins), or silenced altogether. Variation can also alter the function of proteins. Since cells depend on the production of proteins to operate normally, this may trigger substantial changes in their function.

Sequencing systems enable analysis of the genome, transcriptome or epigenome of virtually any organism.

[2] *Ibid.*

a. Developments over last 13 years

Illumina's investments and development activities have driven rapid technological improvements in, and material reductions in the cost of, short read sequencing, thereby significantly expanding the use of short read sequencers. Since its acquisition of Solexa in January 2007, Illumina's innovations have driven down the cost of resequencing a human genome 4,000-fold:



Today, sequencing a genome using Illumina's NovaSeq systems costs approximately [redacted]. Further, Illumina is currently working to develop a system that enables a US$100 genome, and is committed to further reducing the cost of sequencing, because it believes that reducing the cost of sequencing directly increases demand for sequencing:

It is this "virtuous cycle" that drives Illumina's investments in sequencing technology and development. By reducing the cost of sequencing, Illumina creates opportunities for new sequencing use cases and increased volumes in existing use cases. The Transaction will enable it to drive cost reductions and technology improvements in native long read sequencing that are similar to those it has achieved in short read sequencing, thereby increasing demand for both native long read and its current short read sequencing.

Sequencing is a nascent, dynamic and rapidly evolving industry with significant untapped and undeveloped potential for growth. For instance, as of today, less than 0.01% of species and less than 0.02% of human genomes have been sequenced, and the understanding of the human genome is in its infancy.[3] Sequencing has the potential to be a part of everyday life, for instance, where

[3] Illumina presentation, "2019 JP Morgan Healthcare Conference", 7 January 2019, available at https://www.illumina.com/content/dam/illumina-marketing/documents/company/investor-relations/ILMN-at-JPM-2019-7-January-2019.pdf

tumors are sequenced to help with diagnosis and therapy selection, genetic diseases are diagnosed before birth, and your genetics becomes an integral part of personalised medicine.

b. Characteristics of short read and native long read sequencing technologies

The Decision rests on the incorrect premise that short read and native long read technologies (and the systems implementing them) are "technically interchangeable", with read length the distinguishing characteristic of the technologies.

This over simplification fails to capture the fundamentally different technical characteristics of the approaches to sequencing that determine what each type of system can do. These technical differences, including read length, scalability, reads per run, run output, accuracy (whether raw or consensus) and cost determine the use cases for which each technology is (and can be) used. They are inherent in the technologies – today and will persist into the future. As a result, factors such as scalability limit the extent to which current native long read technologies can improve their performance on key parameters such as run output.

Short read systems sequence up to hundreds of base pairs per read, have high throughput (or run output), are scalable and are economical. Native long read systems sequence up to thousands of base pairs per read, have lower throughput (by at least an order of magnitude), are not scalable (an enduring characteristic) and are (and will remain) materially more expensive.

Further, despite their longer lengths, native long reads are not "better" than short reads. While there are specific use cases where a native long read system is required to obtain different or complementary information, native long read systems are not used when either a short read system can provide the same information (at significantly lower cost), as is the case with the vast majority of use cases, or the DNA from the sample being sequenced is short (*e.g.*, NIPT and cfDNA).

Given the above, and the fact that the costs of short read sequencing (however measured) are materially lower than those of native long read sequencing, customers will only use native long read systems when short read systems are unable to provide an answer to the question at hand (*e.g.*, because the read length required is too long).

c. Cost differences

The Decision erroneously dismisses the importance of cost as a factor considered by users of sequencing systems when choosing the appropriate system, and goes on to state that the costs of sequencing using PacBio's Sequel II and Illumina's sequencers are "much more comparable".[4]

Short read and native long read systems differ in a number of cost-determinative performance parameters that are important to customers, including reads per run, output per run, genomes per year[5] and the resulting cost per Gb, as shown in the table below:

Parameters	NovaSeq 6000	Sequel II	Magnitude of Difference
Length of Read	[redacted]	[redacted]	[redacted]
Reads per Run	[redacted]	[redacted]	[redacted]
Output per Run	[redacted]	[redacted]	[redacted]
Genomes per Year	[redacted]	[redacted]	[redacted]

[4] At paragraph 84(b).

[5] "Genomes per year" is used in the industry as a proxy for the number of samples that a system can sequence in a year.

$/Gigabase	[redacted]	[redacted]	[redacted]

There are different ways of describing sequencing costs, including Total Cost of Ownership ("TCO"), cost per Gb, cost per run, cost per million reads, cost per genome, and cost per project. When comparing systems that have different run outputs, it is important to use metrics that normalise for differences in system output, such as cost per Gb, per million reads, per genome/sample, or TCO. These reflect cost of ownership taking into account the manner in which a system is designed to be used over time.

Operating costs of short read systems are an order of magnitude lower than that of native long read systems as a result of the fundamental differences in the respective technologies. Similarly, because, as acknowledged in paragraph 23 of the Issues Paper, sequencing markets are systems markets, the TCO is a relevant parameter to use to compare costs. For example, the TCO differential between Illumina's and PacBio's systems are clear when looking at the relative cost of (re)sequencing a human genome. For a laboratory sequencing 1,000 whole human genomes per year, the cost per genome sequenced using PacBio's Sequel II is [redacted] while the cost per genome sequenced with Illumina's NovaSeq is [redacted]. This is more than seven times lower and represents a difference of more than [redacted] across 1,000 genomes. For a lab sequencing 10,000 genomes per year, the cost of each genome sequenced using a Sequel II is [redacted], while the cost of each genome sequenced using a NovaSeq is [redacted]. This is more than [redacted] times higher, and represents a difference of [redacted] across 10,000 genomes:

		Volume of Whole human genomes per year			
		1,000	**10,000**	**100,000**	**500,000[6]**
Number of systems required	Illumina	[redacted]	[redacted]	[redacted]	[redacted]
	PacBio	[redacted]	[redacted]	[redacted]	[redacted]
	Differential	[redacted]	[redacted]	[redacted]	[redacted]
Total cost of ownership	Illumina	[redacted]	[redacted]	[redacted]	[redacted]
	PacBio	[redacted]	[redacted]	[redacted]	[redacted]
	Differential	[redacted]	[redacted]	[redacted]	[redacted]
Normalised price per genome	Illumina	[redacted]	[redacted]	[redacted]	[redacted]
	PacBio	[redacted]	[redacted]	[redacted]	[redacted]

Further, sequencing a high number of genomes requires many more Sequel IIs than NovaSeqs. In short, a single NovaSeq can sequence approximately as many genomes in a [redacted] run as a Sequel II system can sequence in [redacted]. While [redacted] Sequel IIs are necessary to sequence [redacted] genomes a year, this can be done with just one NovaSeq. A laboratory sequencing [redacted] genomes a year would only need [redacted] NovaSeqs, but would need [redacted] Sequel IIs.[7]

Illumina is unaware of any circumstances for which the metric proposed by the CMA in Table 1, "cost per million reads per 300 bp fragment," is appropriate or ever used by customers as a cost-comparison metric. In use cases requiring identification and

[6] While Illumina does not have any customers that currently sequence [redacted] genomes per year, Illumina understands that there are current and prospective customers that are considering sequencing projects of this size, and as such has established discounts for customers that may operate at that volume.

[7] The presentation to the CMA on 23 May indicated that [redacted] NovaSeqs and [redacted] Sequel IIs would be required to sequence [redacted] genomes in one year. The lower numbers shown (for both systems) in the table do not reflect updated utilisation assumptions provided by PacBio.

quantification of individual fragments of DNA and RNA, customers are interested in the number of ***independent reads*** from each fragment , e.g., counting RNA transcripts to measure gene expression, or counting fragments of cell free DNA to measure the ratio of chromosomes (aneuploidy detection) for NIPT. Once a fragment has been identified, additional reads derived from that same fragment do not add additional insights and are therefore neither necessary nor valuable. Shorter 'sub-reads' of a native long read, as implied by the "cost per million reads per 300bp fragment" are not independent read counts and, therefore, are not useful for the purposes of quantification or other use cases in which customers are interested in the number of reads.

d. Complementary use of sequencing technologies

As noted above, the Decision erroneously takes the position that there is no clear cut demand-side distinction between native long read and short read systems, such that native long read and short read systems are interchangeable.

As a result of the fundamentally distinct technical characteristics and economics described above, customers only use native long read systems when short read systems are unable to provide an answer to the question at hand. In other words, if a use case can be addressed using a short read system, a short read system will be used. However, there are use cases for which short read results are insufficient (*e.g.*, when larger SVs need to be discovered and be detected or repetitive regions need to be sequenced).

Each customer has a set of use cases that it needs to perform (*e.g.*, research questions to address or clinical tests to perform), and each use case has a set of requirements which determine whether a short read or native long read system is used. These requirements include the following:

a. *Technological requirements*: these include read length, accuracy, cost per sample, samples per day (scale), samples per run (batching), depth (number of reads), run time, turnaround time and library preparation requirements (*e.g.*, duration);

b. *Customer context*: whether the customer is carrying out basic research, translational research, lab developed clinical testing or CE-IVD approved clinical testing, and whether it uses automation in its lab, *etc.*; and

c. *Sample types and quality*: the amount of input DNA required (DNA sample preparation for short read systems is less complex than for native long read systems, because less DNA is required to prepare a sample and there is no requirement to keep long samples intact), and the sample type available, both source (*e.g.*, blood, FFPE, stool) and quality (*e.g.*, DNA from FFPE samples is of lower quality than other types and typically is in shorter fragments).

The Decision mischaracterises the complementary use of short read and native long read systems. For example, in the context of *de novo* sequencing of whole genomes it incorrectly concludes that the use of both native long read and short read systems in *de novo* sequencing, with the potential for improved native long read results to reduce the amount of "polishing" of the draft reference genome using short read systems, means that the systems are "interchangeable". This reflects a fundamental misunderstanding of both the complementary nature of the use cases, and the nature of complementarity itself.

Both short read and native long read systems can be used in *de novo* sequencing, but they address distinct and complementary use cases:

a. If the relevant genome is complex (like plant genomes), native long read sequencing is required for *de novo* assembly of a reference genome. Short read sequencing can be used for *de novo* sequencing of certain small, non-complex genomes, such as microbial

genomes. Native long read systems enable assembly of larger continuous fragments, but short read technologies cannot deliver *de novo* sequencing of longer, complex genomes. *De novo* sequencing of plant and animal genomes, which frequently contain repetitive DNA, particularly benefits from native long read systems because they span repeats.

Jeremy Schmutz, a faculty investigator at the HudsonAlpha Institute for Biotechnology, and an early-access customer of the Sequel II, made the distinct complementary uses clear when he said that "*he is interested in using the* [Sequel II] *to do* ***de novo assembly of plant genomes***" and has used it to complete the *de novo* assembly of the Sorghum plant.[8] He went on to elaborate about the differences between short read and native long read systems in plant genomics studies in the following terms: *"... for plant genomics studies, while resequencing with Illumina yields a lot of information about plant diversity and SNPs, much variation remains undetected…* [because] *plants tend to be hypervariable… when you view* [the data] *through the lens of a reference, you avoid portions of the genome."* *By contrast, long-read sequencing will lead to the "ability to start to build up more comprehensive pan-genome references in plants, so that when we do association studies, we have reference blocks for those plants," which will enable linking of traits and variants."*[9]

b. Apart from being used to create draft reference genomes for small, non-complex reference genomes, short read systems enable economical polishing (error correcting) of reference genomes produced by native long read systems to achieve high accuracy. The fundamental limitations on the accuracy, lower run output, higher costs and lower sample throughput of native long read systems limit their usefulness in polishing. Accordingly, customers polish using lower cost, higher accuracy short read systems.

c. Resequencing entails aligning reads from a sample against an existing reference genome for the relevant species or population. Both short read and native long read systems can be used for resequencing in different use cases: (i) Short read systems are used in resequencing to identify variants such as SNVs, small indels involving 1 to 50 base pairs, and small tandem repeats because they offer high run output, high sample throughput, high accuracy, and favourable economics; and (ii) Native long read systems are used to resequence when short read systems cannot be used (*e.g.*, because the variant of interest is too long).

In that regard, the relevant decision practice makes clear that products which "technically" could serve the same or similar purposes but are in practice used by customers for distinct uses because of their distinct characteristics and price are complements, not substitutes.[10] For example, in *Ambu A/S/ Unomedical Limited*, the OFT found that high quality electrodes and more basic electrodes were complements rather than substitutes because of the price difference and the fact that they were used by customers for different purposes.[11] In *General Electric Company/ Invision Technologies Inc.*, the OFT found that systems used to detect explosives and other illegal substances supplied by each party were complements (rather than substitutes) as a result of the substantial price difference and the fact that each system provided different valuable information about the substances.[12]

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[8] https://www.pacb.com/wp-content/uploads/GenomeWeb_PacBio_early_access.pdf; https://www.youtube.com/watch?v=VAshkMhhPZY.

[9] *Ibid*.

[10] OFT, Decision of 17 February 2011, *FGX Europe Limited/ Framed Vision Limited*, 32-42; OFT Decision of 14 May 2012, *Ambu A/S/ Unomedical Limited*, para. 35; OFT, Decision of 26 January 2005, *General Electric Company/ Invision Technologies Inc.,* para 18.

[11] OFT Decision of 14 May 2012, *Ambu A/S/ Unomedical Limited*, para. 35

[12] OFT, Decision of 26 January 2005, *General Electric Company/ Invision Technologies Inc.,* para 18.

Customers are of the view that native long read systems and short read systems are complementary, as illustrated in their public statements:

a. Genome Centre of the University of California Davis: the Genome Centre owns a Sequel as well as several Illumina mid- and high-throughput systems, states on its website that they: "*offer the two complementary Next Generation Sequencing (NGS)* technologies*: Illumina sequencing, and PacBio (long read) sequencing, and provide the full spectrum of sequencing options and a wide range of library preparation services for both platforms"*.[13]

d. Earlham Institute: the Institute explains on its website that "*PacBio sequencing for larger genomes is often combined with short-read sequencing data (e.g., from the Illumina HiSeq) in a 'hybrid' assembly which will give you greater contiguity than the HiSeq data alone*".[14]

e. The University of Exeter: the university states that PacBio's systems "*can also be used in conjunction with short read data to improve existing assemblies*".[15]

f. Novogene: a large provider of sequencing services advertises on its websites that it "*not only offers PacBio Sequel-based de novo sequencing services, but also provides combined services using various platforms, including Illumina HiSeq, PacBio Sequel, and 10X Genomics Chromium, to match the needs of researchers*".[16]

g. VIB: following the launch of PromethION, researchers from Belgium's VIB explained that their laboratory owned both Illumina and ONT systems and they anticipated that they would *"… use different technologies for different applications…"* but said the group is still figuring out each system's sweet spot. *"It will depend on the organism and the research question*".[17]

h. Oxford Genomics: following the launch of the PromethION, David Buck, researcher at the Oxford Genomics centre, explained that he "*…sees potential in the technology for applications like phasing genomes and identifying structural variants. It could also be combined with Illumina sequencing, which would improve the accuracy and enable SNV calling.*"

i. Garvan Institute: one of the first laboratories certified by ONT as a sequencing services provider, the Garvan Institute's website states that "*Nanopore sequencing provides alternative yet complementary capabilities to our existing short-read technologies, allowing us to rapidly identify genetic features that can be difficult to assess with other approaches, such as large genome rearrangements or epigenetic marks*".[18]

e. Migration to native long read

Finally, there may be a limited number of customers who, in the past, have used short read systems to perform use cases for which native long read systems are better-suited and are now switching those runs to native long read systems. However, such limited migration from one technology to the other does not mean that the technologies compete.

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[13] https://dnatech.genomecenter.ucdavis.edu/.
[14] http://www.earlham.ac.uk/pacbio-rsii.
[15] http://sequencing.exeter.ac.uk/pacific-biosciences-overview/.
[16] https://en.novogene.com/technology/pacbio-sequel-system-applications/.
[17] https://www.genomeweb.com/sequencing/oxford-nanopore-customers-europe-australia-discuss-initial-runs-promethion#.XOj9cuQ0N9B.
[18] https://www.garvan.org.au/news-events/news/reading-dna-in-real-time-garvan2019s-new-long-read-sequencing-capability.

Pursuant to the European Commission's and the CMA's decision practice, two products fall within the same relevant market if a small but significant increase in the price of one product would result in a degree of switching to the other product that would render that price increase unprofitable.[19] However, migration from an existing product to a new product that better satisfies the needs of certain customers in the absence of any change in the price or quality of the existing product, is insufficient for the two products to be interchangeable and fall within the same relevant market.[20]

In the case at hand, migration to native long read is not due to a change in the short read offering but to the introduction of new long read systems that better satisfy the specific needs of the switching customers. Due to the differences between the two technologies, those customers do not consider them as interchangeable. Rather, they consider that the new native long read system is best-suited for the relevant use case(s). The customers would not switch back to short read systems in the event of a 5 to 10% decrease in the price of those systems.

4. Recent Developments in Native Long Read Technologies

The significant differences in the characteristics and performance of short read and native long read systems have not been materially reduced by recent systems launches by PacBio and ONT, and, if anything, will increase in the medium- to longer-term.

a. PacBio's Sequel II

Following the launch of the Sequel II (and 8M chip), there remains a significant technological and cost gap as compared to short read systems (*e.g.*, Illumina and its short read competitors). Illumina anticipates that the gap will widen as it continues to improve its systems to produce hundreds to thousands of Gb (for its medium throughput systems) and thousands to tens of thousands of Gb (for its high-throughput systems), while the technological limitations of PacBio's methodology constrain its ability to make further improvements to its current yield.

The figure below compares the run outputs of PacBio's systems, on the one hand, and Illumina's [redacted],[21] and shows that PacBio's technological innovations (including both the Sequel II system and its potential successors) will not reduce the significant differential in run output or operational costs. That difference will range from at least [redacted] today to more than [redacted] in the medium- to long-term (for Illumina's high throughput systems).[22] Further, the current run throughput performance gap between Illumina's and PacBio's systems is currently the narrowest it will be.

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[19] OFT, *Guidance on Market Definition*, December 2004, p.7 para.3.3, CMA, *Merger Assessment Guidelines*, September 2010, p.31 para.5.2.10; European, Commission, *Notice on the definition of relevant market for the purposes of Community competition law*, OJ C 372, 9.12.1997, p.7, para.17. General Court, Judgement of 30 January 2007 in case T-340/03, *France Telecom*, para. 87.

[20] CMA Decision of 26 July 2016 in *Ladbrokes/ Coral*, p.42 para. 6.29 ; See also CMA Decision of 14 November 2016 in Future plc / Miura, p.12 para 51 ; Commission Decision of 30 October 2001 in case COMP /M.2420 – Mitsui/CVRD/Caemi, para.134, Danish Competition Council, Decision of 16 August 2017, Imerco Holding/ Inspiration A/S ; General Court, Judgement of 30 January 2007 in case T-340/03, *France Telecom*, para. 88.

[21] [redacted]

[22] [redacted]

PacBio's native long read technology cannot scale in a manner that would enable it to deliver run outputs that are closer to, let alone comparable with, those delivered by Illumina's systems. These differences stem from the sequencing approaches themselves:

a. Cameras/Sensors PacBio's technology is single molecule and real-time, effectively requiring a "movie" to be filmed of the sequencing process using a one-time use camera that is part of the consumable flow cell.

b. Single-molecule approaches are significantly less accurate than short read approaches, requiring throughput to be traded for accuracy. The Sequel II has not changed this.

c. Real-time approaches have demanding and costly compute requirements, constraining their scalability.

As the figure above makes clear, the run output for the Sequel II is currently approximately of data,[23] compared with a single flow cell that can generate of data (a 1 difference). Because of the significant difference in output per flow cell, the price per Gb using the is a nearly lower ( ). Even Illumina's can generate of data - times greater than Sequel II's run output at less than ( ).[24]

As this makes clear, while the Sequel II has delivered a run output improvement, it has not made PacBio's system "much more comparable" with Illumina's.

[23] Using Circular Consensus Sequencing (CCS), the raw read output of the Sequel II can be improved to accuracy. However, this results in an almost reduction in output.

[24]

b. ONT

[redacted]

5. Competitive Assessment

The Transaction will not allow the merged company to profitably raise prices, lower quality, reduce its range of services or reduce innovation for three main reasons:

a. The shares of supply relied on in the Decision provide a misleading static picture which fails to account for recent developments in the short read and native long

[redacted]

read markets and the significant amounts of entry that will occur in the short- to medium-term.

b. The parties are not each other's closest competitors.

c. There are many other providers that are already significant competitors with the parties in their respective markets or are well placed to enter in the short- to medium-term.

PacBio does not compete with Illumina. Further, Illumina has, both before and after PacBio began offering its native long read systems, a strong record of driving short read sequencing price reductions, increasing quality (whether in relation to throughput, run output, accuracy or any other measure), offering a range of systems to enable customers to carry out short read sequencing in the manner that best suits them, and investing heavily in innovation. The parties will continue to face material (and growing) competition in both short read and native long read sequencing.

a. Short Read Systems

Illumina's conduct is constrained by direct competition from other providers of short read sequencing systems. There are three companies in particular that currently compete with Illumina in the supply of short read systems and short read sequencing services: Beijing Genomics Institute ("BGI"), Thermo Fisher Scientific ("Thermo Fisher"), and Qiagen N.V. ("Qiagen"). Customers view the systems supplied by these companies as competitive alternatives to Illumina's systems and essentially every sale made by one of these companies is a sale that Illumina could have made. Consistent with developments in the last two years, Illumina expects intensified competition over the next three years from those competitors. There is no basis for concluding that "there are limited alternatives to the Parties… [and] that those other available suppliers of sequencing systems are generally not good alternatives to the Parties".

BGI launched its first short read sequencing system, the BGISEQ-500, in 2015,[28] and currently sells several systems, including the BGISEQ-50 launched in 2016,[29] the MGISEQ-200 and MGISEQ-2000 (both launched in 2017),[30] and its highest throughput system, the MGISEQ-T7, in October 2018. BGI also launched a modular NGS workstation, called MGIFLP, in 2017,[31] designed to integrate the entire NGS process.[32].

[redacted]

[28] https://www.bgi.com/global/company/careers/bgi-launches-its-desktop-sequencer-bgiseq-500/. Previously, BGI had released the BGISEQ-100 and BGISEQ-1000 for its sequencing-as-a-service business. See http://www.bio-itworld.com/2015/10/28/bgi-retools-complete-genomics-technology-new-high-throughput-benchtop-sequencer.html

[29] [redacted]

[30] https://www.bgi.com/global/company/news/bgis-mgi-tech-launches-two-new-ngs-platforms/

[31] https://www.bgi.com/global/company/news/bgis-mgi-tech-launches-two-new-ngs-platforms/

[32] http://en.mgitech.cn/product/detail/MGIFLP.html

[33] See Annex 058 submitted on 2 April 2019, including slides on a third-party report comparing BGISEQ-500 to NovaSeq and finding similar computational performance and error rates for the two models.

[redacted]

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a. [redacted]
b. [redacted]
c. [redacted]
d. [redacted]
e. [redacted]

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[redacted]

[redacted]

Thermo Fisher is the world's largest maker of scientific and laboratory equipment, with 400,000 clinical, applied and research customers across the globe.[42] Thermo Fisher is the leading supplier of Sanger sequencing systems, with a total installed base of around [redacted] sequencers,[43] and the second largest supplier of short read systems with approximately [redacted] systems installed at the end of 2017),[44] giving it the largest installed base of sequencing systems worldwide. Thermo Fisher acquired Life Technologies, which marketed and sold the SOLiD and Ion Torrent short read sequencing systems in 2014.[45, 46] Life Technologies had already launched the Ion Torrent systems prior to its acquisition by Thermo Fisher, *i.e.*, the Ion PGM (2010) and Ion Proton (2012). In 2015, it launched the Ion S5 and Ion S5 XL systems, and in 2018, the Ion GeneStudio S5, Ion GeneStudio S5 Prime, and Ion GeneStudio S5 Plus.

[redacted]

a. [redacted]

b. [redacted]

c. [redacted]

d. [redacted]

e. [redacted]

f. [redacted]

g. [redacted]

h. [redacted]

i. [redacted]

[42] Thermo Fisher 2017 Annual report, p. 3, available at http://d18rn0p25nwr6d.cloudfront.net/CIK-0000097745/7bc424cd-7525-4fb2-8de0-a33bc5b10c6b.pdf

[43] [redacted]

[44] [redacted]

[45] [redacted]; See also https://www.thermofisher.com/be/en/home/about-us/news-gallery/press-releases/2014/thermo-fisher-scientific-completes-acquisition-of-life-technologies-corporation.html

[46] Life Technologies, in turn, had acquired Ion Torrent for up to GBP 562 million in 2010. Applied Biosystems, which merged with Invitrogen to form Life Technologies in 2008, had acquired Agencourt Personal Genomics, owner of the SOLiD brand, for GBP 93 million in 2006. Thermo Fisher's SOLiD systems were discontinued as of May 1, 2016. In addition, Life Technologies had acquired Visigen Biotechologies, which was developing a single molecule sequencing technology known by the codename "Starlight", in 2008 for GBP 15.5 million. These figures have been converted from USD to GBP using the Bank of England's 2017 average exchange rate of GBP 1 = USD 1.29 (rounded to two decimal places). See https://www.businesswire.com/news/home/20100817006643/en/Life-Technologies-Announces-Agreement-Acquire-Ion-Torrent, https://www.businesswire.com/news/home/20060530005289/en/Applied-Biosystems-Acquire-Agencourt-Personal-Genomics-Privately-Held, and http://allseq.com/knowledge-bank/ngs-necropolis/visigen/

j. [redacted] and

k. [redacted]

Qiagen entered the market for short read systems in 2012 through the acquisition of Intelligent BioSystems, which had released the MAX-Seq in 2011 and was working on the Mini-20.[47] Qiagen launched its GeneReader system in 2015. Qiagen's continued expansion is illustrated by its targeted 22% increase in sequencing revenues in 2018 (including revenue generated from its GeneReader system, library prep solutions, assays, and bioinformatics).[48] At the beginning of 2018, Qiagen announced several enhancements to the GeneReader, including upgraded NGS chemistry increasing output.[49] Qiagen has undertaken multiple strategic initiatives to expand the use cases in which its GeneReader can be used. For example, in 2018, it announced a partnership with Natera, a provider of sequencing assays for NIPT and ctDNA, to develop NIPT assays for GeneReader.[50] [redacted]

a. [redacted]

b. [redacted]

c. [redacted]

d. [redacted]

e. [redacted]

f. [redacted]

b. Native Long Read

[redacted]. ONT currently commercialises three native long read systems: the MinION, GridION and PromethION, [redacted] As of May 2018, ONT had placed approximately 6,000 to 7,000 MinIONs systems globally.[51] Also in May 2018, ONT reported that there were over 100 GridIONs customers in 24 countries, and that at least 40 PromethIONs systems had shipped, with another 20 expected to ship by the end of June 2018, and further orders received.[52]

Demand for ONT's systems has "increased exponentially" in the last five years.[53] On 8 July 2019, ONT announced that its global revenues grew by 246% in 2018.[54] Specifically, its revenues increased to USD 43.7 million last year, up from USD 17.8 million in 2017.[55] Orders also more

[47] [redacted]

[48] Qiagen 2017 Annual Report, p. 56, available at https://corporate.qiagen.com/-/media/project/qiagen-corporate/corporate-microsite/documents/investor-relations/2017/reports/2017-ifrs-annual-report-r101-final.pdf.

[49] https://corporate.qiagen.com/newsroom/press-releases/2017/20180108_ngs_portfolio_expansion.

[50] https://corporate.qiagen.com/newsroom/press-releases/2018/20180312_qiagen_natera_partnership.

[51] https://nanoporetech.com/about-us/news/clive-g-brown-cto-plenary-london-calling.

[52] https://nanoporetech.com/about-us/news/clive-g-brown-cto-plenary-london-calling.

[53] As stated by Gordon Sanghera, ONT's CEO, upon the opening of the MinION Building. See https://nanoporetech.com/about-us/news/scale-oxford-nanopores-new-high-tech-factory-comes-online

[54] https://twitter.com/nanopore/status/1148115409595449347

[55] *Ibid*.

than doubled in 2018 to USD 60.6 million, from USD 24.5 million the previous year.[56] In addition, ONT announced that it expects a two to three-fold increase in revenues and orders this year.[57]

	2015	2016	2017	2018
Revenue ($M)	1.1	6.2	17.8	43.7
Orders ($M)	1.4	7.2	24.5	60.6

ONT also announced that its new 34,500 square foot manufacturing facility (the "MinION Building") started manufacturing in July 2019 and that full, end-to-end production is being phased in.[58] The MinION Building, which enables ONT to scale up to large-scale production, will produce flow cells for the MinION, GridION, PromethION, and Flongle systems, and for future systems such as the SmidgION and Plongle.[59] Finally, ONT's R10 flow cells started shipping on 10 July.[60]

ONT has attracted funding of GBP 451 million in various fundraising rounds.[61] Most recently, in March 2018, ONT received GBP 100 million from investors from China, Singapore and Australia, alongside existing investors.[62] The funds were raised to support ONT's next phase of commercial expansion, development of new products[63] and the MinION Building.[64]

[redacted]

a. [redacted]
b. [redacted]
c. [redacted]
d. [redacted]
e. [redacted]
f. [redacted]
g. [redacted]

[56] *Ibid*.
[57] https://twitter.com/IPGroupplc/status/1147845361194741760
[58] https://nanoporetech.com/about-us/news/scale-oxford-nanopores-new-high-tech-factory-comes-online
[59] https://nanoporetech.com/about-us/news/scale-oxford-nanopores-new-high-tech-factory-comes-online; The Plongle ("plate Flongle") is a device with 96 individual, disposable flow cells for routine use. The Plongle is designed for users who wish to carry out larger numbers of small, quick tests in parallel. See https://nanoporetech.com/products/plongle and https://twitter.com/nanopore/status/1131629881266245632.
[60] https://twitter.com/nanopore/status/1148258720113135616; "R10" is a new design of nanopore and has delivered consensus accuracy of Q50 on a small genome sample. See https://nanoporetech.com/about-us/news/grandomics-collaborates-oxford-nanopore-deliver-dbsv-100k-project-sequence-100000
[61] https://nanoporetech.com/about-us.
[62] *Ibid.*
[63] ONT 2017 Annual Report, p. 6, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0.
[64] https://nanoporetech.com/about-us/news/oxford-nanopore-announces-ps100-million-140m-fundraising-global-investors.

c. The Parties are not Competitors

As explained in Sections 3(b) and (c), above, there are fundamental differences in the technical characteristics of native long read and short read sequencing that determine how each type of system is used. These technical differences, including read length, scalability, reads per run, run output, accuracy (whether raw or consensus) and cost, determine the use cases for which each technology is (and can be) used. As a result, the Parties' systems do not compete. [redacted]

d. Significant Investment and Imminent Entry

The material recent growth and significant forecast future growth in demand for sequencing has attracted new entrants and has generated significant investment interest from venture capital, pharmaceutical companies, diagnostics companies and governments in recent years.[65] While researching, developing and commercialising new sequencing systems requires significant investment, a large number of companies have made that investment, and due to ongoing and rapid growth and expansion of the sequencing industry, new entrants are able to find willing investors. Sequencing companies have attracted substantial investments from angel investors, investment firms, venture capitalists, governments, and large life science companies. For example, information in the public domain makes clear that, over the last year investment in only [redacted] sequencing companies (*i.e.*, [redacted] exceeded US$295 million. Across the industry as a whole, the investment was significantly greater.

The material number of entrants in the last decade is remarkable, particularly when compared with the number of companies that offered sequencing systems in the twenty years before that. Since 2007, 12 companies have shipped unique sequencing systems, with nine continuing to sell systems today.[71] Between 1986 and 2006, there were only four companies that offered sequencing systems:

[65] Market analysts, for example, have forecast that global NGS revenues will reach GBP 12.67 billion in 2024, up from GBP 4.42 billion in 2018, reflecting a CAGR of 19.2%. See https://www.marketsandmarkets.com/PressReleases/ngs-technologies.asp.

[66] [redacted]

[67] [redacted]

[68] [redacted]

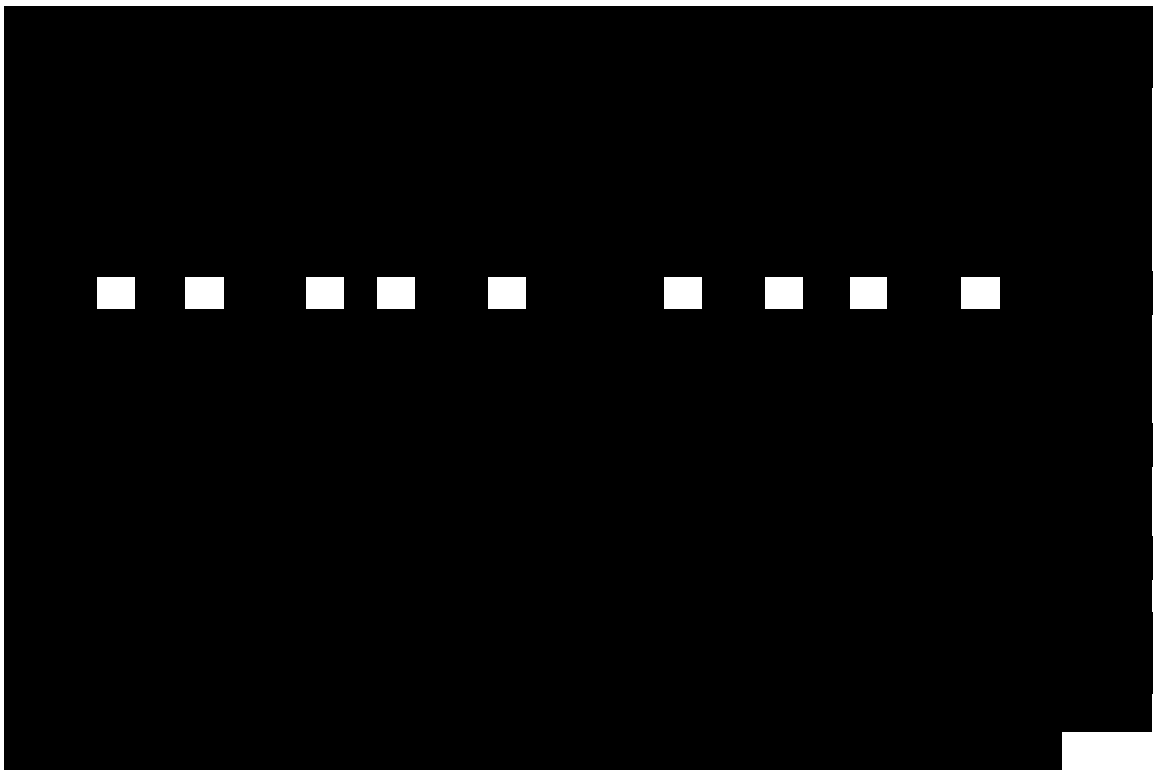
[69] [redacted]

[70] [redacted]

[71] [redacted]

As the level of investment suggests, many of the companies currently developing sequencing technologies are expected to announce, or have announced, the intention to enter the market in the next two years.

6. **Counterfactual**



7. The Transaction will be pro-competitive and will not harm competition or customers

Illumina is seeking to acquire PacBio because it believes that by doing so it will be in the position to:

a. Expand and accelerate uses for both short read and native long read sequencing;

b. Broaden customer access and improve user experience for PacBio's products and technology, driving broader uptake;

c. Accelerate development and delivery of PacBio's systems for clinical customers to enable both new and complementary clinical uses; and

d. Accelerate introduction of future generation sequencing technologies that lead to enhanced capabilities and lower sequencing prices to expand and potentially create new end uses.

The Transaction will enable Illumina to broaden customer access to PacBio's products and technology in the short-term, driving uptake, and accelerate development and delivery of systems for and to clinical customers. PacBio on a standalone basis does not have a distribution partner to distribute its products (including Sequel II), and its existing sales organisation (~20 worldwide, with just six in Europe) is insufficient to do so.

Illumina has significant research and development resources that it intends to use to drive the development of systems integrating PacBio's technology, as it has done with prior acquisitions that drove rapid technological improvements in sequencing and materially reduced costs, thereby significantly expanding the use of sequencing. Illumina believes that it can significantly accelerate the development of PacBio's technology, both delivering on the full potential of the Sequel II and developing new systems that maximise the potential performance of PacBio's technology.

As noted above, far from increasing the cost of sequencing, Illumina's history has been to drive down that cost. For example, it has reduced the cost of resequencing a whole human genome 4,000-fold, and is developing a short read sequencing system that should further reduce that cost from approximately [redacted] to approximately US$100. Similarly, since it acquired Verinata in 2013, Illumina achieved a four-fold reduction in the price per sample for NIPT testing (while increasing the number of samples run from 1,000 in 2011 to 1.2 million in 2019).