Case ME/6795/18

Acquisition by Illumina, Inc. of sole control of Pacific Biosciences of California, Inc.

Merger Notice

17 April 2019

CONFIDENTIAL – BUSINESS SECRETS

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PART I – GENERAL INFORMATION

1. Provide the name and contact details of:

***(a)* an individual within each of the merger parties**

Illumina	Pacific Biosciences
[redacted]	[redacted]

***(b)* any authorised representatives of each of the merger parties**

Illumina	Pacific Biosciences
[redacted]	[redacted]

***(c)* if not already provided in response to (a) and (b), the person(s) submitting the Notice**

1. The names and contact details of the persons submitting the Notice are provided in a) above.

***(d)* the person to whom the CMA should address any correspondence.**

2. Please address correspondence to [redacted] and [redacted].

PART II – MERGER DETAILS

The merger situation

2. Describe the arrangements by which the enterprises will cease/have ceased to be distinct (the merger), including:

***(a)* the parties to the merger (the merger parties)**

3. 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. 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.

4. 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.

5. Illumina and PacBio are referred to as the "Notifying Parties" or "Parties" in the Merger Notice.

***(b)* the type of transaction**

6. The transaction involves the acquisition of sole control by Illumina of PacBio. Pursuant to an executed Agreement and Plan of Merger ("Merger Agreement") (see [redacted]), 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. Subsequently, PacBio shall continue as the surviving corporation and as a wholly-owned direct subsidiary of Illumina (the "Transaction" or "Proposed Transaction").

***(c)* the consideration**

7. As consideration, Illumina will pay GBP 6.20 per share, with a total acquisition price of approximately GBP 930.2 million.[1]

***(d)* the key terms**

8. The Merger Agreement is subject to approval by PacBio's shareholders, which occurred on January 24, 2019, as well as customary conditions as described in Article 9 of the Merger Agreement, which states that all required antitrust filings have been made and all required regulatory approvals have been obtained. The UK is a Key Jurisdiction under Section 1.01(a) of the Company Disclosure Schedule to the Merger Agreement, such that approval of the CMA is a condition to closing.

***(e)* the timing**

9. The Notifying Parties intend to close the Transaction no later than three business days following the satisfaction or waiver of the above mentioned conditions.

***(f)* the strategic and economic rationale for the transaction**

10. As discussed in Section 24 below, the Transaction will:

- facilitate wider distribution of/access to PacBio's products and technology by enabling PacBio to benefit from Illumina's global production, and support and service infrastructure;
- increase adoption of PacBio's systems by clinical and diagnostic customers by enhancing PacBio system quality with Illumina's quality systems and system management processes;
- improve PacBio's systems using Illumina's proprietary technologies;
- enable Illumina to develop coordinated solutions (including bioinformatics) to enable customers to harness the complementary nature of the technologies; and
- accelerate innovation.

***(g)* whether it is being notified in any other jurisdictions and, if so, whether the merger parties are willing to offer a waiver to support coordination between the CMA and the competition authorities in those jurisdictions, and**

[1] 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).

11. The Transaction was notified to the U.S.A's Federal Trade Commission ("FTC") on November 29, 2018. The FTC issued a request for additional information and documentary material on December 28, 2018. Each of Illumina and PacBio confirmed substantial compliance with the Second Request on March 29, 2019.

***(h)* the ownership structure pre and post-merger, including any pre-merger links between the merger parties.**

12. Illumina is a publicly listed company with its common stock equivalent traded on the NASDAQ. Approximately 89% of Illumina's common stock equivalent is institutionally owned, but no shareholders or group of shareholders has or have sole or joint control. The list of Illumina's top five shareholders as at March 29, 2018 is provided below:[2]

Shareholder	Shareholding
Baillie Gifford & Co.	12.10%
Blackrock, Inc	7.9%
Capital Research & Management Co. (Global Investors)	7.8%
The Vanguard Group, Inc.	7.0%
The Growth Fund of America	5.50%

13. PacBio is a publicly listed company with its common stock equivalent traded on the NASDAQ. No shareholder or group of shareholders has or have sole or joint control. The list of PacBio's top five shareholders as at January 30, 2019 is provided below:

Shareholder	Shareholding
Consonance Capital Management LP	9.03%
Maverick Capital Ltd.	8.14%
Magnetar Financial LLC	6.30%
Oracle Investment Management, Inc.	6.27%
BlackRock Fund Advisors	6.22%

14. PacBio and Illumina do not have pre-Transaction links. On completion of the Transaction, PacBio will merge with Illumina's wholly-owned direct subsidiary, FC Ops Corp., with PacBio continuing as the surviving corporation, as a wholly-owned direct subsidiary of Illumina.

3. Provide a brief description of the businesses of the merger parties (and, where relevant, their groups).

15. Illumina develops, manufactures and commercialises systems, consumables, bioinformatics and services used for genetic analysis. Illumina's systems include

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[2] https://www.sec.gov/Archives/edgar/data/1110803/000119312518109968/d545922ddef14a.htm#toc545922_32

second generation, short read, DNA sequencers based on its 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 with specific bioinformatics software and applications. 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 genetics analysis, especially in the field of sequencing. Illumina also provides product support services for its systems as well as genetics analysis services powered by its sequencing and microarray technologies.

16. PacBio develops, manufactures and commercialises third generation, native long read, DNA sequencing systems based on its 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 genomic centers). PacBio's customers include government and not-for-profit genomic research institutes, genomics centers, pharmaceutical companies and agricultural companies. PacBio also provides product support services for its native long read sequencing systems.

17. Please see [redacted] for a detailed description of the Notifying Parties' activities.

4. Provide brief details of any other transactions (merger, acquisition, disposal, joint venture) undertaken by:

***(a)* either of the merger parties in the last two years which involve the products or services in any Candidate Market identified in response to question 13, and**

18. On May 15, 2018, Illumina acquired Edico Genome Inc., a provider of data analysis acceleration solutions.[3]

19. Illumina has not undertaken any other transaction in the last two years.

20. PacBio has not undertaken any transaction over the last two years.

***(b)* both or all merger parties in the last two years (that is, where the merger parties were party to the same transaction).**

21. Illumina and PacBio have not been parties to the same transaction over the last two years.

[3] https://www.illumina.com/company/news-center/press-releases/2018/2349147.html

Jurisdiction

5. Explain why:

(a) a relevant merger situation (as per section 23 of the Act) has been created, or

(b) arrangements are in progress or contemplation which will result in the creation of a relevant merger situation.

22. On November 1, 2018, Illumina and PacBio signed the Merger Agreement, pursuant to which Illumina will acquire 100% of the voting securities of PacBio through a merger of its wholly-owned direct subsidiary, FC Ops Corp., with PacBio. Subsequently, PacBio will continue as the surviving corporation, as a wholly-owned direct subsidiary of Illumina. The Merger Agreement is subject to approval by PacBio's shareholders, which occurred on January 24, 2019, as well as customary conditions as described in Article 9, which requires that all necessary antitrust filings must have been made, and approvals obtained. Once these conditions are met and the certificate of merger is filed with the Secretary of State of the State of Delaware, U.S.A., PacBio and Illumina will cease to be distinct enterprises within the meaning of Section 23 of the 2002 Enterprise Act.

23. The turnover test set out in Section 23 of the 2002 Enterprise Act is not met as PacBio's 2017 turnover in the UK amounted to only GBP [redacted] million.[4]

24. However, the "share of supply" test set out in Section 23 of the 2002 Enterprise Act is met. While, as explained in Section 13, below, the Notifying Parties are not active on the same product market, they are both suppliers of sequencing systems with a combined share of supply in the UK of more than 25%. In 2017, Illumina's share of supply of sequencing systems in the UK exceeded 25%, and PacBio's share of supply of sequencing systems in the UK was *de minimis*.

6. Indicate the annual UK, EEA, and worldwide turnover in the last financial year associated with each of:

(a) the acquirer (including group companies where relevant – see Annex B of the Guidance), and

(b) the target (if not already provided under question 5).

25. The 2017 turnover of Illumina and PacBio, respectively, are provided in Table 1 below.

[4] This figure has 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).

Table 1: Turnover of Illumina and PacBio in million GBP[5]

	Illumina[6]	PacBio[7]	Aggregate
UK-wide	[redacted]	[redacted]	[redacted]
EEA-wide	[redacted]	[redacted]	[redacted]
Worldwide	2,100	72.4	2,172.4

26. The breakdown of PacBio's 2017 turnover reflects in part PacBio's [redacted].[8] The U.S. accounted for [redacted] of PacBio's total 2017 revenue.[9]

27. As noted in Section 11 below, PacBio has [redacted] Through the Transaction, as discussed in Section 24 below, PacBio will benefit from acquiring access to Illumina's global distribution and commercialisation infrastructure and customer base (including in the EEA).

7. Explain why the transaction is not subject to the European Union Merger Regulation (EU Merger Regulation),[10] (highlighting whether it is notifiable in the UK by virtue of the 'two-thirds' rule in article 1(2) or 1(3) of that Regulation).

28. The combined aggregate worldwide turnover of the Notifying Parties is below the EUR 5,000 million threshold laid down in Article 1(2)(a) of Regulation (EC) No 139/2004 ("EUMR"). Moreover, PacBio's aggregate EU-wide turnover is less than the EUR 100 million threshold laid down in Article 1(3)(d) of the EUMR. Therefore, the Transaction does not have a Community dimension within the meaning of the EUMR.

PART III – SUPPORTING DOCUMENTS

8. Provide:

(a) **a press release or report and details of all notifications to listing authorities (for example, for admission to the UK Listing Authority Official List and for**

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[5] 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).

[6] [redacted]

[7] [redacted]

[8] See PacBio's 2017 Annual Report, available at http://investor.pacificbiosciences.com/financial-information/annual-reports

[9] See PacBio's 2017 Annual Report, available at http://investor.pacificbiosciences.com/financial-information/annual-reports, p. 9

[10] Council Regulation (EC) No 139/2004 of 20 January 2004.

admission to trading on the London Stock Exchange) or other documentation evidencing that the merger (or merger proposal) has been made public, and

29. The press release announcing the Proposed Transaction is available at: https://www.illumina.com/company/news-center/press-releases/press-release-details.html?newsid=2374913.

(b) **a copy of the documents bringing about the merger situation, including heads of terms, memorandum of understanding, sale and purchase agreement, business purchase agreement or equivalent. Where these are not in final form, please provide the latest draft and keep the CMA informed of subsequent changes to the document, if any.**

30. The Merger Agreement was submitted as an [redacted].

(c) **If the offer is subject to the City Code, copies of the Offer Document and Listing Particulars. If these are not yet available, provide copies of the latest drafts and supply the final versions as soon as they are issued.**

31. Both Illumina and PacBio are registered in the State of Delaware, U.S.A., and traded on the NASDAQ. The Proposed Transaction is, therefore, not subject to the City Code, which applies to companies having their registered offices in the UK, the Channel Islands or the Isle of Man.[11]

(d) **for each of the acquirer and acquirer group (if relevant) and the target (or merger parties in the case of a full merger), the most recent annual report and accounts.**

32. Illumina's 2017 annual report is available at: http://www.annualreports.com/HostedData/AnnualReports/PDF/NASDAQ_ILMN_2017.pdf.

33. PacBio's 2017 annual report is available at: http://investor.pacificbiosciences.com/static-files/1c2a7f88-5fba-4edd-a53c-643c511535b6.

(e) **copies of the most recent business plan of the acquirer and acquirer group (if relevant) and the target (or merger parties in the case of a full merger). Where a horizontal overlap or vertical relationship involves, for example, a specific division or brand of one or both of the merger parties, the most recent business plan for the relevant division or brand should be provided as well.**

34. Illumina's most recent business plan and business plan executive summary were submitted as [redacted].

35. PacBio's most recent business plan and budget presentation were submitted as [redacted].

[11] See section A3 of the City Code.

9. Provide copies of any documents in either of the merger parties' possession which:

(a) **have been prepared by or for, or received by, any member of the board of directors (or equivalent body) or senior management or the shareholders' meeting of either merger party (whether prepared internally or by external consultants), and**

(b) **either:**

(i) set out the rationale for the merger (including but not limited to the benefits of, and/or investment case for the acquisition), or

(ii) assess or analyse the merger with respect to competitive conditions, competitors (actual and potential), potential for sales growth or expansion into new product or geographic areas, market conditions, market shares and/or the price to be paid. This should include but not necessarily be limited to post-merger business plans or strategy (including integration plans and financial forecasts) and Information Memoranda prepared by or for the merger parties that specifically relate to the sale of the target. If no such Information Memoranda exist, explain what information or document(s) given to any of the merger parties is meant to serve the function of an Information Memorandum.

Indicate (if not contained in the document itself) the date of preparation and the identity and role of the author(s) within the merger parties or external consultants.

36. For Illumina, please see [redacted] and [redacted].

37. For PacBio, please see [redacted].

10. Provide copies of documents (including, but not necessarily limited to, reports, presentations, studies, internal analyses, industry/market reports or analysis, including customer research and pricing studies) in either merger parties' possession and prepared or published in the last two years which:

(a) **have been prepared by or for, or received by, any member of the board of directors (or equivalent body) or senior management of either merger party (whether prepared internally or by external consultants), and**

(b) **set out the competitive conditions, market conditions, market shares, competitors, or the merging parties' business plans in relation to the product(s) or service(s) where the merger parties have a horizontal overlap as identified in response to question 12 below.**

38. For Illumina, please see [redacted] and [redacted].

39. For PacBio, please see [redacted].

PART IV – COMPETITION ASSESSMENT

Counterfactual

11. If the notifying parties consider that the CMA should assess the competitive effects of the merger against a counterfactual other than the current or pre-existing competitive situation, please describe that counterfactual and explain why the notifying parties consider it should be used for that assessment.

40. The Notifying Parties submit that the CMA should consider PacBio's historical and forward-looking financial circumstances but-for the merger when assessing the competitive effects of the Transaction. Additionally, the CMA should consider PacBio's fulsome search for a potential partner prior to entering into the current Merger Agreement with Illumina.

[redacted]

41. [redacted]

42. [redacted]

[redacted]

[redacted]

43. [redacted]

44. [redacted]

- [redacted]
- [redacted]

[12] PacBio 2017 Annual Report, p. 15, available at: http://investor.pacificbiosciences.com/static-files/1c2a7f88-5fba-4edd-a53c-643c511535b6

[redacted]

- [redacted]
- [redacted]

II. PacBio's search for a partner

45. [redacted]

46. [redacted]

47. [redacted]

48. [redacted]

[13] *Ibid.*, p. 9.

[redacted]

III. PacBio's failed agreement with Roche

49. [redacted]

50. In an effort to develop clinical applications and the customers using them, PacBio entered into a "Development, Commercialisation and License Agreement" on September 24, 2013 with Roche (the "Roche Agreement") under which PacBio would develop and manufacture certain products intended for clinical use, which it would sell exclusively to Roche.[14] Roche is a large clinical and diagnostic instrument and system supplier, with extensive commercialisation infrastructure (and a large clinical and diagnostic customer base). This agreement was intended to lead to the development of certain targeted, assay-specific tests and additional software for PacBio's Sequel System that Roche could then sell to its *in vitro* diagnostic customers.

51. However, in December 2016, Roche announced that it was electing to terminate the Roche Agreement.[15] [redacted], Roche announced that, following termination of the Roche Agreement, it would "have greater focus on

[14] Development, Commercialisation and License Agreement Between PacBio and F. Hoffmann-La Roche Ltd. (Sep. 24, 2013), https://www.sec.gov/Archives/edgar/data/1299130/000129913013000011/pacb-20130930ex101383eca.htm

[15] [redacted]

[16] Please see Section 22 below.

[its] internal development efforts and drive [its] long-term strategy, which is to be a leader in clinical diagnostic sequencing."[17]

IV. PacBio's commercial strategy and expectations regarding its 8M chip

52. The Transaction does not change PacBio's commercial strategy or expectations regarding the launch of its SMRT® Cell 8M chip. The Transaction would expand demand for PacBio's technology, compared to the counterfactual. As explained in Section 24 below, the Transaction would increase access to PacBio's technology through Illumina's larger and more mature sales force. [redacted]

53. Absent the Transaction, PacBio plans to introduce the new SMRT® Cell 8M chip in the second quarter of 2019. There is a beta program in process and five customers have early access to the new 8M technology and are actively running their Sequel II Systems.[18] The early access program is intended to optimise the performance of the SMRT® Cell 8M chip and other components of the Sequel II System (including chemistry and software), to develop reference materials, and pre-emptively address any technological issues that may arise prior to making the product fully available commercially. [redacted] Based on the early performance of the Sequel II Systems at these early access sites, PacBio expects to begin commercial shipments of Sequel II Systems and SMRT® Cell 8M products in the early part of the second quarter of 2019.[20]

54. [redacted]

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[17] Roche Announces Termination of 2013 Development, Commercialisation and License Agreement with PacBio (Dec. 15, 2016), https://www.prnewswire.com/news-releases/roche-announces-termination-of-2013-development-commercialization-and-license-agreement-with-pacific-biosciences-300379155.html.

[18] PacBio press release, 'Pacific Biosciences Announces Fourth Quarter and Annual 2018 Financial Results', 11 February 2019. Press release available at: http://investor.pacificbiosciences.com/news-releases/news-release-details/pacific-biosciences-announces-fourth-quarter-and-annual-2018. [redacted]

[19] [redacted]

[20] PacBio press release, 'Pacific Biosciences Announces Fourth Quarter and Annual 2018 Financial Results', 11 February 2019. As at April 12, 2019, the current target date for commercial launch is April 24, 2019.

[21] [redacted]

[redacted]

55. The SMRT® Cell 8M chip increases the maximum number of potential observations through its ZMWs (zero-mode waveguides — the wells on the SMRT chip where DNA molecules are analysed) to 8 million, from 1 million on the previous chip. [redacted]

Market definition

12. Describe the product(s) or service(s) and geographic area(s) where the merger parties overlap, where they have a vertical relationship, or where they supply related products/services.

I. Sequencing

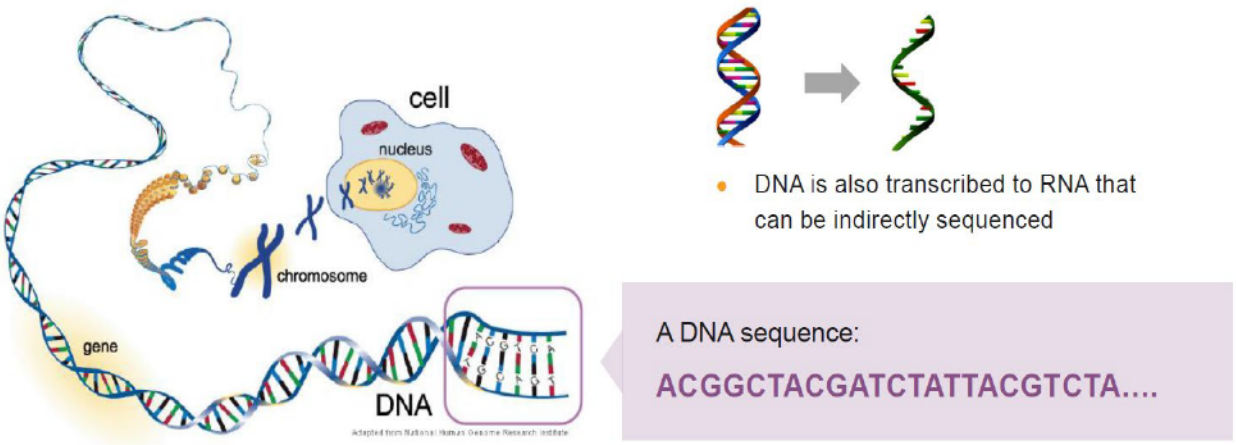
56. DNA and RNA are composed of four nucleotides that are linked together in strands that can reach lengths into the millions of nucleotides. DNA is composed of adenine (A), cytosine (C), guanine (G) and thymine (T); in RNA thymine is replaced by uracil (U). Sequencing is the process of determining the order of nucleotides in a strand of DNA or RNA. Because in DNA A "pairs" with T, and C with G, to create a double-stranded molecule, determining the sequence of one strand is sufficient to know the sequence of the other complementary strand. A strand of DNA with its many nucleotides contains a code that dictates how proteins are made, and proteins control virtually all living functions. RNA serves as an intermediate molecule involved in the translation of the DNA code to proteins. A genome, the collection of DNA for an organism, contains the entire set of instructions for that organism. Sequencing DNA therefore underlies our studies of all organisms, and informs our knowledge spanning basic biology to complex human diseases such as cancer.

[22] [redacted]

[23] See [redacted]

[24] [redacted]

Figure 3: DNA sequencing



57. Genomics is an interdisciplinary field focused on the study of an organism's genome and understanding the structure, function and evolution of genomes.[25] The introduction of Next-Generation Sequencing ("NGS") has made the study of genomes easier, more accurate, significantly less costly and much faster.

58. 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, including:

- **Basic research**: is broadly defined to include activities of scientists who use DNA sequencing to further scientific discovery (*e.g.*, oncology research). Such research takes place at, among other places, universities, research institutes, government institutions, and biotechnology and pharmaceutical companies. For example, in 2005, Harvard University started the "Personal Genome Project" as a pilot program. Basic research enables scientists to connect human genetic information (*e.g.*, human DNA sequence, gene expression, RNA, *etc.*) with human trait information (*e.g.*, disease state and predisposition, medical information, physical traits, *etc.*) and environmental information.[26]

- **Translational research**: builds on basic research to create new therapies, medical procedures or diagnostics. Often described as the practice of transferring scientific knowledge "from bench to bedside", translational research "translates" scientific discoveries into new clinical tools and applications that can improve human health.[27] Knowledge gained from DNA

[25] https://www.genome.gov/19016904/
[26] https://pgp.med.harvard.edu/about
[27] https://www.eupati.eu/non-clinical-studies/translational-medicine/

sequencing has been used by researchers to create new therapies and treatments based on genetic variation. For example:

- Researchers have found that gene expression profiling of breast tumors can identify women at low risk of recurrence, who might safely avoid post-surgical chemotherapy;[28]
- There are ongoing efforts to identify variants linked to certain Mendelian[29] disorders, such as hemophilia or sickle cell anemia.[30] These initiatives provide genetically informed predictions of disease risk and medication safety and efficacy, enabling personalised decisions for disease prevention;[31]
- Determining from a blood sample whether a patient has cancer before symptoms occur is being pursued by companies such as Grail. The idea is to detect cancer early so that the probability of cure is higher.

- **Clinical and diagnostic applications**: use DNA sequencing to evaluate risks, diagnose illness and design treatments for patients. For example, DNA sequencing enables healthcare professionals to perform non-invasive prenatal testing (NIPT) which identifies chromosomal abnormalities in a fetus. NIPT analyses fetal DNA from a maternal blood sample to detect common chromosomal abnormalities such as trisomy 21 (*i.e.*, Down syndrome), trisomy 18 (*i.e.*, Edwards syndrome) and trisomy 13 (*i.e.*, Patau syndrome).[32, 33]

  It is important to appreciate that sequencing currently accounts for a small portion of clinical and diagnostic testing. Clinical laboratories buy a broad range of instruments that are used for other types of testing, including *in vitro* incubators, mass spectrometry, real-time polymerase chain reaction ("PCR"), digital PCR, and end point PCR instruments.[34] These instruments are used to run both regulated (CE-IVD) and laboratory-developed tests (LDT).

  Sequencing is a relatively new technology and is at the early stages of the adoption cycle for clinical applications. Additionally, while sequencing has the potential to address clinical applications that require broad surveys of genes, genomes, epigenomes, or transcriptomes, many clinical applications do not require gene, genome, epigenome or transcriptome information. For example, clinical assays centring around detection and quantification of peptides,

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[28] Wylie Burke and Diane M. Korngiebel, "*Closing the Gap between Knowledge and Clinical Application: Challenges for Genomic Translation*", February 2015, available at https://doi.org/10.1371/journal.pgen.1004978
[29] Mendelian inheritance is the manner by which genes and traits are passed from parents to their children. The modes of Mendelian inheritance are autosomal dominant, autosomal recessive, X-linked dominant, and X-linked recessive. Also known as classical or simple genetics.
[30] https://byjus.com/biology/mendelian-disorders/
[31] Joel B. Krier, Sarah S. Kalia and Robert C. Green, "*Genomic sequencing in clinical practice: applications, challenges, and opportunities*", available at https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5067147/.
[32] https://www.illumina.com/clinical/reproductive-genetic-health/nipt.html
[33] Please see below for more detail on NIPT.
[34] Please see Section 13 below for a discussion of PCR, qPCR, and digital PCR.

proteins, and small molecules primarily use mass spectrometers (*e.g.*, toxicology screening). Clinical assays that survey single point changes in the genome will often use PCR, and those that interrogate changes in gene expression of a small number of targets (typically ranging from 1 to 20 genes) will use quantitative PCR ("qPCR") methods (*e.g.*, HIV viral load). While Illumina only supplies sequencing (and microarray) systems to clinical customers, a number of Illumina's competitors (including Qiagen and Thermo Fisher) offer a broad range of clinical systems and solutions. As a result, these competitors have broad and deep relationships with these customers.

A description of non-sequencing methods of ascertaining genetic information deployed in clinical and diagnostic applications is provided in [redacted].

- **Agrigenomics**: use DNA sequencing to explore the genetic and biological basis for productivity and disease resistance in crops and livestock. This enables farmers and breeders to tailor cultivation and breeding decisions, producing healthier and higher-yielding crops and livestock.

- **Pharmaceutical companies**: use DNA sequencing to develop new therapeutics and develop assays to act as companion testing (companion diagnostics) for certain therapeutics. For instance, many therapeutics only work, or work optimally, on patients having a certain genetic makeup. Pharma companies use or develop sequencing-based assays as "companions" for certain therapeutics to determine or enhance before treatment therapeutic efficacy or applicability for a particular patient. Pharmaceutical companies, such as AstraZeneca and GSK, use pharmacogenomics to analyse how patients' DNA influences their response to new drugs. They also conduct scientific research that is used to improve drug development at a later stage.

- **Consumer genomics**: use DNA sequencing to provide personalised genetic data and analysis regarding disease predisposition and planning around health, wellness, nutrition and fitness for individual consumers. This is an emerging and rapidly growing area, being fed by increasing demand and interest from consumers. For example, in the UK, after the completion of the "100,000 Genomes Project", the NHS and Genomics England are now planning to expand the project to healthy consumers.[35] Volunteers will be able to pay for a personalised report on their unique genetic makeup. Subject to the volunteers' permission, the genetic data will also be made available to researchers and scientists for genomic research.[36]

II. Genetic variation

[35] Please see Section 15 for more information on Genomics England and the 100,000 Genomes Project.
[36] The proposal to recruit 'genomic volunteers' who would pay for a personalised report was part of the Life Sciences Sector Deal 2, announced in late 2018, available at https://www.gov.uk/government/publications/life-sciences-sector-deal/life-sciences-sector-deal-2-2018).

59. 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.[37]

60. Genetic variation accounts for many of the physical differences we see (*e.g.*, height, hair, eye colour). Other than affecting our appearance, genetic variation can also have medical consequences affecting disease susceptibility, including predisposition to complex genetic diseases such as cancer, diabetes, cardiovascular disease, and Alzheimer. In addition, genetic variation can affect individuals' response to certain drug treatments, causing them to respond more or less well, and experience adverse side effects to varying degrees.[38]

61. Identifying variations in an individual's genome requires comparison of the DNA sequence of that individual against a reference genome using the process of alignment.[39] A reference genome is a DNA sequence that provides an appropriate representation of the structure and shared genome sequence for a particular species or population, such that variants amongst individuals within such species or populations can be identified. A reference genome is generally considered to be a very high quality genome that is assembled using multiple complementary technologies, including short reads, native long reads, and in some cases third-party, non-sequencing technologies such as genome mapping.[40] The different complementary technologies are required because each has strengths for different aspects of the assembly. Short read systems provide economical and accurate local assemblies at high depth. These local assemblies have endpoints around regions of the genome that are difficult for short read systems (*e.g.*, repeats). Native long read systems bridge gaps between regions of the genome that short reads do not effectively cover (*e.g.*, repeats). Long-range mapping reads offered by third-parties can provide structural information for variations that are too large for native long read systems in complex genomes, for example over millions of base pairs. Even after substantial effort, reference genomes may still contain some poorly defined regions, such as the large centres and ends of chromosomes that contain many repeat regions that may prove difficult for both short read and native long read technologies. As discussed below, short read and native long read technologies have

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[37] http://www.annualreports.com/Click/24414, p. 4

[38] *Ibid.*

[39] Alignment is the process of determining where a sequencing read from a sample maps (i.e., aligns) with respect to a reference (*e.g.*, a reference genome, see below). Sequencing reads may align perfectly with the reference, in which case there are no identified variants. On the other hand, alignments may reveal differences between the aligned sequence and the reference, thus indicating variation. In some cases, alignment is not possible, for instance, because there is not enough information (*e.g.*, a repeat-rich region), or the reference sequence itself does not contain the sample sequence.

[40] A genome map is less detailed than a genome sequence. A sequence spells out the order of every DNA base in the genome, while a map simply identifies a series of landmarks in the genome. Mapping and sequencing are typically completely separate processes. For example, it is possible to determine the location of a gene—to "map" the gene—without sequencing it. Thus, a map may tell you nothing about the sequence of the genome, and a sequence may tell you nothing about the map.

different strengths and, when errors occur, error profiles[41] such that the use of complementary approaches can be used to best produce a highly accurate reference genome. These differing strengths and error profiles are expected to remain for the foreseeable future.

62. Due to genetic variation between populations of a species, for example humans, population-specific reference genomes may be appropriate. This may be the case when samples include sequences not represented in the reference genome (*e.g.*, large insertions or other SVs), or because a reference genome does not adequately represent population-specific haplotype variation.

63. The process of creating a new reference genome is still an active area of research and development. Whether or not there is a closely-related reference genome in existence, both short read and native long read sequencing can be used to appropriately characterize novel regions, leveraging the strengths of each technology, respectively.

64. Variations in the DNA sequence can result from SNVs, insertions, deletions, inversions, translocations, or duplications of nucleotides over the DNA strand, 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, such changes may trigger substantial changes in their function.

65. There are numerous classes of variation in a genome, each with a specific characteristic. Among them are the following:

- **Single nucleotide polymorphism variant (SNV)**: a change in a single nucleotide that occurs within a DNA sequence. SNVs can be found in regions of the DNA that code for proteins (*i.e.*, in the parts of our genes that dictate production of proteins, also known as exons) as well as in non-coding regions of our DNA. SNVs that do not change the composition of the resulting protein are still functionally important;[42]

- **Insertion – deletion variants (indels)**: a number of base pairs are inserted or deleted from the DNA sequence. When insertion - deletion variation occurs in coding regions of the genome, it may produce mutations that are linked to various pathological conditions;

[41] Short read and native long read technologies have different but largely complementary error profiles in the data that cannot be overcome with consensus sequencing. Because these complementary error profiles are expected to remain for the foreseeable future, users are expected to continue to combine reads from different technologies for a more accurate final result, for example combining native long read and short read sequencing.

[42] [redacted]

- **Block substitution**: a series of base pairs in proximity to the reference genome that are replaced with a different series of base pairs.[43] Block substitutions are, for instance, associated with lung and skin cancers;[44]

- **Duplications:** a series of base pairs is duplicated. Duplications have been associated with, for instance, Duchenne Muscular Dystrophy;

- **Translocations:** occur at a chromosomal level and these re-arrangements can lead to chromosome-length changes in the genome. Translocations are associated, for instance, with the XX Male syndrome and cancer;

- **Inversion variant**: instead of following the sequence of the reference genome, a block of complementary nucleotides occurs in reverse order. Variations in the type of inversions may affect either a small or a large number of base pairs. Hemophilia A and infertility, for instance, are associated with inversion variants;

- **Copy number variant (CNVs)**: occur when there are fewer or more copies of certain genes, segments of a gene, or stretches of DNA (compared to the reference genome). A number of neurodevelopmental disorders have been identified as resulting from CNVs, including mental retardation;[45]

- **Tandem repeats**: copies of DNA sequences that lie adjacent to each other in the same orientation (direct tandem repeats) or in the opposite direction to each other (inverted tandem repeats).[46] They can be small (*i.e.*, up to 6 bp) or larger (*i.e.*, up to 10,000 bp), and are associated with various neurological disorders, including Huntington Disease, Ataxias and Amyotrophic Lateral Sclerosis;

- **Structural variant (SV)**: a variation in the structure of an organism's chromosome. Shorter variants (*e.g.*, SNVs and indels involving 1-50 bp) are considered to be small variants. Insertions, deletions, duplications, block substitutions, CNVs, inversions or translocations that are larger than about 50 bp are considered to be SVs. SVs typically affect a sequence length of anywhere between hundreds to thousands to even millions of base pairs. SVs in human genomes play a role in diseases including neurological/neurocognitive disorders, cancer development and progression and autism.

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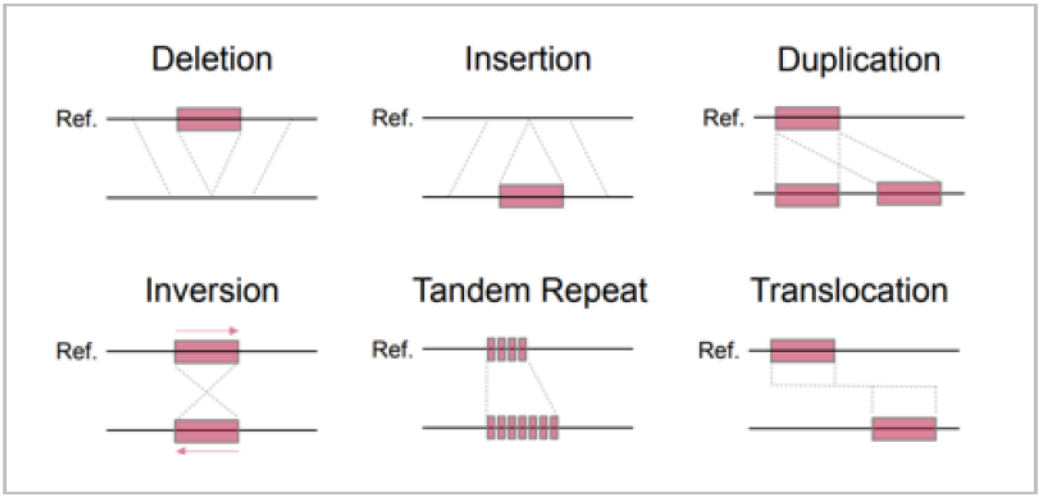
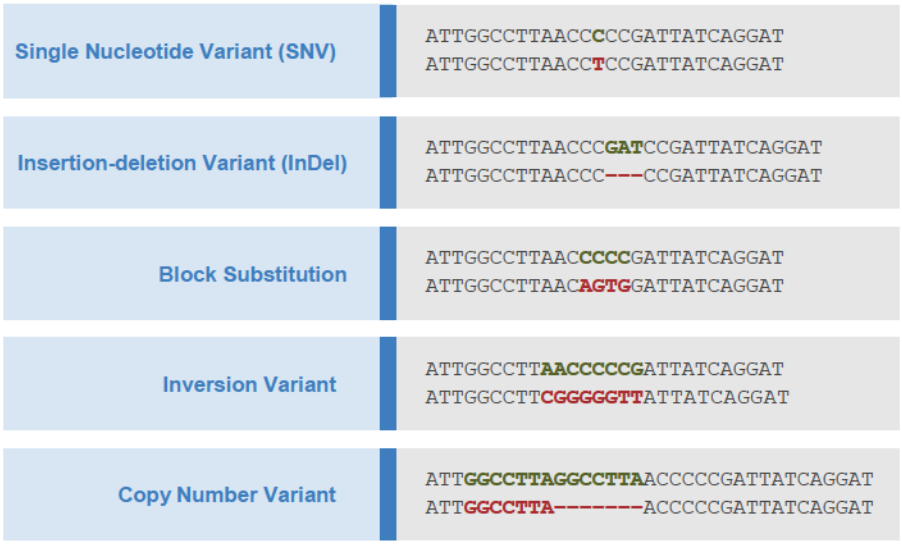
[43] See http://www.completegenomics.com/documents/Small+Variants+FAQ.pdf, p. 7
[44] See https://www.biorxiv.org/content/biorxiv/early/2018/09/20/415133.full.pdf
[45] [redacted]
[46] See https://meshb.nlm.nih.gov/record/ui?ui=D020080

Figure 4: Types of structural variants



Source: *PacBio's website*

Figure 5: Variants and DNA sequencing



Source: *CMA presentation - Tech Tutorial*

III. Sequencing applications

66. Sequencing systems enable researchers to study the genome, transcriptome or epigenome of virtually any organism. Sequencing applications differ largely by the goal of the interrogation (*e.g.*, *de novo* sequencing a genome for the first time, resequencing an entire or targeted area of a genome, or counting mRNA molecules in a sample, to name a few examples), how the DNA or RNA samples are obtained and the data analysis and bioinformatics tools used.

A. Genomics

67. Genomics is the study of an organism's genome (its complete set of genetic material).

- **Whole-genome sequencing (WGS)** refers to the process of determining the variants in an organism's genome. This is typically performed at scale using short reads, such as with Illumina's economical and accurate reads. Because this process relies on a reference genome, in contrast to a *de novo* genome (defined below), this process is also referred to as "resequencing" (*i.e.*, sequencing the genome of a particular species or population that has previously been sequenced and for which a suitable reference genome exists). While WGS is commonly associated with sequencing human genomes, the scalable, flexible nature of the application makes it equally useful for sequencing any species, including livestock, plants or microbes. For example, during the *E. coli* outbreak in Europe in 2011, researchers quickly sequenced the disease-causing bacterial strain, enabling them to track the origins and transmission of the outbreak and identify genetic mutations responsible for its increased virulence.

- **Whole-exome sequencing (WES)** refers to the process of targeting for sequencing the protein-coding genes in a genome (*i.e.*, the exome). Proteins are the molecules that determine nearly all functions in a living organism, so when they malfunction, disease often results. Although the exome represents less than 2% of the human genome, it contains most of the known disease-causing genetic variants, making WES a cost-effective alternative to WGS. WES is a widely-used targeted sequencing application.

- ***De novo* assembly/*De novo* sequencing** consists of sequencing a genome where there is no application-appropriate reference available, for example when sequencing a species for the first time, such as in a research setting, or when sequencing new regions of a genome not represented in a reference. Both short read sequencing and native long read sequencing technologies are ideal for this process, but serve complementary and distinct roles. Native long read systems enable assembly of larger continuous fragments that elucidate structural order. Long-range chromosomal structural mapping may require the use of third party mapping technology for further ordering. Short read systems permit economical polishing of the assembly for high accuracy. *De novo* sequencing is a necessary step in the creation of reference genomes. Importantly, *de novo* sequencing is an assembly of reads, in contrast with WGS, which is an alignment of reads to a reference. *De novo* assembly/*de novo* genome/*de novo* sequencing can also be used for other applications, such as RNA transcript isoform mapping.

- **Targeted sequencing** entails the isolation and sequencing of a subset of genes or regions of the genome. Targeted sequencing enables researchers to focus resources, including sequencer output, to specific areas of the genome. This permits a targeted region to be sequenced multiple times, sometimes hundreds or in certain application thousands of times, resulting in increased coverage of the area. The sequencing depth or coverage level often determines whether variant discovery can be made with a certain degree of confidence, and higher coverage enables identification of rare variants that would be too expensive to identify with WGS, for example. Targeted sequencing is useful for studies in oncology, microbial genomics, and other research involving analysis of rare cell populations. For example, the high coverage of targeted sequencing is required

to identify mutations in tumors, which can be likened to looking for "a needle in the haystack". Tumors are usually a mix of normal and tumor tissue. Identifying mutations in tumors typically requires repetitive sequencing at very high coverage because the important tumor-specific variants tend to be underrepresented in the samples. For example, a tumor that contains 50% normal tissue requires double the sequencing depth to detect mutations, compared to what would be required for a 100% pure tumor sample. As a result, while 30x coverage is typically sufficient for identifying common variants, in cancer sequencing coverage ranging from 100x to 1000x depth is often required.

B. Transcriptomics

68. The transcriptome is the complete set of RNA molecules, including messenger RNA (mRNA) molecules, expressed from the genes of an organism. Transcriptomics is the study of an organism's transcriptome. Often, the mRNA molecules are targeted for sequencing because these transcripts contain protein-coding information, and proteins control almost all living functions. Library preparation for sequencing mRNA samples usually entails "reverse transcription", employing a polymerase that converts the mRNA molecules to DNA by producing complementary DNA strands (cDNA) that are indistinguishable from DNA.[47] The cDNA sample is sequenced in the same way as DNA.

- **Total RNA and mRNA sequencing** or whole transcriptome sequencing entails sequencing the entire RNA or mRNA of an organism. Cellular organisms use mRNA to convey genetic information that directs the production of proteins. Many viruses encode their genetic information using RNA. This sequencing application enables scientists to better understand gene expression[48] and decode viruses' genomes.

- **Targeted RNA sequencing** refers to the process of sequencing a subset of genes. It enables detection of several gene expression (activation) mechanisms such as differential expression (activation of different genes within a cell that define that cell's functions), allele-specific expression (how alleles result in different observable traits), gene-fusions (how two genes can merge), gene isoforms (different forms of mRNA that can be produced by a gene), coding SNVs (variation of a single nucleotide in the genome that differs between members of a species), and splice junctions (location on a transcript that directs gene splicing).

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[47] [redacted]

[48] Refers to the "turning on" of a gene. Most human genes are active, or turn on, only in certain cells under certain conditions. Genes for eye colour are active in eye cells but not in stomach cells. Similarly, some genes may lie dormant for years and then turn on and become malignant later in life. When genes are turned on, they produce mRNA.

- **Small RNA and non-coding RNA sequencing** entails sequencing small, non-coding RNA,[49] or microRNAs, which are short RNA molecules of 18–22 bp nucleotides that play a role in regulating RNA translation to protein.

C. Epigenomics

69. While genomics involves the study of DNA sequences and variants between individuals in a population, epigenomics refers to the study of changes to the chemical makeup of the DNA itself that do not change its base sequence, but may change how a gene is expressed. One common epigenetic modification in humans is the addition of a methyl (CH_3) group to the C base. Such methylation is associated with gene expression changes found in diseases such as cancer. Recent studies show that lifestyle and environmental factors can lead to epigenetic changes to DNA, which can cause or exacerbate disease. There are many different types of epigenetic marks, on both DNA and RNA. The meaning and function of epigenetic marks remains an active area of research, as much remains to be understood.

- **Methylation sequencing** focuses on studying cytosine methylation, an enzyme-mediated modification to DNA. Methylation disorders such as hypomethylation, causing strong expression of a gene, or hypermethylation, silencing a gene, can lead to diseases including cancer, diabetes, cardiovascular and inflammatory diseases and mental disorders.

- **ChIP (chromatin immunoprecipitation) sequencing**[50] targets sequencing towards selected regions of the genome for further characterisation of epigenetic marks.

- **Ribosome profiling** is based on deep sequencing[51] of ribosome[52] protected–mRNA fragments, providing a "snapshot" of all the ribosomes active in a cell. This information enables identification of the proteins being actively translated in a cell.

IV. Short read vs native long read sequencing technologies

70. A key differentiating characteristic of post-Sanger NGS technologies is the read lengths they are capable of providing. Generally, NGS systems to date have fallen into two broad categories of read length:

- **Short read sequencing systems**: generally defined as systems that produce read lengths ranging from tens to hundreds of base pairs per read. Most second-

[49] A non-coding RNA is an RNA molecule that is not translated into a protein.
[50] Chromatin is a complex of DNA, RNA, and protein found in eukaryotic cells. Eukaryotic genomes are packaged into chromatin, and how chromatin is packaged plays a key role in gene regulation and, ultimately, cell phenotype.
[51] This refers to sequencing at high coverage levels.
[52] The ribosome is a cell molecule that synthetises (builds) proteins on the basis of the information provided by mRNA. This process is called the translation.

generation sequencing technologies, including Illumina's SBS-based systems, fall into this category; and

- **Native long read sequencing systems**: generally defined as systems that produce reads lengths in the low thousands to the hundreds of thousands of bases or more per read (5,000 to > 100,000 base pairs). Currently-commercialised native long read systems are sold by PacBio and Oxford Nanopore Technologies ("ONT"). Both of these technologies sequence single molecules. [redacted][53]

- Other key differentiators between short and native long read technologies include:

  - Yield (throughput, determined by the number of total reads or bases sequenced in a single run);

  - Economics (cost per Gb);[54]

  - Sample preparation requirements; and

  - System scalability (ability to increase output).[55]

A. Short read sequencing

71. Short read systems generate tens to hundreds of base pairs per read, and some technologies, like Illumina's, have the ability to produce billions of unique reads in a single sequencing run. Illumina's systems, due to their high raw accuracy, high yield, and favourable economics, are well-suited for counting applications, population genomics efforts, and other high-scale, cost-sensitive applications such as screening panels and cancer diagnostics. In addition, they are complementary to native long read technology for *de novo* assembly/*de novo* sequencing of large, complex genomes. [redacted]

[53] Please see Section 22 below.
[54] Customers consider multiple metrics when considering the cost of sequencing. Depending on the customer, and the context in which it is sequencing, different metrics may be relevant. The importance for a customer of metrics may also vary over time due to changes in sample volumes, applications, sources of funding, *etc*. Commonly used metrics include cost/run, cost/Gb, and cost/million reads. Higher throughput customers are typically most sensitive to cost/Gb, cost/million reads, while lower throughput customers may be more sensitive to system price. The importance of a particular metric also varies across different applications: for applications requiring high amounts of Gb sequencing (*e.g.*, WGS), customers are most sensitive to cost/Gb; for applications requiring high numbers of reads (*e.g.*, RNA-Seq, NIPT), customers are most sensitive to cost/million reads; for applications requiring low amounts of Gb sequencing (*e.g.*, Amplicon sequencing or library QC), customers are most sensitive to cost/run. A metric used by customers when selecting systems is the total cost of ownership, which is a function of depreciated system price and consumable price per sample multiplied by the number of samples run.
[55] Please see Section 15 below.

[redacted]

B. Native long read sequencing

72. Native long read systems generate thousands to hundreds of thousands of base pairs or more per read. As a result, native long read sequencing is well-suited for the initial discovery of previously unknown large SVs because it enables reads that are considerably longer than short read sequencing. These long reads are often longer than a large SV, thus spanning the end points of the large SVs. Knowing the end points allows better alignment against the applicable reference genome (see figure below). An additional ability of native long read technologies is the utility in performing phasing (determining if variants reside on the same chromosome).

Figure 6: Example - Insertion of a repetitive sequence

Source: *CMA presentation - Tech Tutorial*

V. Strengths and limitations of short and native long read sequencing technologies

73. Each technology type has its advantages and limitations that determine its suitability to different applications and experimental parameters such as number of samples in an experiment, types of samples, amount of starting material, sequencing target (DNA or RNA), clinical and diagnostic applications, *etc*.

A. Strengths and limitations of short read sequencing

74. Short read sequencing has several **advantages**, including:

- Short read systems achieve **high output and throughput** by sequencing up to billions of DNA strands in parallel (*i.e.*, in a single run). Therefore, they are well-suited for applications that require sequencing on a large scale;[56]

[56] Short read sequencers can sequence a large number of samples per run making them well-suited for certain applications including Genome Wide Association Studies. A genome-wide association study is an approach that

- Because of their high throughput, short read systems have a relatively **low cost per base**;[57]

- Based on the chemistry used, some short read systems may achieve **high raw read accuracy** with error rates of less than 1%. For example, Illumina's systems typically generate ~75% or more of base calls with average accuracies meeting or exceeding 99.9% ("Q30" quality score) with performance varying based on library type and quality, fragment size, loading concentration, and other experimental factors;[58]

- Short read systems are well-suited for producing high-quality **deep coverage** of small to large genomes;

- In terms of variant detection, short read systems are well-suited for detecting small variants such as **SNVs**, **small indels**, and **small tandem repeats**, which comprise the greatest number of variants in a genome;

- Short read systems are also well-suited for **counting** the number of DNA fragments that match a certain sequence. Counting applications do not require long reads in order to verify the presence of a target. For instance, NIPT counts the number of fetal chromosome fragments circulating in a mother's bloodstream. These fragments are short, so 100-200 bp long sequencing reads are sufficient to characterise them. [redacted]

Short read systems are well-suited for a broad range of applications. This breadth of applications, compared to the relatively limited range of applications for which native long read systems are well-suited, is a material advantage of short read systems.

75. However, short read systems also have a number of **limitations**, including:

- Because of their limited read length, short read systems are not well-suited for the assembly of larger continuous fragments that elucidate structural order in *de novo* assembly/*de novo* genome/*de novo* sequencing.[59] Short reads do not contain sufficient information to permit the accurate assembly of genomic regions that contain a large number of, or long stretches of, repetitive or paralog regions, or highly similar regions, such as duplicated genes, for example. As a

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involves rapidly scanning markers across the complete sets of DNA, or genomes, of many people to find genetic variations associated with a particular disease.

[57] https://www.businesswire.com/news/home/20171016005445/en/Illumina-Releases-NovaSeq-S4-Flow-Cell-NovaSeq

[58] https://www.illumina.com/documents/products/technotes/technote_Q-Scores.pdf; and https://www.illumina.com/systems/sequencing-platforms/novaseq/specifications.html

[59] Please see above.

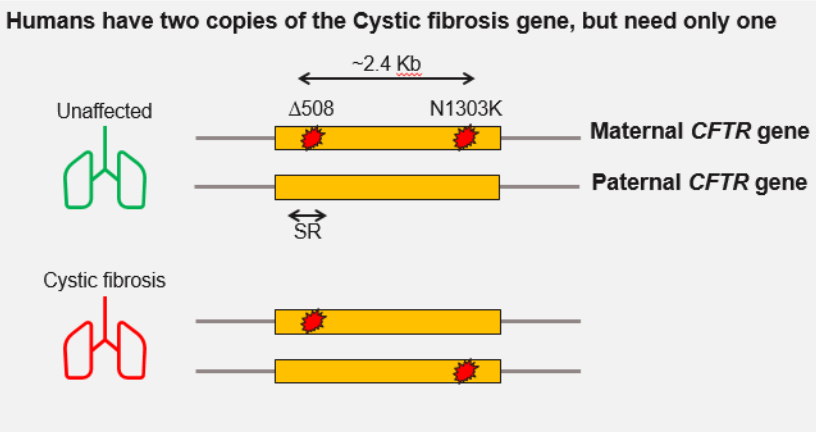
result, accurate assembly of these regions is compromised with short read sequencing, because, depending on the size of the genome, assembly of the reads is otherwise too complex or intractable for short read sequencing. This results from the inability of algorithms to properly order short reads that do not span the junctions with surrounding sequences for these difficult regions;

- Short read systems are not well-suited to detect larger **SVs** because they fail to map the end points of an SV, due to their limitation of only being able to sequence up to hundreds of base pairs.[60] SVs also tend to be clustered in duplicated and repetitive or paralog regions of the genome that are typically difficult for short read sequencing.[61] [redacted]

- Short read systems are not well-suited for **haplotype phasing**. Haplotypes are groups of alleles in an organism that are inherited from a single parent. Phased sequencing identifies alleles on maternal and paternal chromosomes.[62] In other words, phasing identifies which allele belongs to which copy of the chromosome, or alternatively, which alleles appear together on the same chromosome.[63] This is important because certain diseases only occur when both gene copies are defective. For example, cystic fibrosis occurs only when both the maternal and paternal CFTR gene copies are defective. If there are two variants on only one gene copy, the disease does not occur. Phasing the variants allows a determination of whether they reside on the same chromosome.[64] For instance, because variants in the long ~190 Kb CFTR gene may occur at distances longer than short reads can span, it is challenging to ascertain whether the variants are on the same gene copy or not;

[60] https://www.biorxiv.org/content/biorxiv/early/2016/04/13/048603.full.pdf, p. 6
[61] https://community.10xgenomics.com/t5/10x-Blog/Structural-Variant-Analysis-with-Linked-Reads/ba-p/191
[62] https://www.illumina.com/techniques/sequencing/dna-sequencing/whole-genome-sequencing/phased-sequencing.html
[63] https://biology.stackexchange.com/questions/9326/what-does-phasing-mean
[64] https://www.biorxiv.org/content/biorxiv/early/2016/04/13/048603.full.pdf, p. 6

Figure 7: Phasing



- Short read systems have limited utility in resolving **paralogous genes** of the genome. Paralogs are genes that result from duplication during the evolutionary process. As a result, these genes are highly similar. An example is the paralog genes SMN1[65] and SMN2. These two genes are ~30 Kb long and differ by only ~6 bp in the reference genome. As a result, short read systems are not well-suited for mapping variants between these genes.

B. Strengths and limitations of native long read sequencing

76. There are several **advantages** to using native long read sequencing, including:

- Native long read systems can enable ***de novo* assembly/*de novo* sequencing** of larger genomes. Native long read lengths are helpful in spanning repetitive or paralog regions to efficiently assemble genomes.[66] Native long read technologies have been used to produce *de novo* assemblies of hundreds of microbial genomes, dozens of plant and animal genomes, and entire human genomes;[67]

- Native long read systems can enable the capture of **complex or repetitive regions** in a genome. Because native long reads can span the end points of complex and repetitive regions, they are able to produce more contiguous reconstructions of the genome;[68]

- Native long read systems enable discovery and detection of large **SVs,** because the can span the SVs' end points;

[65] The absence of SMN1 leads to 95% of Spinal Muscular Atrophy (the second most common cause of infant mortality).
[66] http://investor.pacificbiosciences.com/static-files/1c2a7f88-5fba-4edd-a53c-643c511535b6, p. 11
[67] https://www.biorxiv.org/content/biorxiv/early/2016/04/13/048603.full.pdf, p. 2-3
[68] Examples of complex regions include HLA and CYP2D6. For these two complex regions it is necessary to "phase" the variants to the same haplotype and thus the reads need to span multiple 1000s of bp.

- Native long read systems are suitable for **haplotype phasing**, enabling identification of whether variants exist on the same copy of the chromosome;

- Native long read systems can span long transcripts in a single read, and consequently enable mapping of **full-length transcripts**, **isoforms** and **gene fusions**. The typical human mRNA transcript is about 2 Kb long and isoforms have different splice junctions. Therefore, in order to map the entire transcript, including splice junctions that define the isoform, native long reads are most suitable. For gene fusions, the ability to sequence on both sides of the fusion and cover the junction is important. Native long read systems are well-suited for transcriptomics because they enable this. Similarly, native long read systems are well-suited for sequencing immune cells (lymphocytes), because the immune proteins secreted from (or on the surface of) cells can be created by combining a much smaller number of DNA sequences. As a result, the ability of native long read technology to sequence splice junctions permits the specific combinations deployed by individual cells to be identified;[69]

- Commercially available native long read systems are capable of direct detection of many **epigenetic modifications**, either by measuring kinetic variation during nucleotide incorporation (such as PacBio) or by measuring the unique electrical blockage of the modified base passing through a nanopore (such as ONT).[70] The ability to detect epigenetic modifications may aid the understanding of epigenetic modifications and their relevance for gene expression, disease status, and ultimately enable pharmaceutical design to better address diseases;

- Native long read systems are well-suited for resolving **paralog regions** of the genome;[71]

- Native long read systems are well-suited for sequencing some **pathogens**, particularly in the case of small viruses with genomes smaller than the read length of a native long read system. For example, the HIV genome is only 8 Kb in size, which means that native long read sequencing of the genome may capture the whole sequence in a single read. This means that native long read systems can identify whether multiple mutations exist on the same molecule (and, therefore, the same virus);[72]

- Current native long read systems are all **real time**. As a result, current native long read technologies are potentially well-suited for near real time experiments.

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[69] *"Nanopore long-read RNAseq reveals widespread transcriptional variation among the surface receptors of individual B cells"*, (2016) *Byrne* et al, Nature Communications, 8:16027.
[70] Epigenetics refers to the study of heritable phenotype changes that do not involve alterations in the underlying DNA sequence.
[71] Please see above.
[72] *"A method for near full-length amplification and sequencing for six hepatitis C virus genotypes"*, (2016), Bull et al, BMC Genomics, 17, 247.

77. However, native long read technologies also have a number of **limitations**, including:

- Native long read systems have **low raw read (non-consensus) accuracy** with error rates of about 10% to 15%. Single molecule techniques are inherently error-prone because a single sequencing pass of the molecule does not provide the redundancy necessary for current high accuracy approaches, whether short or native long read. In some contexts, low raw read accuracy can be overcome by increased coverage, leading to higher consensus accuracy. However, the lower throughput and higher cost of native long read sequencing at high coverage effectively precludes the use of native long read systems in applications that require both high accuracy and scale. As a result, native long read technologies are not well-suited for at-scale sequencing of complex genomes, such as the human genome;

- Because native long read systems achieve relatively **low output and throughput**, the number of bases of DNA or RNA that can be analysed in a single run is much lower (often orders of magnitude less) than with short read systems;

- Because of their lower output and throughput, and their lower raw accuracy, native long read systems have a much **higher cost per base**, especially at the consensus level;

- It is much less economical to achieve deep genome **coverage** using native long read systems;

- Native long read systems are not well-suited to sequence small variant classes such as **SNVs**;

- Native long read systems are not well-suited for **counting** because their read length offers no advantage over short read systems. In most instances, the fragment lengths of the DNA or RNA used in such applications are tens to a few hundred bases long (*e.g.*, a single ctDNA sample will typically require approximately 1 billion reads per sample whereas most native long read systems currently yield between about 1 to 10 million reads per run);

- The **input material** (*i.e.*, DNA sample) requirements for current native long read systems result in increased complexity as compared to short read systems. Native long read input material needs to consist of long fragments of DNA, have high molecular weight,[73] be of high quality and have limited breakage. As a result, it is generally necessary to have a larger amount of input DNA in order to prepare a sequencing-ready sample.[74]

[73] https://academic.oup.com/hmg/article/27/R2/R234/4996216, p. 1
[74] http://www.phgfoundation.org/documents/long-read-sequencing-ready-for-the-clinic.pdf, p. 3

78. As a result of these sequencing technology differences, their suitability for particular applications and in certain customer settings differs significantly.

C. Examples of applications for which short read systems are well-suited

79. The characteristics of short read technologies make them well-suited for particular applications requiring high throughput, high depth, high raw read accuracy, and/or low cost per base.

80. Short read systems are used for both research and clinical applications. In the clinical environment, short read systems are well-suited for applications including, for example, NIPT and liquid biopsy (ctDNA).

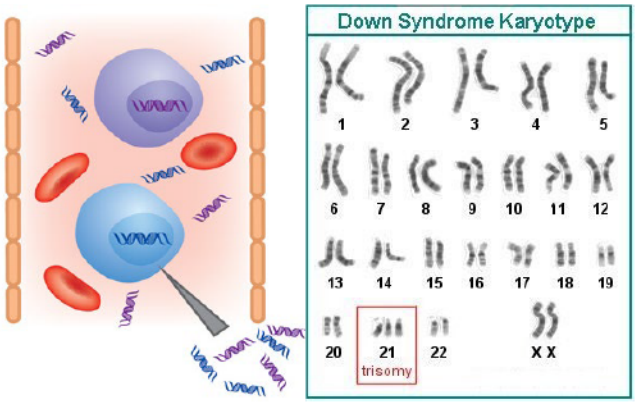
81. **NIPT** is a way of examining cell-free fetal DNA (cfDNA) by taking a sample of blood from a pregnant woman.[75] NIPT takes advantage of the fact that a fetus sheds fragments of its DNA into the mother's blood stream. The sequencer counts how many copies of each chromosome appear by sequencing a blood sample taken from the mother. If the fetus has Down's syndrome, for example, an extra copy of chromosome 21 will be present when compared with the other fetal chromosomes or the mother's chromosome 21.

82. Short read technologies are well-suited for NIPT because of their high throughput and counting capabilities. The fragments of fetal DNA found in maternal blood are short and degraded (the average size of cfDNA is only approximately 200 bp).[76] As a result, reads longer than this length offer no additional value. While native long reads could theoretically be used for NIPT from a technical point of view, because typically 7 million sequence reads, or counts, of the sample are required, native long read technologies are not well-suited for NIPT because they lack the scale to offer this number of counts economically. [redacted]

[75] Cell-free DNA (cfDNA) refers to various forms of non-encapsulated and degraded DNA fragments that are present in blood plasma. The source of DNA can be a tumor clone (referred to as circulating tumor DNA, or ctDNA) or fetal DNA that is present in maternal blood plasma during a pregnancy (referred to as cell-free fetal DNA, or cffDNA). cfDNA can serve as a biomarker for various disorders, such as cancer and prenatal chromosomal aneuploidies.

[76] "*Size distributions of maternal and fetal DNA in maternal plasma". (January 2004) Chan KC, Zhang J, Hui AB, Wong N, Lau TK, Leung TN, Lo KW, Huang DW, Lo YM. Clinical Chemistry. American Association for Clinical Chemistry (AACC). 50 (1): 88–92.* doi:10.1373/clinchem.2003.024893. PMID 14709639).

Figure 8: NIPT



83. **Liquid biopsy** is a non-invasive alternative to surgical biopsies, enabling doctors to discover a range of information about a tumor from a blood sample. The DNA of some tumor cells may be found in the blood. Tumor-derived fragmented DNA in the bloodstream is termed circulating tumor DNA (ctDNA). Non-invasive sequencing is preferred for tumor characterisation and monitoring tumor progression because it enables consistent/continual monitoring in a convenient, economical fashion, unlike invasive procedures that entail risk.[77]

84. There are several factors that make highly accurate short read sequencers ideal for accurately detecting and quantifying low levels of ctDNA in the bloodstream. First, ctDNA fragment sizes are typically under 200 bp, ideally mapping to the read lengths accurately achieved by short read technologies. Second, rare ctDNA variant fragments are present in very low levels in the blood stream and are diluted by the abundance of non-variant DNA in plasma. Therefore, counting and quantifying specific rare ctDNA fragments against the background of non-variant DNA is akin to finding a needle in a haystack, requiring very high depth of sequencing (often in excess of 1,000-fold to 10,000-fold or greater coverage, as compared to the 30x coverage that is typically sufficient for identifying common variants when sequencing a human genome). Lastly, since ctDNA fragments are in low abundance, it is critical that the sequencing technology has high raw read accuracy in order to clearly differentiate between real variants in individual ctDNA fragments and sequencing errors. [redacted].

85. In the research environment, short read systems are well-suited for targeted gene sequencing panels and population genomics. In **targeted sequencing**, only a subset of

[77] https://www.illumina.com/content/dam/illumina-marketing/documents/products/whitepapers/trusight-tumor-15-cfdna-white-paper-1170-2016-016.pdf, p. 1

genes or defined regions in the genome are sequenced.[78] This enables researchers to focus resources on the regions in which they are most interested. Targeted sequencing typically sequences the target region in depth (500-1000x or higher), enabling researchers to identify rare, small variants.[79] Short read systems are well-suited for targeted sequencing because of their high throughput, low cost per base, and their high coverage.

86. **Population Genomics** (PopGen) entails large-scale comparison of DNA sequences within populations of individuals, potentially leading to improvements in individual patient care and translational research with cohort-level knowledge. Short read sequencing is well-suited for PopGen projects because of its high accuracy, high throughput, high scale and low cost per base and, therefore, lower cost per genome.[80]

D. Examples of applications for which native long read systems are well-suited

87. Today, native long read technologies are predominantly used in research applications, rather than in clinical applications. Native long read systems are well-suited for applications requiring discovery and detection of large SVs, haplotype phasing, *de novo* assembly/*de novo* sequencing of larger genomes and applications requiring near real time sequencing.

88. Beyond DNA sequencing, native long read systems are uniquely suited for studying transcriptomes and direct detection of epigenetic modifications.

VI. "Native long read" vs "Linked long read"

89. While short read systems provide read lengths in the tens to hundreds of base pairs per read, library preparation methods can enable a longer DNA "parent" segment (*e.g.*, 50 Kb) to be fragmented, labelled, and sequenced using short read technology with the aim of associating the resulting sequences with the parent fragment. Linked long reads use library preparation methods to enhance the functionality of short read systems. Linked long reads are not substitutes for native long reads. Long read sequencing systems that sequence contiguous fragments of DNA spanning thousands to hundreds of thousands of bases or more are referred to as "native" or "true long read". In contrast, linked long read sequencing approaches may use various strategies, such as unique barcodes identified with the parent fragment on each short read generated from a strand of DNA, to link the short reads together. As explained below, linked long reads are inherently unable to match the quality and information content of native long reads and thus are not a substitute, but rather a complementary technology. [redacted]

[78] Targeted gene panels are focused panels that contain a select set of genes or gene regions that have known or suspected associations with the disease or phenotype under study.
[79] https://www.illumina.com/techniques/sequencing/dna-sequencing/targeted-resequencing/targeted-panels.html
[80] As discussed in Section 13, below, native long read systems could be used in a complementary fashion with short read systems on a small target subset of samples to create reference genomes for the populations being studied.

[redacted]

Figure 9: Linked long read v Native long read

[81]

90. The term "linked long reads" is a misnomer; "associated" short reads is a more appropriate terminology, given that such reads are generated from ordered and assembled short reads rather than a single and contiguous long read. As a result, their characteristics differ significantly from native long reads, including the following:

- Because associated short reads are essentially barcoded assemblies of short reads, they can be produced at much **higher output and throughput**, **lower cost per base**, **higher raw read accuracy**, and more **coverage** than native long reads;
- Associated short reads are well-suited for detecting small variant classes such as **SNVs, small indels, and small tandem repeats**, which benefit from high accuracy and coverage;
- Since current associated short read sequencing is based on short read technologies that are not currently real time, they are not capable of near **real time** sequencing, meaning that they are not well-suited for near real time experiments;
- Because the underlying technology used in associated short read sequencing is entirely based on short read technologies, associated short read technologies also suffer from many of the limitations of short read technologies, discussed above:
    - Because associated short reads generally require a reference and have difficulties with resolving some repetitive regions, they are not well-suited for the assembly of larger continuous fragments that elucidate structural order in ***de novo*** **assembly**/***de novo*** **genome**/***de novo*** **sequencing**;
    - Because associated short reads have the same difficulties with some repetitive regions as short reads, they are not well-suited to resolve **large SVs**. [redacted].

[81] It should be emphasised that the gaps in the results produced by linked long read sequencing contain no useful information.

- Current associated short read technologies do not have the ability to directly detect **epigenetic modifications**;
- Native long reads are the prevailing technology used for **haplotype phasing**,[82] reflecting the combination of the completeness of information and availability of the technology. [redacted];
- The complexity of barcoding transcripts (*e.g.*, various lengths, expression levels and splicing complexity) makes mapping complex structures such as larger **SVs**, as described above, (*e.g.*, PacBio's Iso-Seq® method) and creating **"reference" transcriptomes** difficult using associated short reads;
- Associated short reads are usually **gapped** because they have incomplete coverage of the parent fragment. [redacted].

91. [redacted]
    - [redacted]
    - [redacted]

92. [redacted]:
    - [redacted]
    - [redacted]; and
    - [redacted] is.

93. The limited utility of current associated short reads is further illustrated [redacted]

[82] Please see above.

[redacted]

94. To the best of the Parties' knowledge, all short read technologies can be used to produce associated short reads. As explained above, associated short reads use specialised library preparation methods that effectively barcode samples to assist in piecing together short read results. While different short read technologies may require different barcoding schemes, there are numerous approaches available.

95. Illumina does not currently provide its own associated short read solution. As discussed in [redacted], Illumina discontinued its "TruSeq Synthetic Long-Read DNA Library Prep Kit" in July 2018. [redacted]

96. There are a number of providers of associated short read library solutions which, to the best of Illumina's knowledge, can be used with all short read systems (including [redacted]).[84] These providers include [redacted]. In addition, a number of short read system suppliers offer their own solutions. For example, [redacted] has launched an associated short read solution.[85]

13. Identify (and explain the rationale for identifying):

(a) **the narrowest candidate product/service and geographic market(s) where the merger parties overlap, and (if the parties have a vertical relationship or supply related products/services)[86] the narrowest candidate product/service and geographic market(s) at each level of the vertical supply chain and for each related product/service (the Narrowest Candidate Market(s)).**

(b) **any other plausible candidate product/service and geographic market(s)[87] where the merger parties overlap, have a vertical relationship, or supply**

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[83] https://www.10xgenomics.com/solutions/

[84] [redacted]

[85] [redacted].

[86] These are products or services which do not lie within the same market, but which are nevertheless related in some way; for example, because they are complements (so that a fall in the price of one product/service increases the customer's demand for another), or because there are economies of scale in purchasing them (so that customers buy them together). See guidance note to Question 12.

[87] This may include, for example, the products/services and geographic area(s) in the Narrowest Candidate Market(s) together with other products/services and geographic areas that might be considered substitutes with such products/services and geographic area(s).

related products/services (together with the Narrowest Candidate Market(s), the Candidate Market(s)).

I. Product market definition

A. Short read and native long read systems fall into distinct product markets

97. The Notifying Parties submit that short read sequencing and native long read sequencing are complementary, such that they fall into distinct product markets. As there is no CMA or European Commission ("Commission") precedent on the relevant potential markets for sequencing, the following discussion describes the demand- and supply-side factors that underpin this view.[88]

i. Absence of demand-side substitutability

98. Sequencing systems that perform short reads and native long reads are not substitutable for customers. As explained in Section 12 above, customers use short read sequencing systems and native long read sequencing systems in different contexts, because the sequencing systems and the reads produced have different characteristics, in large part as a result of the fundamental differences in the underlying technologies implemented. These systems address different customer needs and are used in different applications or in a complementary fashion in the same applications.

a. Short read and native long read systems have different characteristics, costs, and uses

99. As described above, short read systems have strengths. Short read systems are characterised by high output and throughput, deep coverage, high raw read accuracy, and low sequencing cost per base. Additionally, the DNA sample preparation requirements for short reads are often less complex because a smaller amount of input DNA is needed in order to prepare a sequencer-ready sample and there is no requirement to keep long DNA molecules intact. Short read systems are well-suited for short circulating DNA fragments in the blood stream that characterise certain sequencing applications (such as NIPT (cfDNA) and liquid biopsy (ctDNA)) and DNA from FFPE[89] samples.[90] Short read systems are also well-suited for detecting small variant classes such as SNVs, which benefit from high accuracy and deep coverage, as well as for "counting" applications.

100. However, short read systems also have limitations. Because of their limited read length, they are not well-suited for the assembly of larger continuous fragments that elucidate structural order in *de novo* assembly/*de novo* genome/*de novo* sequencing, and they are of limited utility in distinguishing highly similar regions, such as duplicated genes, or repetitive or paralog regions with lengths of repeats that exceed the read length

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[88] OFT, *Guidance on Market Definition*, December 2004.
[89] FFPE, or Formalin-Fixed Paraffin-Embedded, is a technique for preserving and preparing tissue samples, including tumor biopsies.
[90] The DNA obtained from FFPE samples is of lower quality as compared to other types of samples and typically consists of shorter fragments.

supported by the sequencer. Short read systems are also not well-suited for detecting larger SVs. Finally, short read systems are not well-suited for haplotype phasing.

101. Native long read systems have different strengths. Native long read systems can enable *de novo* assembly/*de novo* sequencing of larger genomes. They can enable sequencing of complex and repetitive regions in a genome in a single read. Native long read systems also enable discovery and detection of larger SVs. Further, they are suitable for haplotype phasing and enable detection of full-length transcripts, isoforms and gene fusions. Finally, the commercially available native long read technologies can directly detect numerous epigenetic modifications.

102. However, native long read systems have a number of limitations. Commercially available native long read technologies have historically suffered from high error rates, ranging from 10 to 15%. [redacted].

103. The error rates of PacBio's native long read technology have improved over time. [redacted]. PacBio's CCS method involves rotation of the single molecule to create additional reads in order to improve the accuracy of the read. It is important to note that, while CCS improves the accuracy of the native long read, it does so at reduced throughput and, therefore, increased cost.[91]

104. [redacted]

[91] Another common approach to improving accuracy of native long reads involves performing reads of different molecules that span the overlapping region of the sequence and comparing those to reach a consensus sequence with higher accuracy. For example, if one observes a 10% error at a particular base and then runs the read ten times on different molecules that span the region, the read will be right 9 times out of 10, enabling the user to identify and select the correct read. Generally, providers of native long read sequencing technology are always working to improve read accuracy.

[92] [redacted]

[redacted]

105. [redacted]

Figure 10: [redacted]

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93 [redacted]

95 [redacted]

96 [redacted]

97 [redacted]

106. Due to their historically low accuracy rates, native long read technologies have trouble resolving small variant classes such as SNVs. As noted above, although these accuracy rates can be improved through, amongst others, the use of consensus reads (where multiple, identical pieces of DNA are sequenced, or the same piece of DNA is sequenced multiple times, in order to average out sequencing errors), this results in relatively shorter read lengths, a much lower overall throughput, and a higher cost per base. This means that native long read technologies are not well-suited for applications that require the sequencing of many samples. Additionally, native long read systems are not well-suited for counting applications because such applications:

- typically start with highly fragmented DNA less than a few hundred base pairs;
- do not require long read lengths; and,
- require a higher number of reads than native long read technology can economically deliver.[98]

107. Moreover, native long read systems require input material that consists of long fragments of DNA, has high molecular weight, and is of high quality. Consequently, preparing a sequencer-ready sample for a native long read system is more complex as compared to sample preparation for a short read system. These requirements also generally result in the need for a larger amount of input DNA to prepare a sequencer-ready sample. As a result of the limitations described above, it is less economical to create deep genome coverage using native long read technologies.

108. Given these different characteristics, short read and native long read systems are well-suited for different applications.

109. Short read technologies and native long read technologies have no practical interchangeability now (or in the foreseeable future) because of the fundamental differences between the technologies. As a result of these technological differences, users select short read and native long read systems on the basis of various characteristics, including read length, scale, accuracy, number of reads (depth), sample preparation requirements, throughput, and speed and turnaround time, in addition to cost. There are no existing applications for which, on the basis of the differences in these characteristics, a user would replace one technology with the other. For illustrative purposes, some examples are provided below, using the Parties' respective short read and native long read technologies:

- **NIPT**: a single NIPT sample using Illumina's protocol requires approximately 7 million reads whilst using about 10 ng of highly fragmented (~200 bp fragments) circulating DNA (cfDNA) derived from the mother's blood.

[redacted]

[98] Please see Section 12 for more detail on counting applications.

[redacted]

- **WGS**: as discussed in paragraph 67 above, human WGS is a resequencing application that is typically performed at scale, for example in the GEL "100,000 Genomes Project". [redacted]

- **Oncology (liquid biopsy)**: as explained in paragraphs 83 and 84 above, liquid biopsy tests detect cancer biomarker variants in DNA shed by solid tumours into the bloodstream (ctDNA). The advantage of such tests is that a blood draw is less costly and less invasive than a surgical biopsy, and the test can be repeatedly performed during treatment, even when the tumour location is unknown. ctDNA is highly fragmented (typically less than 200 bp), and variants are rare within the isolated DNA because most of the cfDNA derives from healthy cells that do not have the variant. Therefore, counting and quantifying specific rare ctDNA fragments against the background of non-variant DNA is akin to finding a needle in a haystack, requiring a very high depth of sequencing. Lastly, since ctDNA fragments are in low abundance, it is critical that the sequencing technology has high raw read accuracy so that when a variant is observed, there is a high level of confidence that it is not a sequencing error. Even with Illumina's raw read accuracy of approximately 99.9% for the majority of bases sequenced, the sequencing depth for liquid biopsy tests is

[redacted]

often in excess of 1,000-fold to 10,000-fold or greater, such that any given genetic locus must be sequenced this many times before a variant can be confidently identified. [redacted] and

- **'Dark'/'camouflaged' genome regions:** the human genome contains 'dark' or 'camouflaged' gene regions that cannot be adequately assembled or aligned using standard short read sequencing technologies, preventing researchers from identifying mutations within these gene regions that may be relevant to human disease. Short read sequencing is unable to adequately address camouflaged regions because the reads cannot fully span camouflaged regions to properly align homologous nucleotides. Native long read sequencing technologies have the potential to address many camouflaged regions because these technologies have median read lengths measured in thousands of nucleotides, rather than only hundreds of nucleotides from standard short read sequencing technologies.

b. Short read systems and native long read systems are complementary

110. As illustrated in the table below, because short read and native long read systems have different characteristics, customers use them for different applications or for the same application in a complementary fashion.

Table 2: [redacted]

[redacted]

111. As discussed above, in the clinical and diagnostic environments, short read technologies are well-suited for applications including NIPT and liquid biopsy

applications for sequencing cfDNA and ctDNA, respectively. In the research environment, they are well-suited for targeted gene sequencing panels and population genomics.

112. As explained in Section 12 above, native long read technologies are well-suited for *de novo* assembly/*de novo* sequencing, including sequencing of complex plant and animal genomes.[100] In addition, they are well-suited for discovery and detection of SVs, and phasing. Further, they are uniquely suited for mapping transcript isoforms. Current native long read technologies also enable direct detection of epigenetic modifications.

113. There are, however, certain applications for which customers can use both short read and native long read technologies to take advantage of their complementary strengths. These can be broadly categorised as follows:

- "Reflex" testing;
- Initial discovery; and
- Coordinated sequencing.

114. *"Reflex" testing*: this includes applications where short read systems are used in the first instance, due to their higher accuracy, higher throughput and lower cost. For example, short read systems can be used to screen for relevant targeted biomarkers that can indicate the presence or absence of a disease. When justified as illustrated below, further information using native long read systems can be obtained. Examples of such applications include HLA tissue typing, Cystic Fibrosis (CFTR) haplotype phasing, Rare and Undiagnosed Genetic Disease (RUGD), *etc*.

- **Tissue typing** or Human Leukocyte Antigen (HLA) typing entails testing the compatibility of prospective organ donors and recipients prior to an organ transplant.[101] HLA genes are very complex regions that contain many haplotypes over a multiple Kb fragment. Although the majority of HLA typing is currently performed using PCR-based approaches,[102] it can also be done by sequencing and matching the HLA genes of the recipient and those of the usually large number of potential candidate donors.[103] Because most potential donors are incompatible, many donors may need to be tested for a given recipient, making cost and scalability important factors for tissue typing. As a result, short read systems are well-suited to be used for screening because they can identify incompatible donors. However, because short read systems are unable to provide complete information about compatibility, native long read

[100] Animal and plant genomes are complex – they can have multiple copies of each chromosome per cell, for example the strawberries have eight copies, and certain fish have four.
[101] https://www.illumina.com/clinical/hla-sequencing/hla-analysis-ngs.html
[102] https://www.labcompare.com/10-Featured-Articles/142130-Testing-for-Human-Leukocyte-Antigens/
[103] HLA genes are strongly associated with transplant rejection, autoimmune disease, vaccine pharmacogenomics (vaccinomics), cancer, and mate selection. Please see https://www.illumina.com/clinical/hla-sequencing/hla-analysis-ngs.html

systems can then be used to provide additional information that short reads do not.

- **Cystic Fibrosis (CFTR) haplotype phasing** where less costly short read sequencing can be used to screen for certain variants that can cause diseases only when both gene copies of the allele are defective in a given sample, for example. If such variants are present, native long read sequencing can then be used to confirm whether or not such disease-causing variants exist on both the maternal and paternal gene copies, indicating the presence of the disease, or if such variants exist only on one gene copy, indicating the absence of the disease.

- **Rare and Undiagnosed Genetic Disease (RUGD)** sequencing entails the use of sequencing to identify genetic markers for rare diseases. RUGD sequencing also enables the identification of variants that cause inherited disorders.[104] Short read systems are the first line sequencing technology used, due to their lower cost, higher accuracy and throughput, and ability to sequence areas with the most known actionable variants (*e.g.*, SNVs). However, many rare diseases are associated with structural changes that are more readily detected with native long reads systems:

    - First, where the DNA of both biological parents is not available, researchers may require "phasing" to identify the allele causing the disease; and

    - Second, if researchers cannot correlate the disease to variants that can be identified with short read systems, they will use native long read systems to try to identify whether the disease is caused by a larger variant such as a large SV.

  In other words, if short read RUGD test results are inconclusive, native long read tests can be useful to try to identify variants or other abnormalities that were not detected by the short read technology.

115. *Initial discovery*: as explained in Section 12 above, native long read technologies are well-suited for discovery of previously unknown larger SVs, for example. However, once these variants have been discovered using native long read technologies, short read sequencers and algorithms can be trained to re-identify most of these variants in new samples. Examples of such applications include isoform mapping, CNVs, and SVs.

116. *Coordinated sequencing*: this includes applications where short read and native long read sequencing are both utilised to provide complementary information for an application. In these cases, native long read technology is used to access longer range structural information, for example, and short read technology is used for high accuracy due to the ability to sequence economically with high depth. Examples of such applications include:

[104] https://www.illumina.com/clinical/reproductive-genetic-health/genetic-health/rare-undiagnosed-diseases.html

- ***De novo* assembly/*de novo* genome/*de novo* sequencing**: as discussed above, this application relies on the use of both short and native long read technologies;

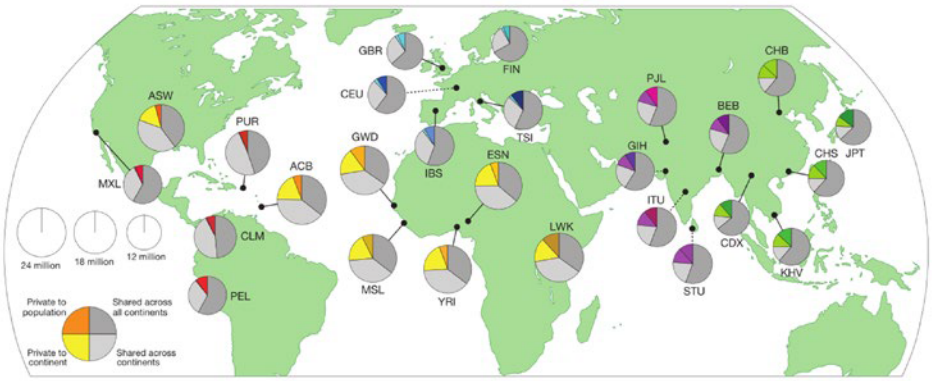
- **Cancer genomes**: sequencing a fresh frozen solid tumour to 10-20x depth with native long read technology can identify SVs, then short reads can be used to obtain additional depth for SNVs. Fresh frozen samples maintain the integrity of DNA such that native long read technology can be applied, as opposed to some samples, such as FFPE, that would be inappropriate for use with native long read technologies;

- As explained in Section 12 above, **population genomics** projects entail the large-scale sequencing and comparison of DNA of populations of individuals (plant or animal, including human). Short read systems are well-suited because of their high accuracy, throughput, scale, and low cost per base for conducting the very large number of runs needed for population-scale projects.

    - Additional valuable genetic information can be added to these projects by using native long read systems alongside short read systems, for instance when short read results are unable to identify disease-causing variants (*e.g.*, larger SVs), native long read systems may be used to sequence subsets of the population-wide samples to identify the disease-causing variants.

    - As discussed in Section 12 above, population-specific reference genomes and databases will be beneficial for PopGen when, for example, samples include sequences not represented in the reference genome (*e.g.*, large insertions or other SVs), or because a reference genome does not adequately represent population-specific haplotype variation. Such population-specific reference genomes (*e.g.*, to take into account ethnic differences) are important in identifying population-specific variants that are linked to population-specific diseases (see figure below). Generation of such new reference genomes and databases benefits from the use of both complementary native long read and short read systems for the reasons explained above in Section 12.

Figure 11: Many variants are specific to populations or continents



Source: *A global reference for human genetic variation, Nature 2015;526(68)*

- When short read results are unable to identify disease-causing variants (*e.g.*, larger SVs), native long read systems can be used to sequence subsets of the population-wide samples to identify the disease-causing variants.

117. As a result, while short read technology and native long read technology are both used in these applications, they are used as complements, rather than substitutes. They are used together to exploit their complementary strengths, thus providing researchers with a greater wealth of information than could be obtained by either technology alone.

c. Short read and native long read technologies are not substitutes

118. As explained above, short read and native long read technologies are not considered to be substitutes by customers, who use them either for entirely different applications or for the same application side-by-side to benefit from their complementarity.[105] This is illustrated by the number of customers that have acquired systems from both Illumina and PacBio over the last three years in the UK. [redacted]

- [redacted]
- [redacted]

[105] [redacted].

119. [redacted][106].

120. As this degree of customer overlap makes clear, customers use Illumina and PacBio systems alongside each other, as complements.

121. As a result, even in the event of a small but significant increase in the cost of short read systems, customer demand would not divert to native long read systems. Conversely, a small but significant increase in the cost of native long read systems, which have a much higher cost per base today, would not divert customer demand towards short read systems.

d. Diverging growth expectations of short read and native long read technologies

122. The use of each of short read and native long read technologies is expected to grow over the next five years, but the Parties do not expect that this growth will either be the result of, or lead to, the technologies being used in the same fashion for the same application(s), due to their fundamental technological differences. While demand for each technology is expected to grow, both in existing (*e.g.*, oncology, PopGen, and RUGD) and new applications, it is anticipated that neither technology will grow as a result of migration of customer demand from the other technology given the specific requirements of customers in terms of applicability to their sequencing needs. For illustrative purposes, the paragraphs below provide some examples of applications for which each of short read or native long read technologies, respectively, could become suitable in the next five years:

- **Clustered Regularly Interspaced Short Palindromic Repeats ("CRISPR") mutation screening**: CRISPR has recently shown great promise for reducing the effort required to create directed mutations to a genome, *e.g.*, in agriculture for the introduction of desirable traits. As the use of CRISPR increases, so will the use of sequencing for the purpose of verifying that mutations were created in the desired manner (*i.e.*, where desired and not in off-target locations). Short read systems are well-suited for this application because screening for mutations over a large number of samples requires scale, depth and accuracy with favourable economics;

- **Tumour Mutation Burden ("TMB") screening**: a new class of cancer drugs called immunotherapies have shown great promise for treating certain cancers such as melanoma, non-small cell lung cancer, bladder cancer, and kidney cancer. Because these drugs are expensive and unfortunately do not benefit all patients, it is important to identify the patients who will respond most favourably. The biomarker TMB shows great promise for this purpose. TMB measures the quantity of different mutations found in a tumour, and a higher

106 [redacted]

number of mutations is correlated with better clinical responses to immunotherapies. Short read sequencing is well-suited for measuring TMB where, again, screening for mutations over a large number of samples requires scale, depth and accuracy with favourable economics;

- **DNA data storage**: DNA data storage solutions, all still in the research phase, aim to mitigate the problem of archiving vast amounts of computer data that are valuable to maintain, but infrequently accessed. For instance, it is estimated that by the year 2020, the digital universe will contain 44 zettabytes, or 1 billion terabytes.[107] DNA molecules are a potential solution to this problem because they can compactly store large amounts of information while maintaining data integrity for many decades, in contrast to current storage media. Microsoft estimates a shoebox worth of DNA could contain data comparable to around 100 giant data centres.[108] Current DNA synthesis methods that could be used to encode information in DNA create relatively short DNA fragments, *e.g.*, less than approximately 200 bases. Therefore, short read sequencing is well-suited for "reading" stored fragments within the template size range of short read sequencers; and

- **The Earth BioGenome Project**, which aims to sequence all 1.5 million known eukaryotic (organisms whose cells have a nucleus enclosed within membranes) species on Earth, is a project in which native long read sequencing could become used in the next five years. The UK's contribution to this effort is known as the Darwin Tree of Life Project, and is targeting 66,000 species of animal, plant, protozoa and fungi.[109] Because this is a *de novo* project, it is well-suited for native long read technologies. The sequencing of 66,000 species' genomes is expected to take approximately ten years.

ii. Absence of supply-side substitutability

123. There is no substitutability between short read systems and native long read systems on the supply side either. Each supplier of sequencing systems has developed a proprietary technology that is protected by IP rights, and developing a short read system or native long read system, respectively, requires the invention and development of an entirely new technology. A supplier of short read systems would therefore not necessarily be able to use its research, development or production assets to invent, develop or manufacture native long read systems to quickly respond to a small but significant price increase of native long read systems and *vice versa*. Even in relation to certain fundamental elements of innovation and development, the different technologies would require different expertise, experience and know-how in the R&D teams.

B. Associated short reads are ordered and assembled short reads

[107] https://www.emc.com/leadership/digital-universe/2014iview/executive-summary.htm
[108] https://www.technologyreview.com/s/601851/microsoft-reports-a-big-leap-forward-for-dna-data-storage/
[109] https://www.ebi.ac.uk/about/news/announcements/darwin-tree-of-life

124. As explained in Section 12 above, associated short read sequencing is performed using short read systems, using specialised library preparation methods that effectively barcode samples to assist in piecing together short read results.

125. The characteristics, cost, and uses of associated short read sequencing differ significantly from those of native long read sequencing. Indeed, because associated short read results are essentially assembled short read results, they do not provide complete coverage of the parent molecule (*i.e.*, they contain gaps).[110] They can, however, be produced at much higher output and throughput, lower cost per base, with higher raw read accuracy, and greater depth than native long read results. Because they are essentially a modified use of short read technology, associated short reads are well-suited for detecting small variant classes such as SNVs, small indels, and small tandem repeats. However, they are not well-suited for the assembly of larger continuous fragments that elucidate structural order in *de novo* assembly/ *de novo* genome / *de novo* sequencing, and are less useful in identifying larger SVs than native long read technology. They also cannot be used to directly detect epigenetic modifications, and are not well-suited for haplotype phasing.

126. [redacted]

127. In short, while associated short read technology enhances the utility of short reads in some contexts, overcoming some of the shortcomings of short reads, they do not provide the level of completeness, or range or span of sequences that is provided by native long read systems. [redacted]

128. As a result, customers do not consider associated short read sequencing to be a substitute for native long read sequencing. Because of the differences in functionality, customers could not use associated short read sequencing in place of native long read sequencing, even in the event of a small but significant increase in the cost of native long read systems.

C. Potential sequencing markets are systems markets

129. The Notifying Parties submit that sequencers and their related consumables fall into systems markets, *i.e.*, markets comprising both the sequencers and their secondary products and services (including sample preparation equipment, library preparation

[110] Please see Section 12 above for a detailed discussion of the differences between associated short reads and native long reads.
[111] https://www.10xgenomics.com/news/mgi-genetic-sequencer-certified-new-10x-genomics-compatible-program/

kits, consumables used in the sequencing process, bioinformatics tools, and related support services).

i. Characteristics of systems markets

130. Customers purchase both short and native long read sequencers taking into account the "total cost of ownership" (or whole life cost) of the sequencing system. Given the need for library preparation kits and consumables used in the sequencing process, customers take the costs of those kits into account when considering the cost per run (and then the cost per sample).[112] As a result of that dynamic, setting a supra competitive price for library preparation or consumable kits would impact on sales of sequencers.[113]

131. Suppliers are well aware of the total cost of ownership approach taken by customers in assessing sequencing solutions. As a result:

- Sequencing system suppliers publish extensive information on sample preparation, library preparation and consumables used in the sequencing process, enabling customers to estimate the number of kits that they are likely to require to undertake the number of sequencing runs necessary to sequence the number of samples that they anticipate testing over the life time of a sequencer;

- The price of (or likely expenditure on) sample preparation, library preparation and consumables used in the sequencing process is a relatively high proportion of the sequencer's price (and can account for a material proportion of the sequencer's price when customers purchase under a reagent rental-type model); and

- A sufficiently large proportion of customers are able and likely to take into account the total cost of ownership such that it would be unprofitable for a supplier to set a supra competitive price for the library preparation kits and consumables used in the sequencing process, given the number of customers that would adapt their sequencer purchasing behaviour (within a reasonable period of time).[114]

132. As a result, system suppliers are not incentivised to increase the price of library preparation kits and consumables used in the sequencing process if that would reduce future sales of sequencers. This is important because customers need to upgrade their systems over time. Further, the increasing number and scope of sequencing applications and tests for any given application that can be performed, coupled with the growing demand for tests, means that both existing customers require additional capacity and new customers acquire sequencing systems. The prospect of this large number of new

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[112] OFT, *Guidance on Market Definition*, p. 21, para. 6.5.
[113] OFT, *Guidance on Market Definition*, p. 21, para. 6.3. See also, OFT Decision of 20 July 2001 in *ICL/Synstar*, para. 25.
[114] OFT, *Guidance on Market Definition*, p. 21, para. 6.6.

and repeat customers disciplines pricing, particularly since suppliers cannot price discriminate between new or repeat customers.[115]

133. The European Courts[116] and the Commission have considered similar markets in the past.[117] In its *Luxury Watch* judgement, the General Court found that primary and secondary products belonged to a unified market if a price increase of the secondary product would cause a shift in the demand for the primary product.[118] The Court distinguished such markets from those in which customers did not take into account the price of secondary products when purchasing the primary product, *i.e.*, if they did not take into account its total cost of ownership.[119] In *Pelikan/Kyocera*, the Commission considered that the markets for printers and ink cartridges should be assessed jointly given that customers did buy on the basis of whole life costing.[120]

134. Further, the Commission has also found that primary and secondary products belong to a unified market if secondary products of one supplier cannot be used with the primary products of another supplier. In particular, in *Danaher/Beckman Coulter*, the Commission considered that laboratory instruments and related equipment (consumables, reagents, parts, software, *etc.*) belonged to a unified market because suppliers of instruments supplied consumables and reagents only for their instruments and not for their competitors' instruments.[121] In *Panasonic Healthcare/Bayer's Diabetes Care Business*, the Commission considered that instruments and reagents for *in vitro* diagnostics ("IVD") belonged to a unified market because IVD instruments were usually proprietary, such that reagents supplied by one manufacturer could not be used with instruments from another supplier.[122]

ii. Systems markets for short read and native long read sequencing

135. The potential markets for short reads and native long reads, respectively, have all the characteristics of systems markets. Customers are sophisticated and engage in whole life costing when purchasing sequencers. Such customers include major sequencing services providers (*e.g.,* [redacted]), genomics centers, pharmaceutical companies, universities, and clinical laboratories. They consider the costs of consumables, product support services and bioinformatics tools of different suppliers and will take these into account when selecting and purchasing a sequencer. This is even more the case given that, in the longer run, these costs will exceed the cost of the sequencer.

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[115] OFT, *Guidance on Market Definition*, p. 21, para. 6.7.
[116] See Judgement of 15 December 2010 in Case T-427/08, *CEAHR v. Commission* and Judgement of 12 December 1991 in Case T-30/89, *Hilti AG v Commission*.
[117] Decision of 22 September 1999 in Case IV/34.330 *Pelikan/Kyocera*, para. 61-69; Decision of 18 January 2017 in Case M.8087 *Smiths Group/Morpho Detection*, para. 39-42.
[118] Judgement of 15 December 2010 in Case T-427/08, *CEAHR v. Commission*, para. 103.
[119] Judgement of 15 December 2010 in Case T-427/08, *CEAHR v. Commission*, para. 106.
[120] Decision of 22 September 1999 in Case IV/34.330 *Pelikan/Kyocera*, para. 61-69.
[121] Decision of 16 June 2011, Case M.6175 *Danaher/Beckman Coulter*, para. 20.
[122] Decision of 23 November 2015, Case M.7787 – *Panasonic Healthcare/Bayer's Diabetes Care Business*, para. 22.

136. Suppliers also consider sequencers and their related library preparation kits and consumables used in the sequencing process, and product support services to fall within single unified markets, and determine their (pricing) strategies accordingly. For example, Illumina sets the price of its consumables to ensure that it will not negatively affect its sales of sequencers. Its pricing seeks to ensure that customers can economically run its sequencers at capacity to maximise efficiency. Certain other suppliers, including [redacted], provide sequencers at relatively low upfront cost and spread the remainder of the price across the sales of library preparation kits and consumables used in the sequencing process (and related services) supplied over time. While this reflects a different pricing model, it makes it clear that both suppliers and customers look at the total cost of sequencing when supplying or acquiring systems.

137. A large number of market participants supply library preparation kits. However, each system supplier supplies the consumables used with its own sequencers in the sequencing process. As a result, they compete with each other for the sale of the entire sequencing system.

D. Chain of substitution between short read and native long read systems, respectively

138. There is a chain of substitution between different short read systems. While the smallest and highest throughput systems are clearly not direct substitutes for each other, it is clear that customers weigh up the characteristics of different systems and their needs in selecting sequencers. For example, customers performing amplicon sequencing may choose between iSeq, MiniSeq, MiSeq or NextSeq, with sample volumes and their preference for batching being a key determinant of which platform is the best system for a particular customer. Similarly, customers running higher throughput methods, such as whole transcriptome analysis, exomes, or liquid biopsy, may take into account sample volumes and preference for sample batching levels in choosing between NextSeq and NovaSeq systems. In many cases, NextSeq is used as a production-level system for high throughput processing of samples (and sequencing methods). The NextSeq may be used in these instances due to batching considerations and desire to have redundancy of instrumentation. Three examples of customers that use the NextSeq as such are [redacted].

139. Further, as existing customers' requirements change, they can choose whether to run existing systems more intensively, acquire additional lower throughput systems or acquire higher throughput systems (like Illumina's NovaSeq). While at least [redacted] of Illumina's customers start with lower throughput systems, more than [redacted] of those customers will subsequently add a higher throughput system as their sample volumes increase (and approximately [redacted] add an additional lower throughput system). To illustrate, the purchasing history of three UK-based Illumina customers over the last five years is as follows:

140. [redacted][123] For example, a native long read customer may choose between [redacted], taking into account sample volume and preference for batching levels as key determinants.

141. However, as already noted, short read systems and native long read systems are not substitutable.

E. Sequencing and alternative methods of ascertaining genetic information are not substitutes

142. Alternative methods such as microarrays, PCR (PCR, qPCR and digital PCR), fluorescence in situ hybridization ("FISH") and DNA mapping are not methods of sequencing, nor are they substitutes for sequencing, even though they can be used to ascertain genetic information. Sequencing technologies enable previously never-before sequenced DNA to be ascertained (*i.e.*, *de novo* sequencing) and unanticipated variants of any type (*e.g.*, SNVs, indels, SVs) in nearly any location to be determined. In contrast, non-sequencing alternative technologies require prior knowledge of the relevant sequence, including anticipated variants. This prior knowledge is derived from sequencing.

143. The alternative technologies may be used for a number of reasons, including sample volume (*e.g.*, microarrays), turnaround time (*e.g.*, PCR), sensitivity (*e.g.*, digital PCR), established clinical utility (*e.g.*, FISH), because they provide complementary information (*e.g.*, mapping), or cost (*e.g.*, PCR and microarrays). However, they only enable determination of whether known sequences or particular variants are present (or not) in a sample, not actual sequencing of the sample.

144. The Parties do not consider that these alternative technologies are substitutes for either short read or native long read systems. In all of these alternative technologies, prior

[123] [redacted]

knowledge of the sequence to be investigated is required. However, further information about each of these alternative technologies is provided in [redacted].

II. Geographic market definition

145. The Notifying Parties submit that the potential markets for short read systems and native long read systems, respectively, are worldwide in scope. While there is no CMA or Commission precedent on the relevant geographic market for sequencing, the CMA's predecessor agency, the OFT,[124] and the Commission,[125] have previously found that laboratory instrument markets are at least EEA-wide or worldwide in scope. In particular, in *Thermo Electron Manufacturing Limited/GV Instruments Limited*, the OFT found that the market for mass spectrometer instruments was worldwide in scope, as the geographic location of the supplier was not important for customers, and distribution costs were not significant compared to the overall cost of the products.[126]

146. Similarly, for customers of short read and native long read systems, the location of suppliers is not particularly relevant. Suppliers are generally active globally and typically offer, from centralised production facilities, identical products regardless of the customer's location. Moreover, transport costs are not significant and there are no significant price differences between jurisdictions worldwide:

- For Illumina, [redacted][127]
- For PacBio, [redacted]

[redacted]

[124] Decision of 15 December 2006, *Thermo Electron Manufacturing Limited/GV Instruments Limited,* para. 22-23.
[125] Decision of 16 June 2011, Case M.6175 *Danaher/Beckman Coulter*, para. 32.
[126] Decision of 15 December 2006, *Thermo Electron Manufacturing Limited/GV Instruments Limited,* para. 22-23.
[127] [redacted]

[redacted]

[redacted][128]

147. While system suppliers must provide support services to customers (given the sensitive nature of the instruments), [redacted]

[redacted]

148. The potential markets for short read systems and native long read systems, respectively, therefore have the main characteristics of being global, or at least EEA-wide, in scope.

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128 [redacted]

129 [redacted]

130 [redacted]

131 [redacted]

Shares of supply

14. Provide the shares of supply (by value and, where appropriate, volume) for the merger parties and each of their principal competitors for the Candidate Markets (see question 13).

149. As discussed in Section 13 above, the Notifying Parties submit that there are distinct short read and native long read systems markets. Further, they submit that the potential markets are worldwide, or at least EEA-wide, in scope.

150. The Notifying Parties are unaware of publicly available sources that provide either estimates of the total market size or shares of supply for the potential markets for short read and native long read systems, respectively, either globally or in the UK.

151. The tables below reflect Illumina's best estimates of its, and its competitors' shares of supply by value on the potential market for short read systems for 2017, in the UK.

Table 3: Estimated shares of supply by value for the potential market for short read systems

Supplier	UK (2017)[132]
[redacted]	[redacted][133]
[redacted]	[redacted][134]
[redacted]	[redacted]
[redacted]	[redacted][135]

152. [redacted]

153. In relation to the potential market for native long read systems, [redacted] has reported that, as of May 2018, there were approximately 6,000 to 7,000 [redacted] shipped

132 [redacted]

133 [redacted]

134 [redacted]

135 [redacted]

to users globally.[136] [redacted][138]

154. The Notifying Parties do not have access to UK-specific data concerning [redacted].

155. The Notifying Parties submit that shares of supply are not a relevant indicator of the competitive situation in the potential markets for short read and native long read systems respectively. As explained in Sections 18 and 22 below, the potential markets for short read and native long read systems are nascent and rapidly growing, with forecasts suggesting that global NGS revenues will reach GBP 12.67 billion by 2024 (up from GBP 4.42 billion in 2018).[139] Further, these potential markets have seen the launch of disruptive new technologies which can rapidly gain wide adoption and expand significantly, with further entry anticipated in the short-term.

156. In this regard, the Commission's decisional practice[140] and the case law of the European Courts[141] make it clear that, in nascent and fast growing markets that are innovation-driven, market shares (or shares of supply) need not necessarily indicate market strength. For example, in *Cisco Systems Inc. v. Commission*, the General Court confirmed the Commission's view that the combined market shares of Microsoft and Skype on the potential markets for consumer communication services, including a combined market share of 80-90% on the potential segment for video calls, were not indicative of market strength. The Court found that "*the consumer communications sector is recent and fast-growing sector which is characterised by short innovation cycles in which large market shares may turn out to be ephemeral. In such a dynamic context, high market shares are not necessarily indicative of market power …*".[142]

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[136] [redacted]

[137] [redacted]

[138] [redacted]

[139] https://www.marketsandmarkets.com/PressReleases/ngs-technologies.asp

[140] Commission, Decision of 2 September 1991 in Case IV/M.129, *Digital/Philips*, para. 18; Commission, Decision of 2 March 2001 in Case COMP/M.2256 *Philips/Agilent Health Care Solutions*, para. 31; Commission, Decision of 7 October 2011 in Case COMP/M.6281 *Microsoft/Skype*, para. 78.

[141] Judgement of the General Court of 11 December 2013 in Case T-79/12, *Cisco Systems Inc. v. Commission*, para. 69.

[142] Judgement of the General Court 11 December 2013 in Case T-79/12, *Cisco Systems Inc. v. Commission*, para. 69.

Horizontal effects

15. Provide a description of how competition works in each Candidate Market where the merger parties overlap. The description of such competitive dynamics in the Candidate Market should include (but not necessarily be limited to):

***(a)* information on the competitive constraint posed by each of the merger parties on each other and on the competitive constraint posed by the other principal suppliers in the Candidate Market(s);**

***(b)* an explanation of what drives customer choice for the overlap product/services. Where relevant, the response should include the identification of separate customer groups, if any, and an explanation of how the competitive dynamics differ across these customer groups (see 5.2.28 to 5.2.31 of Merger Assessment Guidelines);**

***(c)* a description of the parameters of competition (for example, price, quality, service, innovation) and their importance relative to one another;**

***(d)* an explanation of the role and significance of product/service differentiation (including an explanation of the extent to which the merger parties' products/services are differentiated);**

157. As explained in Section 13 above, the Notifying Parties submit that short read and native long read systems fall into distinct product markets. As a result, the activities of Illumina and PacBio do not overlap. The Notifying Parties are not and, absent the Transaction, would not, become competitors.

I. Differentiation of the Notifying Parties

158. In addition to the strengths and weaknesses of short read and native long read sequencing technologies generally, as described in Section 12 above, there are material yield differences between Illumina's short read and PacBio's native long read technologies. Further, these differences are not expected to diminish, even in the medium-to-longer-term. [redacted] Indeed, the differential between Illumina's and PacBio's technologies' output per flow cell is expected to increase even further over the next five to seven years, absent the Transaction.

159. [redacted].

160. [redacted]

161. [redacted]

162. [redacted]

163. [redacted]

164. [redacted]

165. [redacted]

166. [redacted]

167. In light of the expected continued divergence in yield between Illumina's short read and PacBio's native long read technologies, the Notifying Parties expect that the respective strengths and limitations of Illumina's and PacBio's respective technologies will remain as described in Section 12. As a result, sequencing applications that, today, are well-suited for either Illumina's short read sequencing technology or PacBio's native long read technology, will continue to be well-suited for that technology. In addition, continued significant reductions in the cost per base for each technology will likely lead to the emergence of new sequencing applications not available today that will be well-suited for one technology over the other, based on the inherent characteristics of the technologies, including cost per base.

II. Competitors

168. For the sake of completeness, the Notifying Parties describe the competitive dynamics of the potential markets for short read and native long read systems.

169. Market reports have predicted that global NGS revenues will reach GBP 12.67 billion[143] in 2024, up from GBP 4.42 billion[144] in 2018, reflecting a CAGR of 19.2%.[145] This growth has been catalysed by the rapid expansion of DNA sequencing's utility in medical and scientific applications. These factors have led to increased adoption of the technology in existing and new applications (*e.g.*, WGS, *de novo* assembly/*de novo* sequencing, oncology and reproductive health). Due to the differential types of information, attributes and economics, illustrating their fundamental complementarity, it is anticipated that the growth of each of the potential short read and native long read system markets will not be at the expense of the other.

A. Competitive landscape of the potential market for short read systems

170. The potential market for short read systems is a rapidly-expanding, dynamic market characterised by an increasing number of sequencing platforms, rapid improvements in system performance, lower costs, and reduced complexity of generating sequencing data (*e.g.*, improvements in workflow) and analysing the results (*e.g.*, improvements in bioinformatics and analytics).

171. As explained further in Section 22, below, the potential market for short read systems has recently drawn in new entrants, alongside launches of new systems by existing market participants.

172. Currently, Illumina competes globally with three major diagnostics and instruments companies to supply short read systems and sequencing services: Thermo Fisher Scientific ("Thermo Fisher"), Qiagen N.V. ("Qiagen"), and the Beijing Genomics Institute ("BGI"). [redacted]

173. A material number of third parties have developed and supply library preparation kits and bioinformatics solutions (*e.g.*, sequence alignment to sequence interpretation solutions) which can be used with Illumina's sequencers. These suppliers include, among others, the following:

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[143] This figure has 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).
[144] This figure has 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).
[145] https://www.marketsandmarkets.com/PressReleases/ngs-technologies.asp; Please see [redacted]

Library preparation	Bioinformatics
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	
[redacted]	
[redacted]	
[redacted]	

174. However, given that Illumina and PacBio supply entire short read systems (Illumina) and native long read systems (PacBio), including sequencers, consumables, bioinformatics tools and product support services, the Notifying Parties have only described below suppliers who also supply entire systems.

i. Thermo Fisher

175. Thermo Fisher is the world's largest maker of scientific and laboratory equipment, with global revenues of more than GBP 16.2 billion[146] in 2017[147] and approximately 70,000 employees.[148] Its commercial reach provides access to 400,000 clinical, applied and research customers across the globe.[149]

176. Thermo Fisher is the leading supplier of first-generation Sanger sequencing systems, with a total installed base of around [redacted].[150] It is also the second largest supplier of NGS short read systems. At the end of 2017, it had an estimated global installed base of NGS short read systems of over [redacted].[151]

177. Thermo Fisher entered the potential market for NGS (non-Sanger) short read systems in 2014 through its GBP 10.54 billion[152] acquisition of Life Technologies, which

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[146] This figure has 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).

[147] Thermo Fisher 2017 Annual report, p. 23, available at http://d18rn0p25nwr6d.cloudfront.net/CIK-0000097745/7bc424cd-7525-4fb2-8de0-a33bc5b10c6b.pdf

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

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

[150] [redacted]

[151] [redacted]

[152] This figure has 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).

marketed and sold the SOLiD and Ion Torrent short read sequencing systems.[153, 154] Thermo Fisher no longer actively markets the SOLiD systems. Thermo Fisher's Ion Torrent systems are based on SBS technology. However, unlike Illumina's systems, they do not record base additions with cameras. Instead, they rely on the fact that the addition of a nucleotide to a DNA polymer releases a hydrogen ion, and as a result the pH changes. The resulting pH change is measured using semiconductors.[155] According to Thermo Fisher, the advantages of this approach are that it offers a faster run time and simplified workflow.[156] [redacted][157] For instance, the Ion GeneStudio S5 (*see below*) can produce reads up to 600 bp.[158]

178. Thermo Fisher's portfolio currently includes five NGS short read system configurations: the Ion PGM (Personal Genome Machine), Ion Proton, Ion GeneStudio S5, Ion GeneStudio S5 Plus, and Ion GeneStudio S5 Prime. These are low-to-medium throughput benchtop sequencers that are widely used for clinical and translational purposes.[159] Thermo Fisher's GeneStudio S5 series was launched in January 2018.[160] Various consumable semi-conductor "chips" supplied by Thermo Fisher may be used in most of its sequencers, and their performance varies, depending on the chip used.

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[153] [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

[154] 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/

[155] https://www.thermofisher.com/be/en/home/life-science/sequencing/next-generation-sequencing.html

[156] https://www.thermofisher.com/be/en/home/life-science/sequencing/next-generation-sequencing.html [redacted]

[158] https://www.fisher.com/us/en/home/life-science/sequencing/next-generation-sequencing/ion-torrent-next-generation-sequencing-workflow/ion-torrent-next-generation-sequencing-run-sequence/ion-s5-ngs-targeted-sequencing/ion-s5-specifications.html

[159] [redacted]

[160] [redacted]

179. In addition, Thermo Fisher also supplies two library preparation instruments: the "OneTouch 2"[161] and the "Ion Chef".[162] These instruments simplify the workflow for Thermo Fisher's systems by automating library preparation.

Table 4: Thermo Fisher sequencers[163]

[redacted]

[161] https://www.thermofisher.com/order/catalog/product/4474779

[162] https://www.thermofisher.com/be/en/home/life-science/sequencing/next-generation-sequencing/ion-torrent-next-generation-sequencing-workflow/prepare-template/ion-torrent-next-generation-sequencing-ion-chef-system.html

[163] [redacted]

[redacted]

ii. Qiagen

180. Founded in 1986, Qiagen is a major player in the provision of sample preparation and assay technologies for molecular diagnostics (human healthcare), applied testing (forensics, veterinary testing and food safety), pharma (pharma and biotech companies) and academia (life sciences research).[174] It is listed on the New York and Frankfurt Stock Exchanges, with its corporate headquarters in Venlo, the Netherlands, and operational headquarters in Hilden, Germany. It currently has about 35 subsidiaries in over 25 countries, with a global network of distribution partners in more than 60 countries to serve more than 500,000 customers.[175]

181. In 2012, Qiagen acquired Intelligent BioSystems ("IBS"), a company that was developing short read sequencing systems based on a SBS technology similar to Illumina's.[176] IBS had released its first system, the MAX-Seq, in 2011 and was working on a benchtop sequencer called the Mini-20.[177] Over the last few years, Qiagen has acquired a number of additional sequencing-related companies that provide library prep solutions, assays and/or bioinformatics software, including CLC Bio (2013), Ingenuity Systems (2013), Enzymatics (2015), Exiqon (2016), OmicSoft Corporation (2017), and N-of-One (2019).[178]

182. In November 2015, Qiagen commercialised its first system, the "GeneReader", based on IBS' short read technology.[179] The GeneReader is part of a suite positioned by Qiagen as the first end-to-end NGS workflow, from sample to final report.[180] The suite includes a number of different modules and tools that enable (i) sample preparation, (ii) target enrichment and library preparation, (iii) sequencing (using the GeneReader), and

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[174] Qiagen 2017 Annual Report, p. 4, available at https://corporate.qiagen.com/-/media/project/qiagen-corporate/corporate-microsite/documents/investor-relations/2017/reports/2017-ifrs-annual-report-r101-final.pdf

[175] https://corporate.qiagen.com/about-us/global-presence

[176] https://www.genomeweb.com/sequencing/qiagen-acquires-intelligent-bio-systems-maps-out-sequencing-strategy#.XDnaO1xKjcs

[177] [redacted]

[178] https://www.genomeweb.com/informatics/qiagen-acquires-clc-bio#.XFIM1lz7S70, https://www.prnewswire.com/news-releases/qiagen-acquires-ingenuity-systems-adding-leading-solution-for-analysis-and-interpretation-of-complex-biological-data-205279951.html, https://corporate.qiagen.com/newsroom/press-releases/2017/20150111_enzymatics, https://www.prnewswire.com/news-releases/qiagen-announces-successful-completion-of-tender-offer-for-shares-in-exiqon-584079341.html, https://corporate.qiagen.com/newsroom/press-releases/2019/20190107_qiagen_acquires_n_of_one

[179] https://corporate.qiagen.com/newsroom/press-releases/2015/20151104_gr_launch

[180] [redacted]

(iv) data analytics and interpretation.[181] At the end of 2017, the worldwide installed base of the GeneReader was estimated at approximately [redacted].[182]

183. Qiagen offers customers different pricing models for the GeneReader. [redacted].

Table 5: Qiagen sequencer

[redacted]

184. In addition to the GeneReader system, Qiagen also supplies universal solutions which can be used with any NGS sequencer, including Illumina's. These sequencing-related solutions include library preparation, assays, and bioinformatics software.[188]

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181 [redacted]

182 [redacted]

183 [redacted] https://www.qiagen.com/us/products/ngs/mdx-ngs-genereader/library-preparation/qiagen-genereader-platform/

184 [redacted]

185 [redacted]

186 [redacted]

187 [redacted]

188 https://corporate.qiagen.com/newsroom/press-releases/2017/20180108_ngs_portfolio_expansion; 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

185. Qiagen's sequencing revenues (including revenue generated from the GeneReader system, library prep solutions, assays, and bioinformatics) exceeded GBP 89 million[189] in 2017, and Qiagen's sequencing revenue target was more than GBP 109 million[190] for 2018 (*i.e.*, a 22% increase).[191]

186. Qiagen is currently working to expand the applications for which the GeneReader system can be used. In 2018, it announced a partnership with Natera, a leading provider of sequencing assays for NIPT and ctDNA, to develop NIPT assays for the GeneReader system.[192] Prior to this partnership, Natera exclusively used Illumina's sequencing systems to perform its NIPT and ctDNA sequencing assays. It also launched a joint venture with Maccura, a Chinese in vitro diagnostics IVD company, to obtain regulatory approvals and accelerate growth of the GeneReader system in China.[193]

iii. BGI

187. BGI is a genomics company that, [redacted], has expanded significantly in recent years with its 2017 revenue rising by approximately 22%.[194] BGI was founded in 1999 to represent China in the Human Genome Project, and is headquartered in Shenzhen, China. It operates in Europe through offices and laboratories in Riga, Copenhagen and London.[195]

188. BGI provides a wide variety of short read sequencing systems and services, native long read sequencing services, and genetic tests for medical institutions, research institutions and other public and private partners.[196] Today, BGI states that it is the world's largest genomics centre, producing at least a quarter of the world's genomic data.[197]

189. The company first commercialised a short read system in 2015, after acquiring Complete Genomics in 2013. Library preparation is based on Complete Genomics' DNA nanoball approach, termed DNBseq, which amplifies the DNA to be sequenced.[198] DNA nanoballs are placed on a flow cell chip to create ordered arrays.

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[189] This figure has 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).
[190] This figure has 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).
[191] 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
[192] https://corporate.qiagen.com/newsroom/press-releases/2018/20180312_qiagen_natera_partnership
[193] Qiagen 2017 Annual Report, p. 5, available at https://corporate.qiagen.com/-/media/project/qiagen-corporate/corporate-microsite/documents/investor-relations/2017/reports/2017-ifrs-annual-report-r101-final.pdf
[194] http://pdf.dfcfw.com/pdf/H2_AN201804191126386621_1.pdf, p. 27; https://www.asiabiotech.com/12/1201/0011_0013.pdf; https://www.scmp.com/business/companies/article/2106262/chinese-biotech-firm-bgi-genomics-surges-8-fold-ipo-pushing
[195] https://www.bgi.com/global/resources/offices-and-laboratories/; See also http://en.mgitech.cn/page/gsjj.html
[196] [redacted]
[197] https://www.bgi.com/us/company/careers/bgi-opens-seattle-office-for-north-america-expansion/
[198] A nanoball is a long strand of repetitive fragments of amplified DNA, which forms a detectable, three dimensional, condensed, and spherical sequencing object.

Sequencing is then performed via an approach termed cPAS (Combinatorial Probe Anchor Synthesis), a fluorescence-based technology.[199]

190. MGI Tech, a BGI subsidiary, currently commercialises two lines of short read systems: the BGISEQ line and the MGISEQ line. The BGISEQ line includes the BGISEQ-50, a benchtop sequencer, and the BGISEQ-500, a high-throughput sequencer. The BGISEQ-500 has received Chinese clinical regulatory (CFDA) approval and a CE mark for NIPT.[200]

191. The MGISEQ line includes the MGISEQ-200, MGISEQ-2000 and MGISEQ-T7. The MGISEQ-200 and MGISEQ-2000 were released in October 2017 and started shipping in 2018.[201] The MGISEQ-200 is marketed as a benchtop sequencer providing medium throughput, while the MGISEQ-2000 is marketed as a production-scale sequencer providing high-throughput.[202]

192. The MGISEQ-T7 was unveiled in October 2018 and is currently available through an early access program.[203] It is marketed as a production-scale sequencer that MGI states provides a daily throughput of up to 6 Tb, a 50% increase in sequencing speed, and a 20% increase in single flow cell density.[204] MGI also states that the sequencer delivers high accuracy and improved efficiency as a result of upgrades to the flow cell, fluidics, biochemical and optical systems.[205]

193. MGI also commercialises two automated sample prep systems, the MGISP-960 and MGISP100, and a modular workstation that it states provides a fully automated workflow, from sample to report, the MGIFLP.[206]

Table 6: BGI sequencers[207]

[redacted]

[199] https://www.bgi.com/resources/sequencing-platforms
[200] [redacted]
[201] https://www.bgi.com/global/company/news/bgis-mgi-tech-launches-two-new-ngs-platforms/
[202] http://en.mgitech.cn/product/Sequencer.html
[203] https://www.prnewswire.com/in/news-releases/mgi-announces-milestone-of-1-000-sequencers-installed-and-opens-early-access-program-for-groundbreaking-ultra-high-throughput-sequencer-mgiseq-t7-874602836.html
[204] http://www.bio-itworld.com/2018/10/25/new-chinese-sequencer-promises-60-human-genomes-in-a-day.aspx; http://en.mgitech.cn/product/detail/139.html
[205] https://www.prnewswire.com/in/news-releases/mgi-announces-milestone-of-1-000-sequencers-installed-and-opens-early-access-program-for-groundbreaking-ultra-high-throughput-sequencer-mgiseq-t7-874602836.html
[206] http://en.mgitech.cn/product/SamplePretreatmen.html; http://en.mgitech.cn/product/detail/MGIFLP.html
[207] http://en.mgitech.cn/product/Sequencer.html

[redacted]

194. MGI claims to offer the "most competitive sequencing price in the market" using the MGISEQ-T7 at a cost per gigabase of approximately GBP 4.[214]

195. MGI has stated it has installed 1,000 systems in 16 different countries.[215] [redacted]

B. Competitive landscape of the potential market for native long read systems

196. The potential market for native long read systems is a nascent [redacted] PacBio was the first to broadly offer native long read systems in 2011, when it started to commercialise its RS system. Since then, Oxford Nanopore Technologies ("ONT") entered the potential market for native long read systems in 2014/2015.[216]

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208 [redacted]
209 [redacted]
210 [redacted]
211 [redacted].
212 [redacted]
213 [redacted]
214 http://www.bio-itworld.com/2019/01/11/MGI-announces-first-customer-mgiseq-t7-complete-genomics-.asp; http://en.mgitech.cn/article/detail/mgiannouncesearlyaccesscustomerofmgiseqt7highestthroughputsequencerbringspowerofchoicetothemarket.html
215 http://en.mgitech.cn/article/detail/mgiannouncesmiles.html
216 ONT 2017 Annual report, p. 6, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0; The MinION was introduced into early access in Spring 2014 and made commercially available in 2015. See https://nanoporetech.com/about-us and https://nanoporetech.com/about-us/history

197. ONT is a privately held, UK based, company that was spun out from the University of Oxford in 2005 and currently has more than 350 employees.[217] It was the first company to develop and commercialise nanopore sequencing systems. As explained in Section 12 above, ONT's nanopore sequencing technology is based on passing a single strand of DNA or RNA, with a speed-regulating enzyme attached, through a protein nanopore. As the DNA or RNA passes through the pore, an electrical signal across the pore is modulated.[218] The signal is amplified, measured, and subsequently interpreted to determine the bases that passed through.[219] Nanopore sequencing enables real-time sequencing of DNA or RNA. ONT's systems do not have a fixed run time, meaning that users can run the systems for as long as it takes to collect sufficient data before the flow cell lifetime expires (flow cell lifetimes are typically at least 48 hours).[220] Read length is determined by the length of the input DNA fragments, but high quality sample preparation is critical to achieve long reads.[221] ONT claims to have achieved read lengths of more than 2 Mb,[222] and achievable average read lengths are greater than 10 Kb.[223]

198. ONT currently commercialises three native long read systems: the MinION,[224] GridION and PromethION. All three are available in "starter packs" that include the sequencer and consumables. Customers can also choose to purchase the GridION and two new versions of the PromethION (24 and 48) under a model that includes an extended software license and warranty (as compared to the starter packs) alongside the sequencers and consumables.[225] [redacted]

199. The MinION was the first system widely commercialised by ONT in 2015.[226] It is a pocket-sized sequencer that can be connected to a computer through a USB port. ONT states that it is being used in traditional laboratories and has also been used in novel environments, including the jungle, the Arctic and low Earth orbit.[227] Since the

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[217] https://nanoporetech.com/about-us/history; https://nanoporetech.com/about-us
[218] https://academic.oup.com/hmg/article/27/R2/R234/4996216, p. 3.
[219] https://academic.oup.com/hmg/article/27/R2/R234/4996216, p. 3.
[220] https://nanoporetech.com/how-it-works/nanopore-sequencing-workflow; Commercial flow cells have a maximum useful lifetime of around 64-72 hours. See https://nanoporetech.com/products/comparison
[221] [redacted]
[222] https://nanoporetech.com/products/comparison
[223] https://www.nature.com/articles/s41598-017-03996-z
[224] https://store.nanoporetech.com/starter-packs
[225] *Ibid.*
[226] The MinION was introduced into early access in 2014 and made commercially available in 2015. See https://nanoporetech.com/about-us
[227] ONT 2017 Annual report, p. 4, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0

MinION's release, ONT reports that its performance has increased approximately 40-fold.[228]

200. ONT describes the GridION as a medium-throughput benchtop sequencer based on the same technology as the MinION. Unlike the MinION, it includes on-board computing capabilities. It is designed to run up to five MinION flow cells in parallel, offering higher throughput and enabling customers to run up to five experiments concurrently.[229]

201. The PromethION is marketed by ONT as a high-throughput benchtop sequencer that can run up to 48 flow cells, depending on the sequencer configuration, each containing up to 3,000 nanopores.[230] The PromethION has built-in computing capabilities.

202. ONT also commercialises the VolTRAX, a small, programmable device designed for automated library preparation, enabling a user to prepare a sample for sequencing, hands-free.[231]

Table 7: ONT sequencers[232]

[redacted]

[228] ONT 2017 Annual report, p. 4, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0
[229] https://nanoporetech.com/products/gridion
[230] https://nanoporetech.com/products/promethion
[231] https://nanoporetech.com/products/voltrax
[232] https://nanoporetech.com/products/comparison
[233] [redacted]

[redacted]

203. [redacted] ONT reports that, as of May 2018, there were approximately 6,000 to 7,000 MinION sequencers shipped to users globally.[248] Also in May 2018, ONT reported that there were over 100 GridION customers in 24 countries, and that at least 40 PromethION sequencers had shipped, with another 20 expected to ship by the end of June 2018, with further orders received.[249]

[redacted]

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

204. ONT's 2017 annual report states that its revenues increased by 204% since 2016, with its UK revenues increasing by 95%.[250] ONT's average headcount in 2017 was 40% higher than in 2015.[251]

205. Further, ONT has attracted funding of GBP 451 million in various fundraising rounds.[252] Most recently, in March 2018, ONT received GBP 100 million from investors from China, Singapore and Australia, alongside existing investors.[253] The funds were raised to support ONT's next phase of commercial expansion, development of new products[254] and a new 34,000 square foot high-volume manufacturing facility in Oxfordshire necessary to meet demand.[255]

206. Finally, as explained in Section 22 below, ONT is currently developing new systems, including the SmidgION, a highly portable sequencer designed for use with smartphones.[256]

C. Parameters of competition for short read and native long read systems

207. On the potential markets for short read and native long read systems, suppliers compete through innovation, system performance, workflow simplicity, product differentiation, accuracy, product size/portability, scalability and price.

208. Innovation is a key parameter of competition, especially considering the rapid rate of innovation over the past ten years that has resulted in dramatically lower sequencing costs coupled with significantly higher throughput and scalability. Suppliers compete through innovation at various levels: to develop new fundamental technologies, to develop new systems that use existing technology, and to improve the performance, utility and value of existing systems.

209. Depending on their specific needs and applications, customers may favour systems with one or more of the following: higher throughput, higher accuracy, shorter run and turnaround times, simplified workflows, smaller sequencer footprints, or lower costs per datapoint or report. A supplier can outcompete its competitors by supplying a system that is superior on some or all of these metrics due to technological innovation. Improving sequencing systems across some or all of these metrics is also important for expanding the use of sequencing, because it can enable new applications and increase adoption of existing applications, which will increase the number of samples being sequenced.

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[250] ONT 2017 Annual Report, p. 6, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0
[251] *Ibid.*
[252] https://nanoporetech.com/about-us
[253] *Ibid.*
[254] ONT 2017 Annual Report, p. 6, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0
[255] https://nanoporetech.com/about-us/news/oxford-nanopore-announces-ps100-million-140m-fundraising-global-investors
[256] https://nanoporetech.com/products#smidgion

210. For example, in the potential market for short read systems, Illumina has been successful with its recent systems because they offer higher accuracy, higher throughput and lower cost per datapoint (for its high throughput systems) than competing systems.

211. [redacted]

212. [redacted].

213. There is also material competition on the basis of differentiated pricing strategies. [redacted]

D. Sequencing services in the UK

i. Providers of sequencing services in the UK

214. To the best of Illumina's knowledge, [redacted] Illumina are the only suppliers of sequencers that provide sequencing services in the UK.

215. There are also a number of academic and commercial third parties that offer sequencing services in the UK, including:

- **The Wellcome Trust Centre for Human Genetics ("Centre")** is a human genetics research centre of the Nuffield Department of Medicine at the University of Oxford, funded by the University, the Wellcome Trust and other

257 [redacted]

258 [redacted].

sponsors.[259] It boasts more than 400 active researchers and around 70 employees in administrative and support roles.[260] The Centre is an international leader in genetics, genomics and structural biology, and collaborates with research teams across the world on a number of large-scale studies in these areas.[261] Researchers at the Centre spend close to GBP 20 million annually in competitively-won grants, and publish around 300 primary papers per year.[262]

In addition to the research programmes, the Centre also provides services through its "scientific cores". One such core is the **Oxford Genomics Centre ("OGC")**, which provides a comprehensive offering of genomic applications, using many of the latest commercial technology systems. OGC currently uses a number of Illumina systems, but is also trialling ONT systems in routine applications for internal projects. OGC operates on a cost-recovery basis for academic projects, and offers competitive rates for commercial organisations;[263]

- **Deep Seq** is the University of Nottingham's NGS facility.[264] It offers research scientists access to high throughput sequencing technology. As well as running standard sequencing projects, Deep Seq also provides analyses services.[265] Deep Seq currently uses the Illumina's MiSeq and NextSeq 500 systems for low and medium throughput, but also runs ONT's GridION, PromethION and MinION systems, having helped to develop software tools for MinION data analysis.[266] It is also the UK sole supplier of the Bionano Saphyr, an optical mapping platform.[267] For larger projects, Deep Seq can outsource to high throughput sequencing service suppliers while supporting those projects with experiment design, library preparation and bioinformatics;[268]

- **Eurofins Scientific ("Eurofins")** is a public life sciences company which provides a range of analytical testing services to clients across multiple industries.[269] Eurofins is one of the global independent market leaders in certain testing and laboratory services for genomics.[270] It has more than 45,000 employees in more than 650 laboratories in 45 countries in Europe, North

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[259] https://www.well.ox.ac.uk/about-us
[260] *Ibid.*
[261] *Ibid.*
[262] *Ibid.*
[263] https://www.well.ox.ac.uk/ogc/about-ogc/
[264] https://www.nottingham.ac.uk/life-sciences/facilities/deep-seq/index.aspx
[265] https://www.nottingham.ac.uk/deepseq/index.aspx
[266] *Ibid.*
[267] *Ibid.*
[268] *Ibid.*
[269] https://www.eurofins.com/investor-relations/our-business/our-company/
[270] *Ibid.*

America, South America and the Asia-Pacific.[271] The company offers a wide range of NGS services in the UK, using both Illumina and PacBio systems;[272]

- **GENEWIZ ("Genewiz")** is a global provider of genomics services. The company has a global network of laboratories in the US, China, Japan and the UK.[273] The UK office was opened in 2011, driven by the company's European expansion and to address the growing needs of the global scientific community.[274] Genewiz provides the whole spectrum of sequencing applications to its customers, using both Illumina and PacBio systems;[275]

- The **Wellcome Sanger Institute ("WSI")** is a British non-profit genomics and genetics institute specialising in research and innovation, that is funded by the Wellcome Trust. WSI is a UK pioneer in the field of sequencing and was the only British organisation involved in the Human Genome Project, carrying out nearly one third of the work.[276] It can leverage its sequencing capabilities in the context of wider collaborations with academic, industrial and strategic partners, utilising its "DNA Pipelines Operations" facility, which provides the WSI with its sequencing needs.[277] This facility is claimed to be one of the largest sequencing facilities in the world and overseas the delivery of high-quality data via a range of technologies and systems.[278] WSI uses a number of Illumina, PacBio and ONT systems.[279] WSI has approximately 1,000 employees, ranging from scientists to developers and engineers;[280]

- **Novogene** is a privately-owned provider of genomic services and solutions. It has a global footprint with presences in the UK, China, US, Hong Kong and Singapore. Novogene claims to have the largest sequencing capacity in the world, with over 1,800 employees. It also owns 49 NGS-related patents and is the publisher of over 1,850 research papers. It provides a broad range of NGS services across human, plant and animal samples, using both Illumina and PacBio systems.[281] Novogene has performed approximately 10,000 projects in

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[271] https://www.eurofins.com/about-us/eurofins-fact-sheet/
[272] https://www.eurofins.co.uk/our-services/ and https://www.eurofinsgenomics.eu/media/956174/bu4_brochure_ngs_overview.pdf
[273] https://www.genewiz.com/en/Public/Company/About-Us
[274] https://www.genewiz.com/en-GB/Public/Company/News-and-Events/Press-Releases/GENEWIZ-Announces-European-Expansion-Appointment-European-Business-Development-Manager-Andre-Kotze
[275] https://www.genewiz.com/en/Public/Services/Next-Generation-Sequencing
[276] https://wellcome.ac.uk/press-release/finished-human-genome
[277] https://www.sanger.ac.uk/science/dna-pipelines-operations
[278] *Ibid.*
[279] https://nanoporetech.com/sites/default/files/s3/literature/GridION-Brochure-030119.pdf
[280] https://www.sanger.ac.uk/people
[281] https://en.novogene.com/next-generation-sequencing-services/; https://en.novogene.com/technology/technology/; Specifically, Novogene's portfolio of systems includes Illumina's NovaSeq 6000, HiSeq X, HiSeq 4000, and HiSeq 2500 and PacBio's Sequel System. As a result, Novogene provides both short read and native long read sequencing services. See https://en.novogene.com/technology/illumina-systems/ and https://en.novogene.com/technology/pacbio-sequel-system-applications/

a period of four years.[282] Novogene has worked with some of the largest and most prestigious institutions in the world, completing nearly 20,000 projects and sequencing 370,000 samples for more than 10,000 global customers;[283] and

- **Macrogen** serves over 18,000 customers across 153 countries,[284] including in the UK. The company provides a wide variety of genetic technology services to customers. It offers highly specialised sequencing services that have been used by researchers from many prestigious institutions such as the National Institute of Health, the Food and Drug Administration and Stanford University.[285] Macrogen provides short read, associated short read, and native long read sequencing services. Specifically, Macrogen's systems including the following:
    - Illumina's NovaSeq 6000, HiSeq X, HiSeq 4000, HiSeq 2500, NextSeq 500, and MiSeq;
    - Thermo Fisher's Ion PGM and Ion Proton;
    - 10x's Chromium controller; and
    - PacBio's RS II and Sequel Systems.[286]

ii. Relative advantages and shortcomings of sequencing services

216. Customers without consistent high volume demand for sequencing often find it more economical to acquire sequencing services, rather than acquiring a sequencing system. Such customers include customers that: (i) are not operating at scale, but have a specific project that requires scale, (ii) require sequencing sporadically, (iii) have sample types or applications that require specialised equipment or expertise that they lack, (iv) have projects that need to be completed within a timeframe that they cannot meet using internal resources, (v) require informatics or analysis expertise they lack, (vi) require access to a regulated environment, or (vii) require capabilities that they cannot access internally.

217. For such customers, sequencing services offer a number of advantages. First, they do not need to invest in a sequencer and other related equipment or in some cases analytical solutions. Second, they do not need to invest in developing the necessary expertise to prepare sequencing samples and operate a sequencer (whether through hiring specialist staff or training existing staff). In some instances, they might not need to develop expertise in any aspect of the sequencing process (including data analysis or interpretation). Data analysis and expertise is significant for applications for which third-party informatics and analytical tools do not exist. Third, they do not need to invest in complying with regulation relating to their facilities or processes. For example,

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[282] *Ibid.*
[283] https://en.novogene.com/about/about-novogene/
[284] http://www.macrogen.com/en/company/summary.php
[285] http://macrogenlab.com/about-us/what-is-next-generation-sequencing-ngs/
[286] http://www.macrogen.com/en/business/ngs_index.php

certain sequencing must occur in cleared environments or using cleared devices. Finally, it provides additional sequencing capacity when the customer experiences unusual demand (particularly when the increase in demand is expected to only be temporary).

218. That said, there are a number of disadvantages of acquiring sequencing services rather than a sequencer. First, outsourcing samples to a service provider is ordinarily more expensive on a per sample basis than acquiring and running a sequencer. When outsourcing samples to a service provider, the price paid includes a premium on top of the provider's cost, which includes the cost of reagents, depreciated cost of the sequencer, and labor, as is usually the case when outsourcing to a service provider. The location of the service provider typically has limited impact on the cost of outsourcing or time to receive results. Shipping samples outside of the UK would only have a material impact on time to results if there were an issue importing samples into the country in which the service provider's facilities are located. However, this is readily done today. The location of the service provider, including locations outside of the UK, typically has minimal impact on the cost of outsourcing sequencing. However, processing samples in a country with cheap labor (*e.g.*, China) could reduce costs.

219. Second, it typically takes longer to receive the sequencing results. It can take between two and ten times longer for results to be provided, depending on the size of the project, and the range of applications and samples involved. Third, loss of control over the chain of custody of samples and related data can potentially compromise security and privacy. Finally, if the entity acquiring the sequencing services is working on a novel sample or method, it risks compromising intellectual property and know how, by exposing details to the service provider.

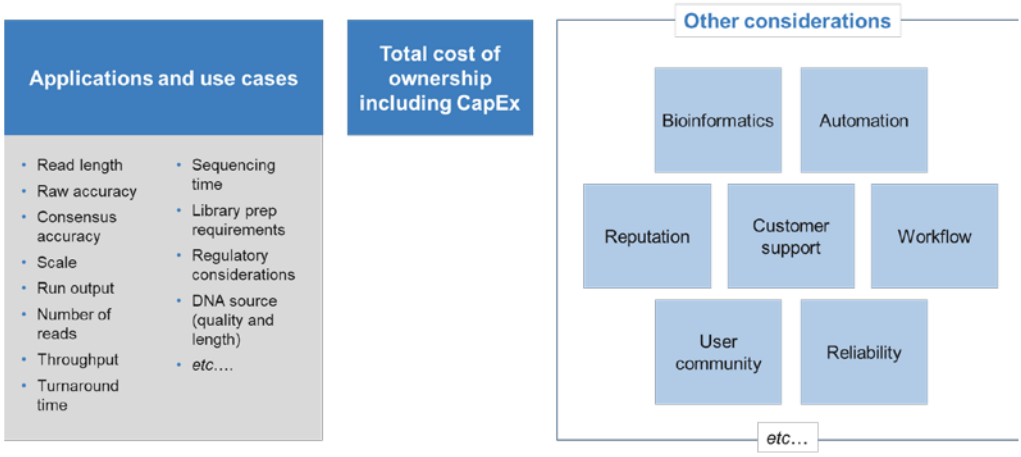
III. Customers

A. Parameters of customer choice

i. Customers take into consideration more than one factor

220. Customers of sequencing systems are typically sophisticated and carefully select the technology that will best address their needs. They do not select a sequencer on the basis of a single factor; rather, they weigh up a set of factors. They will start by considering the applications and use cases that they want to perform. As explained in Sections 12 and 13 above, different sets of applications and use cases may require different attributes, including read length, raw read accuracy, consensus accuracy, scale, output, number of reads (depth), library preparation requirements, run time, and turnaround time. Customers consider the set of applications and use cases that they wish to perform and identify the systems that have the appropriate attributes to best perform across that set of applications and use cases. Then, customers look at the total cost of ownership of those systems (including their upfront cost). Finally, customers often take into account certain secondary considerations, such as bioinformatics, automation, reputation, workflow, customer support, *etc*.

Figure 13: How customers decide to purchase



ii. Customers purchase sequencing systems to perform multiple applications and use cases

221. Customers purchase sequencing systems to perform multiple applications and use cases. It is common for customers to perform multiple applications and use cases on a single system. Sequencing systems suppliers therefore offer systems that support a wide range of applications and use cases.

Figure 14: Applications performed on Illumina systems

	NextSeq Series	HiSeq 4000 System	HiSeq X Series‡	NovaSeq 6000 System
Popular Applications & Methods	Key Application	Key Application	Key Application	Key Application
Large Whole-Genome Sequencing (human, plant, animal)	●	●	●	●
Small Whole-Genome Sequencing (microbe, virus)	●	●		●
Exome Sequencing	●	●		●
Targeted Gene Sequencing (amplicon, gene panel)	●	●		●
Whole-Transcriptome Sequencing	●	●		●
Gene Expression Profiling with mRNA-Seq	●	●		●
miRNA & Small RNA Analysis	●	●		●
DNA-Protein Interaction Analysis	●	●		●
Methylation Sequencing	●	●		●
Shotgun Metagenomics	●	●		●

222. The fact that customers perform multiple applications is also clear from their purchasing pattern of consumables. Approximately [redacted] of Illumina's library preparation kit customers purchase more than one type of kit from Illumina, making it clear that those customers perform multiple applications, as different applications use

different types of library preparation kits. [287] [redacted] [288]

[redacted]

223. Illumina's customers also use more than one type of reagent kit on a single type of sequencer. For example: approximately [redacted] buy more than one type of reagent kit.[290] As different applications use different reagent kits, the purchase of more than a single type of reagent kit for a sequencer indicates that customers are performing multiple applications on a single sequencer.

iii. Customers purchase more than one system

224. Many Illumina systems owners purchase multiple Illumina systems. More than [redacted] of Illumina systems owners have purchased at least two types of sequencers; approximately [redacted] own more than one sequencer of the same type; [redacted] [291] [redacted]:

[287] In addition, certain of these library preparation kits enable customers to perform different applications.
[288] [redacted].
[289] [redacted]
[290] [redacted].
[291] [redacted].

B. Customer groups

225. [redacted] As a result, the Notifying Parties do not consider that the potential markets for either short read or native long read systems should be segmented on the basis of customer groups. However, they describe below the broad types of customers who procure short read and/or native long read systems for indicative purposes.

226. Customers acquiring either or both short read and native long read systems fall into a number of different categories:

- **Basic research customers** use sequencing to further scientific discovery regarding human and non-human genomes. In the UK, these customers include universities and government and not-for-profit genomics research institutes such as the Wellcome Sanger Institute and the Earlham Institute.

  These customers also include entities set up by the government to run major public projects, such as Genomics England. Genomics England was set up by the UK Department of Health & Social Care to run the "100,000 Genomes Project", *i.e.*, to sequence 100,000 genomes from National Health Service ("NHS") patients with a rare disease, plus their families, and patients with various types of cancer.[292] The project is intended to improve knowledge of these diseases.[293] On 5 December 2018, it was announced that the 100,000 Genomes Project is now complete, and that 100,000 genomes have been

[292] https://www.genomicsengland.co.uk/about-genomics-england/how-we-work/
[293] https://www.genomicsengland.co.uk/the-journey-to-100000-genomes/

sequenced.[294] The results will be returned to the NHS throughout 2019, and ultimately to participants.[295]

[redacted][297]

- **Translational customers** build on basic research to create new therapies, medical procedures, or diagnostics to improve human health. In the UK, molecular diagnostics providers such as the [redacted] use sequencing to develop diagnostic tools such as oncology panels.

- **Clinical customers** use sequencing to evaluate risks, diagnose illness, and design treatments for patients. In the UK, they include Public Health England, NHS trusts, and private clinics and clinical laboratory service providers such as Novogene who perform reproductive health tests (NIPT), oncology tests (liquid biopsies, FFPE), genetic disease testing (RUGD) and/or transplant compatibility tests (tissue typing).

- **Consumer genomics customers** use sequencing to provide personalised genetic data directly to consumers (*e.g.*, without a doctor or other intermediary) that analyse ancestry, disease predisposition, and planning around health, wellness, nutrition and fitness to consumers in a non-clinical setting. They include companies such as [redacted]. Companies currently using arrays for consumer genomics testing, including [redacted], are also expected to offer sequencing-based testing in the future.

- **Agrigenomics customers** use sequencing to explore the genetic and biological basis for productivity and nutritional constitution of crops and livestock. Farmers and breeders can tailor their cultivation and breeding decisions to produce disease-resistant, healthier and higher-yielding crops and livestock. In the UK, these customers include agribusiness companies and genomics labs such as [redacted].

- **Pharmaceutical companies** use sequencing to develop new therapeutics and develop assays to act as companion testing (companion diagnostics) for certain therapeutics. For instance, many therapeutics only work, or work optimally, on

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[294] https://futurism.com/100000-genomes-project-success
[295] https://www.genomicsengland.co.uk/about-genomics-england/the-100000-genomes-project/
[296] [redacted]
[297] [redacted]

patients having a certain genetic makeup. Pharma companies use or develop sequencing-based assays as "companions" for certain therapeutics to determine or enhance before treatment the therapeutic efficacy or applicability for a particular patient. Pharmaceutical companies, such as [redacted], use pharmacogenomics to analyse how patients' DNA influences their response to new drugs. They also conduct scientific research that is used to improve drug development at a later stage.

For example, Regeneron Pharmaceuticals, AbbVie, Alnylam Pharmaceuticals, AstraZeneca, Biogen and Pfizer Inc. have formed a consortium to advance the UK Biobank project, which aims to sequence the whole exome of 500,000 volunteers.[298] Regeneron's genetic centre performs the sequencing. The data obtained is then paired with medical and health records in the UK Biobank, including enhanced measures such as brain, heart and body imaging, to create a valuable resource for linking human genetic variations to disease.[299] This sequencing data will be available to members of the consortium for a limited period before being made available to other researchers.[300]

Pharmaceutical companies also outsource this work to contract research organisations or genomics centres, such as [redacted].

C. Customers engage in combinations of basic research, translational research and clinical testing

227. The rapid pace of research and innovation using sequencing to develop novel discovery and testing methods has led to the emergence of new approaches to testing of, and treating, patients. In the context of different applications and use cases, these new approaches range from what traditionally might be considered to be basic research through to clinical testing in a regulated environment. For example, while Illumina recently obtained CE-IVD marking for an NIPT test, the laboratories in Europe have been carrying out NIPT tests for much of the last decade on an LDT basis. In a similar vein, liquid biopsy testing in Europe is currently carried out on an LDT basis. In contrast, TMB testing occurs by laboratories using approaches to testing more commonly associated with translational research, and RUGD testing occurs in the basic/translational research environment. Figure 15 below illustrates this development continuum from basic research through to clinical use (including tests with regulatory approvals):

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298 https://newsroom.regeneron.com/news-releases/news-release-details/regeneron-forms-consortium-leading-life-sciences-companies

299 https://newsroom.regeneron.com/news-releases/news-release-details/regeneron-forms-consortium-leading-life-sciences-companies

300 https://newsroom.regeneron.com/news-releases/news-release-details/regeneron-forms-consortium-leading-life-sciences-companies

Figure 15: Example phases of activities

228. The development of new tests requires customers to sequence samples in a range of contexts from basic research through to clinical testing. Table 8 illustrates how the activities of a number of customers span across basic research, translational research and clinical use:

Table 8: Examples of customers performing a broad range of applications across spaces

[redacted]

229. [redacted]

(e) **an explanation of how pricing is determined (for example, whether set by suppliers, negotiated between suppliers and customers, or the result of a bidding process organised by customers), including, in appropriate cases (as explained below), supporting documentation; and**

IV. Pricing and Supply chain

[redacted]

230. As explained in Section 13, the Notifying Parties submit that short and native long read systems fall into distinct product markets, such that the activities of Illumina and PacBio do not overlap. However, for the sake of completeness, the Notifying Parties describe below pricing in the potential markets for short read and native long read systems.

A. Determination of prices in the potential market for short read systems

231. As explained above, when customers consider the price of short read systems, they take into account the total cost of sequencing the relevant number of samples in the range of their relevant applications. In short, customers take into account the "total cost of ownership" (or whole life cost) of the sequencing systems they are considering. This includes the cost of the sequencer along with consumables used in the library preparation and the sequencing process, and related support services, labor, overhead, facilities, and other auxiliary costs such as data storage, analysis, and security.[304]

232. Short read system suppliers offer different pricing models. However, the prices for sequencers and consumables are interrelated, such that all suppliers price the combination of sequencers and consumables to be considered together. For example,

[redacted]

233. In the potential market for short read systems (comprising both the sequencers and their consumables and services), suppliers take into account a combination of different factors when setting the prices for their systems as a whole. We list below the main factors that short read systems suppliers usually take into account. The weight that each supplier places on these (and potentially other) factors will depend on that supplier's commercial strategy and may change as strategies evolve over time:

- enabling the broader adoption of sequencing in existing applications and the development of new applications;
- the value that the new system will provide to the customer;
- enabling customers to attract third party or institutional funding to conduct their projects;

[304] Please see Section 13.

- expanding their customer base;
- competitors' system prices;
- costs of producing the elements of the system; and
- positioning new systems within their portfolio.

234. In addition, many suppliers offer discounts, such that actual prices reflect discounts offered, rather than list prices.

235. [redacted].

i. Illumina

236. When setting the prices of its systems, Illumina takes into account the factors listed above, weighting certain factors more heavily than others. [redacted].

237. As explained in Section 18 below, Illumina's R&D efforts have enabled it to be the driving force in reducing the cost of sequencing. Illumina was the first company to enable a human genome to be sequenced at a cost of USD 1,000 with the launch of its HiSeqX system in early 2014. Prior to this milestone announcement, the cost per genome was approximately USD 5,000. The HiSeq X was a new product introduction created and marketed for the sole purpose of reducing whole genome sequencing costs to enable the USD 1,000 genome, and to stimulate WGS amongst others.

238. Further innovation, including the NovaSeq announced in 2017, has enabled Illumina to reduce the cost of sequencing a genome by significant amounts. Today the current cost of sequencing a genome using a NovaSeq system is approximately [redacted][305] Further, when it launched the NovaSeq system in 2017, Illumina announced its intention to drive the cost of sequencing a genome down to USD 100 through further development work based on the architecture of the NovaSeq system.

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305 [redacted]

239. Illumina also recently announced in February 2019 that it would reduce the price of two types of flow cells for the NovaSeq, the S1 and S2, by 25% and 10%, respectively, following discussions with customers in order to offer greater flexibility in their workflow.[306] [redacted].

240. Illumina offers systems that meet the needs of existing and new customers (whether for existing or new applications) to broaden its customer base. For example, the iSeq is intended to enable smaller labs and academic institutions, who may not have the capital budget or volume of samples, to use short read systems. [redacted].

241. [redacted].

242. [redacted]

306 https://www.genomeweb.com/sequencing/illumina-expands-clinical-business-internationally-discounts-novaseq-flow-cells?utm_source=Sailthru&utm_medium=email&utm_campaign=GWDN%20Wed%20PM%202019-01-30&utm_term=GW%20Daily%20News%20Bulletin#.XFc8iOSQyzk

ii. Other suppliers of short read systems

243. As discussed above, different suppliers adopt different pricing models and give different weight to the factors listed above], depending on their commercial strategy. [redacted].

244. [redacted]

245. [redacted].

B. Determination of prices in the potential market for native long read systems

246. As explained in Section 13, customers in the potential market for native long read systems also take into account the "total cost of ownership" (or whole life cost) when selecting systems for purchase. As a result, the description above also applies to native long read systems. The total cost calculations made by customers in the potential market for native long read systems mean that different companies have adopted different pricing strategies. For example, [redacted].

247. In addition, actual prices also reflect discounts offered by each supplier to its customers.

248. Finally, actual prices are negotiated between suppliers and customers, unless the customer is required to comply with the public procurement procedures outlined in Section 16.

249. [redacted]

i. PacBio

250. [redacted]

[redacted]

251. [redacted]

252. [redacted].

253. [redacted]

254. [redacted]

ii. [redacted]

255. [redacted]

256. [redacted].

(f) **an explanation of the supply chain (including distribution channels) for the product(s)/services(s), and of any differences between separate geographic areas, where the merger parties overlap, in relation to the supply of the same products/services.**

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[307] https://globenewswire.com/news-release/2018/09/13/1570423/0/en/Large-Scale-Global-Genome-Projects-Choose-PacBio-Sequencing-to-Help-Decode-Life.html and https://www.pacb.com/press_releases/pacific-biosciences-the-wellcome-trust-sanger-institute-and-public-health-england-collaborate-to-finish-genomes-of-3000-bacterial-strains/.

[308] https://store.nanoporetech.com/starter-packs

257. As explained in Section 13, the Notifying Parties submit that short and native long read systems fall into distinct product markets, such that the activities of Illumina and PacBio do not overlap. However, for the sake of completeness, the Notifying Parties describe below the supply chains in the potential markets for short read and native long read systems.

258. The supply chain in each of the potential markets for short read and native long read systems has three main levels.

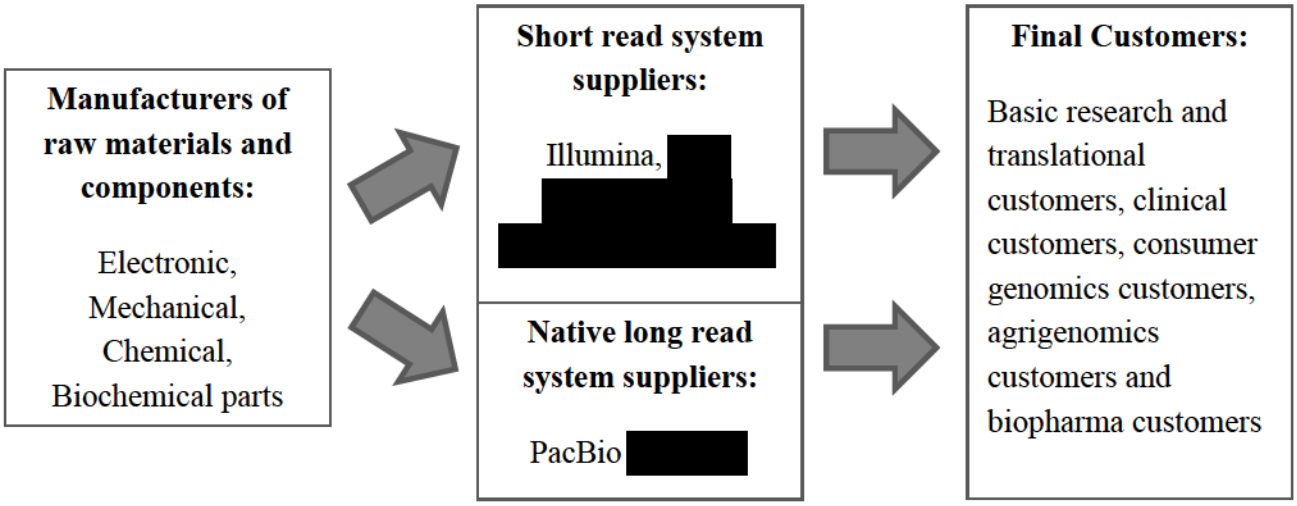
259. The value creation process in both potential markets starts with suppliers of raw materials and components that are used as inputs in the manufacture of the elements of the sequencing systems. There are many specialised suppliers, supplying electronic, mechanical, chemical and biochemical inputs (such as valves, cameras, flow cells, computers, *etc.*). Suppliers include [redacted]

260. In the next step, manufacturers use these inputs to produce their sequencers and consumables. As explained earlier, the current commercialising manufacturers of short read systems are Illumina, [redacted], and of native long read systems are PacBio and [redacted]. The extent to which system suppliers outsource the manufacturing of their sequencers and consumables varies per supplier and may evolve over time. In addition to manufacturing components and potentially sub-assemblies or modules, contract manufacturers also test and validate the inputs that they supply to ensure that they meet the sequencing system supplier's specifications.

261. Finally, short read and native long read systems suppliers sell directly or through authorised distributors to their customers (*i.e.*, to research and/or translational, clinical, consumer genomics, agrigenomics and pharmaceutical customers).[309] To the best of the Notifying Parties' knowledge, all short read and native long read systems suppliers distribute directly to customers in the UK.

[309] Please see Section 15. III above.

Figure 16: Supply Chain



262. The Notifying Parties provide information regarding the production capacity of their manufacturing facilities, together with a brief description of their manufacturing activities, in [redacted].

16. For Candidate Markets characterised by bidding processes and/or where customers typically issue requests for quotations, provide bidding data setting out any bids made by each of the merger parties to win business in the overlapping markets.

263. As discussed in Section 13 above, short read and native long read systems belong to distinct product markets. The Notifying Parties' activities, therefore, do not overlap. However, for the sake of completeness, the Notifying Parties describe below the tender processes that are used in the procurement of their systems in the UK.

I. Types of tender procedures used to procure sequencing systems in the UK

264. As explained in Section 15 above, purchasers of sequencing systems in the UK include public authorities, such as universities, government research institutes, Public Health England, Genomics England, and the NHS and NHS trust funds. The purchasing decisions of these organisations are ordinarily subject to the Public Contracts Regulations 2015 ("PCR"), which implements Directive 2014/24/EU on public procurement (the "Directive").

265. For Illumina, in 2018, [redacted] of those customers were obtained through a tender covered by the Directive.[310] For PacBio, as discussed below, [redacted]

[310] As explained below, [redacted]

[redacted]

266. When a procurement falls within the scope of the PCR, the contracting authority must ensure that the process is run in accordance with the principles, and follows one of the procedures, set out in the PCR. This means that the authority must set out clearly its requirements and the criteria against which awards are made. The PCR also imposes a number of transparency and publication obligations. As a general principle, an authority must award a contract to the "most economically advantageous tender" ("MEAT") (also referred to as "best value for money").[311]

267. There are three relevant types of competitive tender procedures used to procure sequencing systems in the UK:

- **open procedures:**[312] any potential supplier can participate. The authority assesses all bids received in the specified timeframe and scores them against the predetermined award criteria. The contract is awarded to the supplier which submitted the MEAT;

- **framework agreements:**[313] a special type of contract that provides the contracting authorities with some flexibility that is usually tendered through open procurement. Framework agreements typically do not specify or guarantee specific order volumes. Rather, they operate as an "umbrella", under which contracting authorities place orders using "call-off contracts". These call-off contracts are not subject to separate tender processes.

  Authorities can use framework agreements in different ways. One authority can enter into a framework agreement, and then issue call-off contracts to meet its own needs. Alternatively, an authority can enter into a framework agreement that enables other authorities to enter into call-off contracts. For example, Public Health England may enter into a framework agreement that enables other NHS organisations (*e.g.*, hospital trusts) to enter into call-off contracts.

  Authorities can enter into framework agreements with one or more suppliers. A framework agreement will set out the process for awarding call-off contracts, *i.e.*, a contracting authority can (a) directly award a call-off contract to a specific supplier and/or (b) where there are several suppliers under the framework, run another competition among suppliers (also known as "mini-competitions");

[311] Regulation 67(1) of the PCR.
[312] Regulation 27 of the PCR.
[313] Regulation 33 of the PCR.

- **below threshold procurement:**[314] the PCR sets out general principles for procurement processes that fall below the specified thresholds.[315] In essence, contracting authorities must publish opportunities and award notices on Contracts Finder.[316] General principles of transparency and non-discrimination also apply.

268. The PCR permit public authorities to enter into contracts directly with a certain supplier without running a full tender process in certain circumstances (*i.e.*, Regulation 32). This applies, for example, where only one supplier can supply the relevant product. Further, an authority may also award supply contracts directly to a certain supplier "where the products involved are manufactured purely for the purpose of research, experimentation, study or development". Where an authority relies on this procedure, it must clearly document its reasons for doing so, and publish a VEAT notice in the Official Journal of the European Union in accordance with Directive 2004/18/EC on the coordination of procedures for the award of public works contracts. The VEAT notice must also state the justification for using this procedure. The contracting authority must then wait ten days from publication of the notice before concluding the contract, which enables challenges by other suppliers which feel they could have met the contracting entity's requirements.

269. Concretely, if another sequencer supplier feels that it is unfairly excluded from bidding for a contract and has the technical ability to meet the requirements, it is entitled to challenge the award. As a result, even VEAT notices are technically open to competition.

II. Illumina bidding data

270. [redacted].

271. [redacted]

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[314] Regulations 109-112 of the PCR.
[315] The thresholds differ depending on the type of contract and the authority involved. For supply contracts they are set at GBP 118,133 (for central government, including NHS Trusts) and GBP 181,302 (for sub-central government).
[316] https://www.gov.uk/contracts-finder
[317] [redacted]
[318] [redacted]

[redacted]

272. [redacted]

273. [redacted]

274. [redacted]

---

319 [redacted]

320 [redacted]

321 [redacted]

323 [redacted]

Table 9: Illumina bidding data since May 2018

[redacted]

324 [redacted]
325
326

[redacted]

327 [redacted]
328 [redacted]

[redacted]

329 [redacted]

275. [redacted]

276. [redacted][330].

277. [redacted][331]

III. PacBio bidding data

278. [redacted].

- [redacted]:
  - [redacted].[332],
  - [redacted]

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330 [redacted].

331 [redacted]

332 [redacted]

[redacted][333]

- [redacted]s:
  - [redacted]

279. [redacted][334]

280. [redacted]

Increase in the merger parties' buyer power

17. If applicable, for any product(s) (including raw materials) or service(s) which the merger parties both purchase, provide details of the merger parties' ability to obtain more favourable commercial conditions from suppliers as a result of this merger and the effects, if any, of such increased ability on competition at any levels of the supply chain.

281. The Notifying Parties submit that they will not acquire significant buyer power as a result of the Transaction. In particular, their combined share of procurement in any potential procurement market will be materially less than 25%. As explained below, Illumina does not currently have significant buyer power *vis à vis* any of its suppliers, and the *de minimis* increment that will result from PacBio's purchases from some of these suppliers will not change this situation.

---

333 [redacted]

334 [redacted]

335 [redacted]

336 [redacted]

I. The Notifying Parties do not have the ability to impose onerous terms on their suppliers

282. At present, Illumina [redacted]. Most of Illumina's suppliers are global companies that have a wide customer base that includes customers active not only in potential sequencing system markets. Illumina estimates that its purchases do not represent more than [redacted] of the revenue of the vast majority of its suppliers, such that it cannot be considered to be an indispensable customer for its suppliers.[337]

283. This situation will not change post-Transaction. As the table below shows, the Notifying Parties have only a limited number of suppliers in common for certain inputs.

Table 10: Notifying Parties' common suppliers

Input	Supplier
Lasers	[redacted]
Optics	[redacted]
Flow cells/SMRT Cells	[redacted]
Inputs for library preparation kits and consumables used in the sequencing process	[redacted]

284. Further, PacBio estimates that its purchases from these suppliers do not represent more than [redacted] of their revenue. [redacted]

285. Finally, Illumina has neither the ability nor the incentive to impose onerous commercial conditions on its suppliers. As explained in [redacted] Qualifying suppliers able to do this requires time and other investments by Illumina. As a result, it seeks to establish long-term commercial relationships with its suppliers. Such relationships cannot be maintained if the

[337] [redacted]

purchaser were to seek to impose conditions that a supplier would not accept. The Transaction will not in any way change Illumina's incentive to establish and maintain these relationships with its suppliers.

Loss of potential competition

18. Describe whether any merger party has plans or has attempted in the last three years to start supplying product(s)/service(s)/geographic area(s) which it does not currently supply but which the other merger party is already supplying (or expected to supply). If so:

(a) **Provide any internal documents setting out plans of any merger party to expand in the overlapping product(s), service(s) and/or geographic area(s) or to enter a market where another merger party is operating.**

(b) **Explain what barriers to entry or expansion exist for each merger party to start supplying product(s)/service(s)/geographic area(s) which it does not currently supply but which the other merger party is already supplying (or expected to supply).**

I. Illumina's strong and continued commitment to R&D

286. Illumina has historically made substantial investments in R&D. This is motivated by Illumina's goal of increasing the use of sequencing through creating competitive offerings that meet new customer needs, and increasing uptake of existing applications by continuing to drive down sequencing costs and otherwise. To this end, Illumina's significant investment in R&D is a strategy that Illumina remains committed to.

287. In 2017, Illumina invested USD 546 million in R&D, approximately 19.8% of its total revenues for that year.[338] That increased to USD [redacted] in 2018. As the table below illustrates, Illumina has invested approximately [redacted] of its annual revenue in R&D in each of at least the last six years. Further, over that period, Illumina has more than doubled its R&D spend in actual terms.

Table 11: Illumina's R&D expenses[339]

Fiscal year	Illumina R&D expenses (both sequencing and microarrays)[340]	% of total Illumina revenues
2018	[redacted]	[redacted]

[338] [redacted]

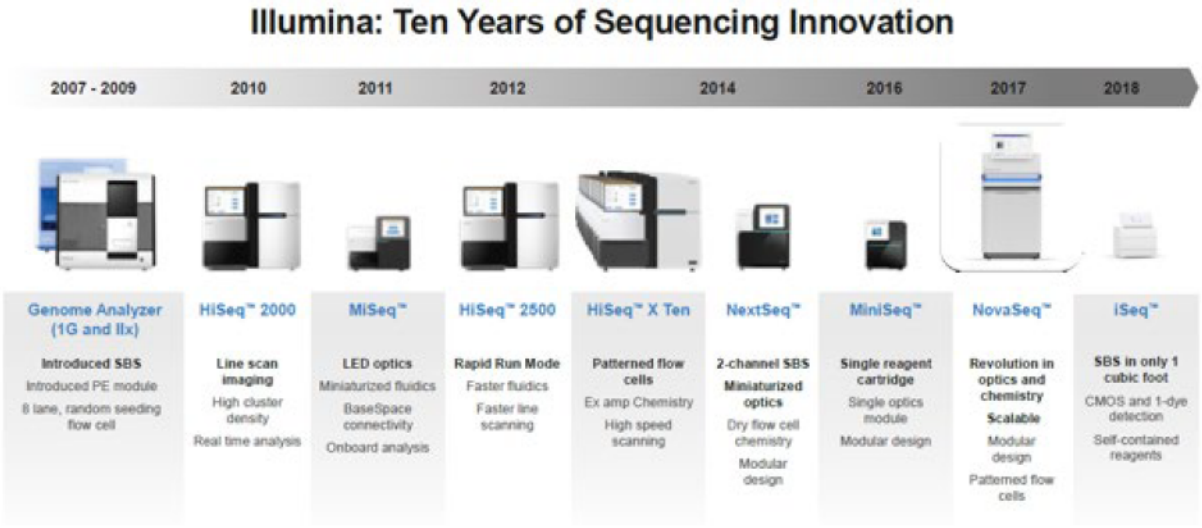
[339] The figures in this table were taken from Illumina's Annual Reports, available at https://www.illumina.com/company/investor-information/financial-information/sec-filings.html

[340] [redacted]

2017	USD 546 million	19.8%
2016	USD 504 million	21.0%
2015	USD 401 million	18.1%
2014	USD 388 million	20.8%
2013	USD 277 million	19.5%

288. Illumina's commitment to R&D is demonstrated by the fact that it invests more in R&D than any other sequencing system developer. If measured as a percentage of revenue, Illumina spends materially more than its industry peers. The primary driver of the additional R&D spend over industry peers is reflected by increased headcount as Illumina recruits scientists, engineers and others to work on R&D for both new products and enhancements to its existing systems.

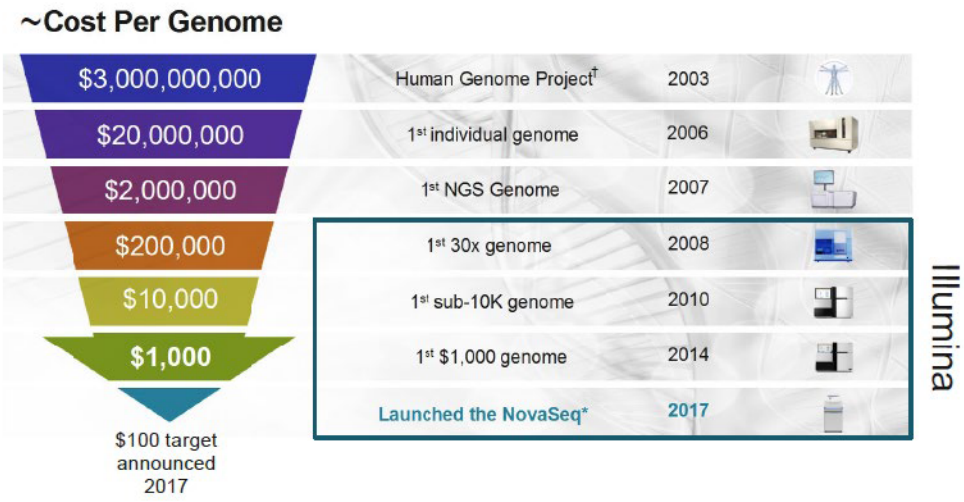
Figure 17: Illumina's innovation track record



289. Reflecting Illumina's goal of reducing the cost of sequencing, Illumina's R&D efforts have enabled it to repeatedly reduce the per genome and per Gb cost of short read sequencing. Illumina was the first company to enable a genome to be sequenced for USD 1,000, with the launch of its HiSeq X system in early 2014. Prior to this milestone, the cost per genome was approximately USD 5,000. The HiSeq X was a new product created and marketed for the sole purpose of reducing WGS costs to enable the USD 1,000 genome, and to stimulate WGS amongst users.

290. Further innovation, including the NovaSeq announced in 2017, has enabled Illumina to reduce the cost of sequencing a genome by significant amounts. Today, the current cost of sequencing a genome using a NovaSeq system is [redacted]. Further, when it launched the NovaSeq system in 2017, Illumina announced its intention to drive the cost of sequencing a genome down to USD 100 through further development work based on the architecture of the newly launched NovaSeq system. Illumina views lowering sequencing costs as essential to expanding the utility and uses of sequencing.

Figure 18: Evolution of cost per genome



291. The potential sequencing markets are nascent, implying that there is a great deal of growth opportunity remaining. For instance, as of today, less than 0.01% of species and less than 0.02% of human genomes have been sequenced, less than 1% of variants in the human genome have been fully characterised, and the understanding of complex structure features of the human genome is at its beginning. Therefore, to continue to increase demand, Illumina believes that it needs to continue to innovate because this will lead to both increased demand for existing applications and the creation of new applications.

292. The importance of innovation to meet increasing expectations of customers and continue to drive down costs is reflected in the rapid technological development in the sequencing sector and frequent introduction of new technologies (and products and services using those technologies).

293. Illumina believes that its continued growth and success in sequencing is heavily dependent on developing and commercialising new technologies, systems and services, and enhancing its existing technologies, systems and services, in order to address evolving market requirements and to catalyse yet unknown or emergent market needs, on a timely basis. If Illumina fails to innovate or adequately invest in new technologies, its products and services may not be attractive in the light of evolving customer needs and competitive offerings.

294. These strategies drive Illumina's significant and varied investments in R&D. It invests to develop new systems (*e.g.*, increasing ease of use, increasing throughput and decreasing turnaround time) and to enhance and improve its existing systems (*e.g.*, increasing throughput and increasing reliability). Illumina also invests to deliver faster, simpler, and lower-cost workflows. Finally, Illumina also makes significant investments in bioinformatics and analytics software, including its cloud computing

environment for analysing sequencing data, BaseSpace. In 2018, Illumina also acquired Edico Genome Inc. ("Edico"), a provider of data analysis acceleration solutions.[341]

295. Illumina has facilities around the world that engage in R&D, *i.e.*, in Cambridge (UK); San Diego, California (U.S.); San Francisco Bay Area, California (U.S.); Madison, Wisconsin (U.S.); and Singapore. In early 2017, Illumina opened a new 27,000 square-meter R&D facility in San Diego.[342] [redacted]

II. Illumina's R&D process

296. Illumina's R&D process is designed to maximise innovation through the efficient use of its R&D budget. This objective is achieved both organisationally and through a phased R&D process to select for the most commercially viable products.

297. [redacted]

298. [redacted]

[redacted]

[redacted]

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[341] https://www.illumina.com/company/news-center/press-releases/2018/2349147.html; [redacted]

[342] https://www.biospace.com/article/booming-illumina-expands-with-a-spanking-new-building-in-san-diego-hiring-more-than-100-/

[redacted]

- [redacted]

[redacted]

299. [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

[redacted]

III. Illumina's sequencing R&D programs

300. The Transaction will not reduce Illumina's incentives to pursue its existing R&D programs. [redacted]

[redacted]

301. [redacted]

A. [redacted]

302. [redacted]

i. [redacted]

303. [redacted]

ii. [redacted]

304. [redacted]

---

343 [redacted]
344 [redacted].

[redacted]

iii. [redacted]

305. [redacted]

306. [redacted]

307. [redacted]

308. [redacted]

345 [redacted].

309. [redacted]

B. [redacted]

310. [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

311. [redacted]

312. [redacted]

- [redacted]
- [redacted]
- [redacted]

313. [redacted]

346 [redacted]

[redacted]

- [redacted]

[redacted]

- [redacted]

- [redacted]

314. [redacted]

[redacted]

315. [redacted]

C. Illumina has no incentive to discontinue or delay its R&D programs

316. [redacted].

317. [redacted]

318. [redacted].

319. [redacted][347]

320. [redacted]

[347] [redacted].

Vertical effects

19. If the merger parties are active in "related" markets (e.g. products that are complementary or that belong to a range of products generally purchased by the same set of customers) and their individual share in any such related Candidate Market exceeds 30%, describe the impact of the merger on the ability and incentive of the merged entity to foreclose rivals (including partial and/or full foreclosure) post-transaction, either by limiting the supply of inputs or access to customers.

321. The Notifying Parties do not operate at different levels of the same supply chain, and neither of them currently supplies any input to the other. Following the Transaction, there is only one foreseen input produced using PacBio systems that could be used by Illumina: sequencing data, including structural information, haplotype phasing and potentially epigenetic information, which is in many cases, published to external, publicly accessible repositories by PacBio and/or its customers and collaborators.

I. Sequencing data as an input for bioinformatics

322. Bioinformatics are important tools used to analyse raw sequencing data. The typical bioinformatics workflow on sequencing systems follows the following main steps:[348]

- **Sequence generation**: the process of identifying the sequence of nucleotides for each of the fragments of the DNA sample sequenced;
- **Sequence alignment/assembly**: the process of determining where each read aligns with each other and/or a reference genome;
- **Variant calling**: the process of identifying variants between the reference genome and the sample sequenced;
- **Variant filtering**: the process by which false-positive variants are flagged or filtered;
- **Variant annotation**: queries multiple databases to characterise each called variant with a set of metadata, such as variant location, predicted cDNA and amino acid sequence, minor allele frequencies, *etc*.

323. Suppliers of sequencing systems use sequencing data to improve the algorithms used by their bioinformatics tools in order to improve the analysis. This data (including PacBio's data) can enable more accurate and complete identification of variants. However, it does not obviate the need, in many cases, to carry out further interpretive analyses to understand the significance or actionability of variants, including identifying the diseases, if any, that identified variants cause.

[348] https://www.ncbi.nlm.nih.gov/pubmed/29154853 p. 5

324. [redacted]:

- [redacted];
- [redacted];
- [redacted]

325. [redacted];

326. [redacted].

II. Absence of input foreclosure concerns

327. The Transaction does not raise any concern related to possible reduced access to PacBio's sequencing data.

A. The practice regarding data as an input

328. As the existing decisional practice of the Commission regarding data-related transactions makes clear, foreclosure concerns arise if the data concerned is unique or non-replicable, such that it cannot be obtained by competitors through other means.[350]

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[349] https://www.illumina.com/products/by-type/informatics-products/basespace-sequence-hub/apps.html

[350] Commission, Decision of 6 September 2018 in Case COMP/M.8788 *Apple/ Shazam*, paras. 316-319 and 324; Commission, Decision of 3 October 2014 in case COMP/M.7217 *Facebook/ WhatsApp*, para. 189; Commission, Decision of 6 December 2016 in Case COMP/M.8124 *Microsoft/ LinkedIn*, paras. 262-264 and 276; Commission, Decision of 11 March 2008 in Case COMP/M.4731 *Google/ DoubleClick*, para. 269.

For example, in *Facebook/WhatsApp*, the Commission examined whether the transaction would materially strengthen Facebook's position in the provision of online advertising services as a result of access to data collected from WhatsApp users.[351] The Commission noted that WhatsApp did not collect user data at the time and that, even if this changed post-transaction, there would remain a large amount of valuable user data collected by competitors that would not be under Facebook's control.[352] The Commission concluded that potential access to WhatsApp user data would not materially strengthen Facebook's position on the market for online advertising.

329. In *Microsoft/LinkedIn*, the Commission considered whether Microsoft could foreclose its competitors on the market for customer relationship management (CRM) software by refusing to grant them access to LinkedIn's full data.[353] The Commission observed that, at the time of the transaction, LinkedIn did not offer access to its data to third parties,[354] and noted that, to the extent that Microsoft could use LinkedIn's full data to improve its CRM software, the transaction would be pro-competitive, as it would provide customers with improved products.[355] The Commission further observed that LinkedIn's data was not essential such that, even if Microsoft decided to use LinkedIn's full data and refused access to its competitors, there would remain many alternative sources of data for CRM software suppliers.[356] The Commission therefore ruled out any foreclosure concerns.

B. <u>PacBio's sequencing data is not unique or non-replicable</u>

330. The Transaction also does not raise foreclosure concerns, as PacBio's native long read sequencing data, including its library of reference genomes, is not unique or non-replicable. There are many other sources of native long read sequencing data available to Illumina's competitors, including native long read sequencing data generated by users of native long read systems [redacted].

331. First, native long read sequencing data is in the vast majority of cases produced by users of native long read systems [redacted]. Those users are the owners of that data and a substantial part of them make that data publicly available. Many research organisations upload their sequencing data to publicly available databases, [redacted].[357] Further, most peer reviewed journals require publication of sequencing data and the US' National Institutes of Health also require the publication

[351] Commission, Decision of 3 October 2014 in case COMP/M.7217 *Facebook/ WhatsApp*, paras. 180-189.
[352] Commission, Decision of 3 October 2014 in case COMP/M.7217 *Facebook/ WhatsApp*, para. 189.
[353] Commission, Decision of 6 December 2016 in case COMP/M.8124 *Microsoft/LinkedIn*, para. 246-245.
[354] Commission, Decision of 6 December 2016 in case COMP/M.8124 *Microsoft/LinkedIn*, para. 247.
[355] Commission, Decision of 6 December 2016 in Case COMP/M.8124 *Microsoft/ LinkedIn*, para. 249.
[356] Commission, Decision of 6 December 2016 in Case COMP/M.8124 *Microsoft/ LinkedIn*, paras. 262-264 and 276.
[357] [redacted]

of sequencing data gathered during federally-funded projects (absent patient privacy concerns).

332. After the Transaction, customers who use applications available on BaseSpace to store and analyse data produced with PacBio's systems will remain in control of their data. They will be free to give access to it to Illumina and third party developers, or not, and may also decide whether to provide it to Illumina's competitors or make it otherwise publicly available.

333. Further, as explained above, sequencing data can be procured by suppliers of sequencing systems in many ways, including by performing native long read sequencing themselves. [redacted]. Competing suppliers can also acquire data from their own customers or from research bodies, as Illumina does today. Native long read sequencing data is also produced by [redacted] and [redacted] customers. That data will also remain available to short read systems suppliers after the Transaction. Further, it is likely that data generated [redacted]

334. Finally, access to PacBio's sequencing data is pro-competitive, as it will enable Illumina and third party developers of BaseSpace applications to improve and develop new bioinformatics applications to the benefit of customers.

Conglomerate effects

20. If the merger parties are active in "related" markets (e.g. products that are complementary or that belong to a range of products generally purchased by the same set of customers) and their individual share in any such related Candidate Market exceeds 30%, describe the impact of the merger on the ability and incentive of the merged entity to foreclose rivals (including partial and/or full foreclosure) post-transaction, either by limiting the supply of inputs or access to customers.

335. As discussed in Section 13 above, short read and native long read systems are complementary, as they are used by customers either for different applications or in a complementary fashion for the same applications.

336. Irrespective of the market shares of Illumina and PacBio, the Transaction does not raise concerns regarding conglomerate effects through bundling or tying practices in the potential markets for short read systems and native long read systems.[358, 359]

337. It follows from the Commission's and the CMA's decisional practice that conglomerate mergers are usually benign or even pro-competitive because they give rise to efficiencies.[360] Bundling and tying as such are common practices that often have no anticompetitive consequences.[361] Companies engage in tying or bundling to provide their customers with better products and offerings in cost-effective ways. Concerns only arise if such strategies could significantly lessen competition by foreclosing competitors.[362]

338. In the case at hand, the Transaction will lead to consumer benefits and does not raise foreclosure concerns, given that:

- customers would continue to be able to use Illumina's systems and PacBio's systems separately and not exclusively in combination, and [redacted] in order to enable users to exploit the complementary nature of Illumina's short read systems and PacBio's native long read systems would not result in a technical tie; and
- Illumina will have neither the ability nor incentive to foreclose competitors through bundling.

I. The Notifying Parties will not engage in technical tying

339. As discussed in more detail in Section 24 below, following the Transaction, [redacted] to enable customers to exploit the complementary nature of short read sequencing and native long read sequencing.

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358 [redacted].

359 [redacted].

360 Commission, *Guidelines on the assessment of non-horizontal mergers under the Council Regulation on the control of concentrations between undertakings*, OJ C 265, 18.10.2008, para. 93; CMA, Decision of 26 May 2009, *The Coca-Cola Company/Fresh Trading Limited*, para. 28; OFT, Decision of 10 February 2010, *The Ambassador Theatre Group Limited/Live Nation (Venues) UK Limited,* para. 95.

361 Commission, *Guidelines on the assessment of non-horizontal mergers under the Council Regulation on the control of concentrations between undertakings*, OJ C 265, 18.10.2008, para. 93.

362 Commission, *Guidelines on the assessment of non-horizontal mergers under the Council Regulation on the control of concentrations between undertakings*, OJ C 265, 18.10.2008, para. 93.

340. [redacted].

A. Existing practice on technical tying

341. As the Commission's Guidelines on the assessment of non-horizontal mergers make clear, tying involves customers purchasing one product (the tying product), also being required to purchase another product (the tied product).[363] Tying can occur contractually[364] or technically. Technical tying occurs where a tying product is designed in such a way that it only works with the tied product, and not with alternatives offered by competitors.[365]

342. The Commission has made clear that technical tying could consist of either (i) combining the merging parties' products in a persistent form[366] or (ii) degrading interoperability between the merging parties' products and competitors' products.[367] For example, in *Intel/McAfee*, the Commission considered that embedding McAfee's security solutions into Intel's CPU/chipset platforms would result in the technical combination of these products in a 'persistent form' and thus in a technical tie.[368]

343. In *Marel/SFS*, the Commission assessed whether Marel and SFS could degrade the interoperability between their products for the processing of poultry and their competitors' products. It found that, while Marel and SFS would be able to provide new solutions integrating their products, they would have neither the ability nor the incentive to reduce existing interoperability of their products with competitors' products.[369] Customers would remain free to purchase Marel and SFS products on a standalone basis and to use them in combination with competitors' products.

B. [redacted]

344. [redacted]

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[363] Commission, *Guidelines on the assessment of non-horizontal mergers under the Council Regulation on the control of concentrations between undertakings*, OJ C 265, 18.10.2008, para. 97.
[364] Contractual tying forces customers to buy the tying product and the tied product together, even though they are separate and can work independently. This is akin to a pure bundling and it is as such discussed below in section B on bundling.
[365] Commission, *Guidelines on the assessment of non-horizontal mergers under the Council Regulation on the control of concentrations between undertakings*, OJ C 265, 18.10.2008, para. 97.
[366] Commission, Decision of 26 January 2011 in Case COMP/M.5984 *Intel/McAfee* paras. 175-221.
[367] Commission, Decision of 22 May 2017 in Case M.8314 *Broadcom/Brocade,* paras. 148-207; Commission, Decision of 22 May 2017 in Case COMP/M.5125 *Marel/SFS*, paras. 48-55; Commission, Decision of 05 March 2008 in Case COMP/M.4747 *IBM/Telelogic*, paras. 248-256.
[368] Commission, Decision of 26 January 2011 in Case COMP/M.5984 *Intel/McAfee*, paras. 175-176.
[369] Commission, Decision of 22 May 2017 in Case COMP/M.5125 *Marel/SFS*, paras. 37 and 48-55.

[redacted]

345. [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]

346. [redacted]

347. [redacted]

348. Finally, Illumina operates an open platform model. It publishes its primer sequences, which enable third parties to develop library preparation kits for its systems. [redacted]. Illumina also enables third party developers to develop analysis software for its platforms, and has strong incentives to encourage as many third party providers as

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370 [redacted]

371 Please see Section 24 below.

possible to continue to develop analytical and other software for users of its services in order to accelerate discovery and broaden the utility of sequencing information. Many companies currently offer analysis software and data storage and sharing solutions, and the widespread use of cloud storage capacity for sequencing data will further drive this development.[372] These solutions can be used across a broad range of sequencers. Most, if not all, third party analysis and storage solutions are sequencing platform agnostic, such that they are not optimised for any particular sequencing system.

349. Third parties could, therefore, also develop solutions to facilitate the use of [redacted] or any other third party's systems together with Illumina's systems.[373] The Parties believe that, as the number of customers using both short read and native long read systems together grows, an increasing number of third parties will be incentivised to develop such solutions. Because Illumina believes that its open model encourages the growth of sequencing, both in terms of the number of applications for which it is used and the number of samples that are run for each application, Illumina intends to maintain this model following the Transaction. PacBio is not a significant provider of analytics software, such that the Transaction will have no impact on Illumina's incentives in this context.

II. Bundling

350. The Transaction will not enable Illumina to leverage its position in the potential market for short read systems into the potential market for native long read systems through bundling.

A. Existing practice on bundling

351. The CMA's and the Commission's practice clearly distinguish between: (i) pure bundling, whereby products are only sold jointly in fixed proportions;[374] and (ii) mixed bundling, where the products are available separately, but the individual prices of the products stand-alone is higher than the bundled price.[375]

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[372] Suppliers of analysis software in the UK include [redacted].

[373] [redacted]

[374] OFT, Decision of 10 February 2010, *The Ambassador Theatre Group Limited/Live Nation (Venues) UK Limited,* para. 106. Commission, Decision of 21 January 2004 in Case COMP/M.3304 *GE/Amersham*, para. 43.

[375] OFT, Decision of 29 July 2003, *Decision of the Office of Fair Trading under section 47 relating to decision CA98/20/2002: alleged infringement of the Chapter II prohibition by BSkyB,* para. 164 ; Commission, Decision of 01 March 2018 in Case M.8394 *Essilor/Luxottica*, para. 196.

352. In assessing the likelihood of such bundling, the key issues are whether:

- the merged entity will have the **ability** to foreclose rivals;
- it will have the economic **incentive** to do so; and
- the **effects** of such a strategy would be to significantly lessen competition (or significantly impede effective competition in the Commission's case).[376]

353. In relation to the assessment of the merging parties' economic incentives, the focus of a competition authority's investigation is on the profitability of a bundling strategy.[377] They also examine whether the merging parties have engaged in bundling in the past.[378] For example, in *GE/Amersham*, the Commission examined whether the merged entity would have the economic incentive to engage in pure bundling with regard to GE's diagnostic imaging equipment and Amersham's diagnostic pharmaceuticals. It concluded that such a strategy would deny the merged entity significant sales as GE would need to forego sales for diagnostic imaging equipment to users that would prefer to use non-Amersham diagnostic pharmaceuticals. Given this, there was no incentive to engage in pure bundling.[379]

354. In *Coca-Cola/Fresh Trading*, the OFT reviewed The Coca-Cola Company (TCCC)'s acquisition of a minority interest in Fresh Trading Limited (Fresh Trading) that enabled it to materially influence the policy of Fresh Trading. In its analysis, the OFT examined whether TCCC had the incentive to bundle its products with those of Fresh Trading in order to foreclose competitors. The OFT considered that the incentive to foreclose was dependent on whether the bundling would be profit enhancing, and concluded that TCCC was unlikely to have an incentive to engage in such behaviour as its minority interest in Fresh Trading meant that it would only receive a portion of the profit resulting from a bundling strategy.[380]

B. <u>The Notifying Parties have no incentive to foreclose competitors through bundling</u>

355. [redacted] Illumina's incentive or ability to engage in pure or mixed bundling of systems will not change following the Transaction.

356. Illumina will not engage in pure bundling as this strategy would most likely lead to losses. [redacted]

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[376] CMA, *Merger assessment guidelines,* para. 5.6.6 and 5.6.13 ; Commission, *Guidelines on the assessment of non-horizontal mergers under the Council Regulation on the control of concentrations between undertakings*, OJ C 265, para. 94. ; Commission, Decision of 1 March 2018 in Case M.8394 *Essilor/Luxottica*, para. 194.
[377] OFT, Decision of 26 May 2009, *Coca-Cola Company/Fresh Trading Limited,* para. 62-64.
[378] OFT, Decision of 26 May 2009, Coca-Cola Company/Fresh Trading Limited, para. 70; OFT, Decision of 10 February 2010, The Ambassador Theatre Group Limited/Live Nation (Venues) UK Limited, para. 113.
[379] Commission, Decision of 21 January 2004 in Case COMP/M.3304 *GE/Amersham*, para. 43.
[380] OFT, Decision of 26 May 2009, *Coca-Cola Company/Fresh Trading Limited,* para. 62-64.

[redacted]

357. On the other hand, Illumina could lose a significant number of customers if it tried to force them to buy a PacBio system using a pure bundling strategy. [redacted]

358. A mixed bundling strategy would be equally ineffective as [redacted].

359. [redacted]

[381] Please see https://nanoporetech.com/about-us/news/new-r10-nanopore-released-early-access. [redacted].

Entry or expansion

21. Where notifying parties would like the CMA to consider whether or not the merged entity will be subject to constraints from potential entry or expansion, provide a description of the barriers to entry and expansion with respect to the Candidate Market(s).

360. The Notifying Parties submit that there are no significant barriers to entry to (or expansion in) the potential markets for either short read or native long read systems, respectively. A number of companies have entered these potential markets in recent years, and several others are expected to enter in the short-term.[382]

361. Illumina estimates that it takes between [redacted], and on average over [redacted], to invent, research, develop and commercialise a new sequencing technology, and another [redacted] to achieve scaled commercialisation. On launch, innovative sequencing technologies can rapidly gain wide adoption and expand significantly, [redacted].[383] The time required to invent, research, develop and commercialise a sequencing technology depends on many factors, including a company's available financial and human resources, and ability to innovate. However, the table below illustrates that the time required has not significantly differed to date depending on whether the relevant sequencing technology is short read or native long read.

[redacted]

[382] Please see Section 22 below.
[383] [redacted]
[384] [redacted]
[385] [redacted]
[386] [redacted]
[387] [redacted]
[388] [redacted]

[redacted]

362. Illumina estimates that the invention, research, development and commercialisation of a new sequencing technology would cost a new entrant [redacted].[395] Illumina estimates that these costs could be lower for a company which already has a sequencing technology because much less investment would be needed in, among other things, advertising and product-support services. The cost of inventing, researching, developing and commercialising a sequencing technology depends on many factors, including the anticipated sequencing chemistry, the type of sequencing system (*e.g.*, benchtop vs production-scale), and the system's envisaged attributes. However, these costs are not driven by whether the anticipated technology is short read or native long read. [redacted]

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389 [redacted]

390 [redacted]

391 [redacted]

392 [redacted]

393 [redacted]

394 [redacted]

395 [redacted]

396 [redacted]

363. While researching, developing and commercialising a new sequencing technology requires significant investment, a large number of companies have made that investment, and due to the growth and expansion of the sequencing markets, new entrants are able to find willing investors. Sequencing companies have attracted substantial investments from angel investors, investment firms, venture capitalists, and large life science companies. For example:

- [redacted][397]
- [redacted][398];
- [redacted][400]
- [redacted]
- [redacted]
- [redacted] and
- [redacted]

364. The Notifying Parties believe these investment activities reflect the fact that there is significant potential for broader use of sequencing technology. As discussed in Section 18, above, the potential sequencing markets are nascent, with a significant growth opportunity remaining. For instance, as of today, less than 0.01% of species and less than 0.02% of human genomes have been sequenced, less than 1% of variants in the human genome have been fully characterised, and the understanding of complex structural features of the human genome is at its beginning. Sequencing has the potential to be a part of everyday life, for instance, where every tumor is sequenced to

397 [redacted]
398 [redacted]
399 [redacted]
400 [redacted]
401 [redacted]
402 [redacted]
403 [redacted]
404 [redacted]

help with diagnosis and therapy selection, genetic diseases are diagnosed before birth, and knowing your DNA sequence becomes an integral part of understanding personal health and personalised medicine.

365. There are no significant tariff or non-tariff barriers to imports of sequencing systems from outside the EEA. In addition, transportation costs are not significant. There are also no barriers preventing companies from having access to raw materials.

366. Brand image is not an important competitive differentiator, as the majority of sequencing system suppliers have positive reputations. Reputation is primarily driven by offering a technology that meets customers' needs, including by producing results that can be relied on.

367. As explained in Section 15 above, in the UK, Illumina currently competes [redacted] on the potential market for the supply of short read systems, and PacBio competes with [redacted] on the potential market for the supply of native long read systems. [redacted]. To the best of Illumina's knowledge, all sequencing system providers hold intellectual property claiming certain aspects of their sequencing technology. [redacted].[405, 406]

368. The Notifying Parties also believe that switching costs are not significant. Sequencing platforms from various manufacturers can be installed into the same lab or production setting, as none require customised facilities. As explained below, system suppliers release new systems quite frequently, and attract customers, suggesting that customers are able and willing to switch supplier(s) if a system better meets their requirements.

369. Further, suppliers have made and continue to make substantial investments in simplifying their workflows, thereby reducing the time required to retrain the technicians running sequencers. Such simplification is a competitive attribute that facilitates uptake. Additionally, emergence of numerous library preparation, data management and data analysis/bioinformatics companies have simplified and standardised workflows for most applications. Unlike a decade ago when users had to conceive and develop their own library preparation and bioinformatics solutions, today users can simply purchase off-the-shelf library preparation kits and

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405 [redacted]

406 [redacted]

analysis/bioinformatics software for nearly all applications of interest, meaning that library preparation and data analysis may increasingly become more similar irrespective of the system used. Availability of a wide array of off-the-shelf kits and analysis software further simplifies switching from one platform to another. In addition, as explained in Section 22 below, several of the new systems being developed are expressly intended to provide low cost, simple and fast solutions.

370. Finally, a material number of customers who buy sequencing systems are new to sequencing and do not face switching costs. [redacted]. Illumina believes that innovation will lead to both increased demand for existing applications and the creation of new applications.[407]

371. The following bullet points specify the costs customers would incur if they were to switch between different providers of sequencers, sequencing services, secondary products/consumables, and data analysis software and data storage and sharing solutions, respectively. The Parties also provide examples of customers switching between the respective providers:

- *Different providers of sequencers*: the primary costs of switching between systems include the price of the new sequencer (which can range between USD 20,000 and USD 1 million, although this cost could either be charged as an upfront cost or be spread across the sales of library preparation kits and consumables over time), and the (relatively limited) time invested to train employees on the new workflow. Training is typically included with the purchase of a sequencer and lasts between two and five days.

  Otherwise, the cost of switching between providers of sequencers is negligible since most of the non-sequencer infrastructure and workflow that would be in place for one sequencing system can readily be used for another sequencing system. Sample and library preparation for most sequencing systems can be accomplished manually or using standard laboratory automation solutions which are generally all purpose and not specific to any particular sequencing system or technology.

  The cost of switching related to data storage and informatics infrastructure is also negligible. This is because users generally use standard cloud-based storage offered by providers such as [redacted] These storage solutions can be used interchangeably with different sequencing systems. Lastly, since there are a broad range of academic and commercial-grade informatics solutions that work with nearly all sequencing systems, users can select solutions that interoperate with their sequencer of choice.

[407] Please see Section 18 above.

Clinical customers may incur additional costs for revalidation of tests and workflows, depending on the initial technology used or the new technology selected. Such costs range, depending on the tests and applications in issue.[408]

Over the years, many customers have switched between providers of short read sequencing. [redacted] Customers switch between different short read systems for a number of reasons, including the features (higher output and faster turnaround time), greater accuracy, improved workflows, regional- or country-specific clearance status, and cost.

As explained in Section 13 above, short read systems and native long read systems are not considered to be substitutable by customers. Customers use short read systems and native long read systems either for entirely different applications or for the same application side-by-side to take advantage of their complementarity. As a result, customers do not switch between short read and native long read systems, and the Notifying Parties are not aware of any instance where a customer has switched between native long read and short read systems (or *vice versa*).

- *Different providers of sequencing services*: the cost of switching between providers of sequencing services is negligible, as different service providers use similar protocols for any given application. As a result, customers can easily switch between sequencing service providers.

[redacted]

408 [redacted]

- *Different providers of secondary products/consumables*: as explained above, there are a material number of third-party providers of library preparation kits that can be used on third-party sequencers. As a result, customers regularly switch between library preparation kit providers.

  Examples of customers that switched between different providers of library preparation kits include:

  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]
  - [redacted]

- *Different providers of data analysis software and data storage and sharing solutions*: most, if not all, third-party data analysis software and data storage solutions are sequencing platform agnostic, such that they are not optimised for any particular sequencing system. As a result, a customer using third party analysis and/or storage solutions who chooses to switch to a different sequencing system, would ordinarily have no need to switch data analysis and storage solutions. Customers are also able to use different providers simultaneously.

  Recent examples of customers switching between, and combining, solutions include:

  - [redacted]
  - [redacted]

- [redacted]
- [redacted]
- [redacted]

372. For a description of the regulatory requirements of supplying sequencing systems in the UK, please see [redacted].

22. If the notifying parties wish the CMA to consider potential entry or expansion in its competitive assessment, notifying parties should provide:

(a) **details of any expansion, entry or exit in any of the Candidate Markets over the past five years, and**

(b) **details of any companies that the notifying parties believe are likely, post-merger, to enter or expand into any of the Candidate Markets in a sufficiently timely manner so as to adequately constrain the merged entity,**

including, in either case, any available evidence for that submission and contact details for any companies named.

I. Growth and expansion of the potential sequencing markets

373. The material recent growth and significant forecasted future growth in demand of sequencing applications has attracted new entrants and has raised significant investment interest from venture capital, pharmaceutical companies, diagnostics companies and governments.[409] The growth and expansion of the sequencing industry in large part reflects the increasing number of sequencing platforms, rapid improvements in system performance, lower costs, and reduced complexity of generating sequencing data (*e.g.*, improvements in workflow) and analysing the results (*e.g.*, improvements in bioinformatics and analytics).

374. The demand for sequencing systems has grown significantly, as technology improvements and enhancements have expanded the number of applications, driven novel discoveries and led to increased clinical utility. New applications enabled by the economics and high throughput of short read systems have greatly increased the number and diversity of users. Continued improvements are expected to drive further expansion in the adoption of existing sequencing applications and expansion into new applications. As noted above, the potential sequencing markets are nascent and, as of

[409] 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.

today, less than 0.01% of species and less than 0.02% of human genomes have been sequenced, less than 1% of variants in the human genome have been fully characterised, and the understanding of complex structural features of the human genome is at its beginning. The expansion of applications (and potential customers) will drive further growth, maintaining incentives for further investment (including by new entrants).

II. Recent entry and expansion

375. Many of the companies that currently commercialise sequencing technologies entered the potential markets for short read and native long read systems, respectively, in the last few years. In just a few years, these companies have significantly expanded their offerings and are expected to keep developing and launching new products and enhancing their existing ones.

A. Potential market for short read systems

376. **Thermo Fisher** entered the potential market for short read systems in 2014 through its GBP 10.54 billion[410] acquisition of Life Technologies, which marketed and sold the SOLiD and Ion Torrent short read sequencing systems.[411, 412] While Life Technologies had already introduced the Ion Torrent technology to the market prior to its acquisition by Thermo Fisher, *i.e.*, the Ion PGM (2010) and Ion Proton (2012), Thermo Fisher has expanded the Ion Torrent portfolio. In 2015, Thermo Fisher launched its Ion S5 and Ion S5 XL systems. More recently, in 2018, Thermo Fisher launched three additional sequencing systems, *i.e.*, the Ion GeneStudio S5, Ion GeneStudio S5 Prime, and Ion GeneStudio S5 Plus. While these three systems use similar underlying technology to the earlier S5 systems, they claim to have materially upgraded computing capabilities and enable increased output and faster analysis. According to Thermo Fisher, its systems are highly configurable, using various consumable chips that enable the

[410] 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).

[411] [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

[412] 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/

devices to provide several throughput options, also enabling flexibility within a single system.[413]

377. **Qiagen** entered the potential market for short read systems in 2012 through its acquisition of Intelligent BioSystems, which had released its first system, the MAX-Seq, in 2011 and was working on a benchtop sequencer called the Mini-20.[414] 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).[415] At the beginning of 2018, Qiagen also announced several enhancements to its GeneReader system, including upgraded NGS chemistry that would enable increased output.[416]

378. Over the last few years, Qiagen has acquired a number of additional sequencing-related companies that provide library prep solutions, assays and/or bioinformatics software, including CLC Bio (2013), Ingenuity Systems (2013), Enzymatics (2015), Exiqon (2016), OmicSoft Corporation (2017), and N-of-One (2019).[417] OmicSoft Corporation, for instance, was acquired by Qiagen to expand its bioinformatics offering with the aim to enable scientists to visualise and mine large institutional and publicly available "omics" datasets. The OmicSoft software solutions are intended to assist in discovery and translational research to access and manage large amounts of data on DNA, RNA and other variables identified through sequencing.[418]

379. In July 2018, Qiagen announced a partnership with multiple organisations to support the creation of a global genomics campus in Manchester, UK, for innovation, life sciences, translational science and molecular diagnostics.[419] Qiagen is working with Health Innovation Manchester, a partnership bringing together the region's public, academic and clinical resources, to develop a world-leading genomics campus in Manchester's health innovation district.[420] Qiagen stated that its existing Manchester site remains central to the company's strategic plans for global innovation and

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[413] https://tools.thermofisher.com/content/sfs/brochures/Ion-S5-S5XL-SpecSheet.pdf; https://tools.thermofisher.com/content/sfs/brochures/Ion-S5-S5XL-SpecSheet.pdf

[414] [redacted]

[415] 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

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

[417] https://www.genomeweb.com/informatics/qiagen-acquires-clc-bio#.XFIM1lz7S70, https://www.prnewswire.com/news-releases/qiagen-acquires-ingenuity-systems-adding-leading-solution-for-analysis-and-interpretation-of-complex-biological-data-205279951.html, https://corporate.qiagen.com/newsroom/press-releases/2017/20150111_enzymatics, https://www.prnewswire.com/news-releases/qiagen-announces-successful-completion-of-tender-offer-for-shares-in-exiqon-584079341.html, https://corporate.qiagen.com/newsroom/press-releases/2019/20190107_qiagen_acquires_n_of_one

[418] Qiagen 2017 Annual Report, p. 7 and 24, available at https://corporate.qiagen.com/-/media/project/qiagen-corporate/corporate-microsite/documents/investor-relations/2017/reports/2017-ifrs-annual-report-r101-final.pdf

[419] https://corporate.qiagen.com/newsroom/press-releases/2018/20180711_manchester

[420] *Ibid.*

development.[421] Qiagen currently has approximately 270 employees in Manchester and stated that it is committed to further growth.[422] Qiagen's Manchester operation will move to a new state-of-the-art facility in 2020 at the new genomics campus.[423]

380. **BGI** acquired Complete Genomics in 2013 and launched its first short read sequencing system, the BGISEQ-500, in 2015.[424] [redacted], BGI has expanded significantly in recent years with its 2017 revenue rising by approximately 22%.[425] It currently sells several systems, including the BGISEQ-50 launched in 2016,[426] and both the MGISEQ-200 and MGISEQ-2000 launched in 2017.[427] BGI also launched a modular NGS workstation, called MGIFLP, in 2017,[428] designed to integrate the entire NGS process.[429] Also in 2017, BGI's initial public offering (IPO) on the Shenzhen Stock Exchange raised USD 81 million,[430] with funds being used to support BGI's continued growth and innovation.[431] BGI has also recently unveiled its highest throughput system, the MGISEQ-T7, in October 2018, with early-access expected to begin in 2019.[432] In January 2019, MGI announced that it has installed 1,000 systems in 16 different countries.[433]

381. [redacted]

382. [redacted]

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[421] *Ibid.*
[422] *Ibid.*
[423] *Ibid.*
[424] 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
[425] http://pdf.dfcfw.com/pdf/H2_AN201804191126386621_1.pdf, p. 27
[426] [redacted]
[427] https://www.bgi.com/global/company/news/bgis-mgi-tech-launches-two-new-ngs-platforms/
[428] https://www.bgi.com/global/company/news/bgis-mgi-tech-launches-two-new-ngs-platforms/
[429] http://en.mgitech.cn/product/detail/MGIFLP.html
[430] https://www.bgi.com/global/company/news/bgi-genomics-announces-pricing-initial-public-offering/; https://www.genengnews.com/topics/omics/bgi-genomics-raises-81m-in-ipo/
[431] *Ibid.*
[432] https://www.prnewswire.com/in/news-releases/mgi-announces-milestone-of-1-000-sequencers-installed-and-opens-early-access-program-for-groundbreaking-ultra-high-throughput-sequencer-mgiseq-t7-874602836.html
[433] http://en.mgitech.cn/article/detail/mgiannouncesmiles.html

[redacted]

383. [redacted]

B. Potential market for native long read systems

384. **ONT** entered the potential market for native long read systems with its MinION pocket-sequencer, offering early access in 2014 and broadly commercialising in 2015.[435] ONT has since significantly expanded through rapid uptake of its systems, frequent updates to its bioinformatics software, base calling hardware, operating software, chemistry, kits, flow cells, library preparation instruments, and new platforms, as well as significant backing from a range of investors. ONT introduced the GridION and PromethION benchtop sequencers in 2017 and 2018, respectively.[436] In addition, in 2017, ONT introduced the USB device VolTRAX,[437] a portable, automated library preparation device.[438]

385. ONT reports that, as of May 2018, approximately 6,000 to 7,000 MinION sequencers had shipped to users globally.[439] Also in May 2018, ONT reported that there were over 100 GridION customers in 24 countries, and that at least 40 PromethION sequencers had shipped, with another 20 expected to ship by the end of June 2018, with further orders received.[440]

386. ONT's 2017 annual report states that its revenues increased by 204% since 2016, with its UK revenues increasing by 95%.[441] ONT's average headcount in 2017 was 40% higher than in 2015.[442]

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[434] [redacted]

[435] The MinION was introduced into early access in Spring 2014 and made commercially available in 2015. See https://nanoporetech.com/about-us

[436] https://nanoporetech.com/about-us/news/introducing-gridion-x5; https://nanoporetech.com/about-us/history

[437] http://www.dnacoil.com/tag/voltrax/

[438] VolTRAX v1 has been available in early access program, and VolTRAX v2 has been released in 2018. See https://nanoporetech.com/products/voltrax

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

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

[441] ONT 2017 Annual Report, p. 6, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0

[442] *Ibid.*

387. Further, ONT has attracted funding of GBP 451 million to date in various fundraising rounds.[443] Most recently, in March 2018, ONT received GBP 100 million from investors from China, Singapore and Australia, alongside existing investors.[444] The funds were raised to support ONT's next phase of commercial expansion, development of new products[445] and a new 34,000 square foot high-volume manufacturing facility in Oxfordshire necessary to meet accelerating demand.[446]

388. ONT continues to invest in research and development, manufacturing build-out and commercial expansion.[447] Its development pipeline is robust, and includes frequent updates to its flow cells, chemistry, bioinformatics software, base calling hardware, VolTRAX library preparation instrument, and platforms, including the SmidgION, a portable sequencing device designed to be used with a smartphone.[448] ONT's website states that the SmidgION is "coming soon".[449] ONT has also developed the "Flongle", an adaptor for the MinION or GridION systems designed to enable direct, real-time DNA or RNA sequencing on smaller, single-use flow cells that will have a low price point, averaging about USD 100 USD per flow cell that is expected to yield at least 1 Gb of sequencing data.[450] The Flongle was released into early access in late 2018, and broader release will follow in 2019.[451]

389. Recently, ONT also announced the MinION Mk1c - a self-contained combination of the MinION, MinIT (a simple, preconfigured IT solution) and a screen, which is networkable using Wi-Fi/Bluetooth/SIM - is being developed for release in mid-2019.[452] Further planned introductions in 2019 include two new versions of the PromethION (24 and 48).[453]

Table 12: ONT's product portfolio expansion

Product	Date of commercial release
Sequencers	

[443] https://nanoporetech.com/about-us
[444] *Ibid.*
[445] ONT 2017 Annual Report, p. 6, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0
[446] https://nanoporetech.com/about-us/news/oxford-nanopore-announces-ps100-million-140m-fundraising-global-investors
[447] ONT 2017 Annual Report, p. 6 and 25, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0
[448] ONT 2017 Annual Report, p. 8, available at https://beta.companieshouse.gov.uk/company/05386273/filing-history/MzIwNzA3NzQ4MWFkaXF6a2N4/document?format=pdf&download=0; https://nanoporetech.com/about-us; https://nanoporetech.com/products
[449] https://nanoporetech.com/products
[450] https://nanoporetech.com/products/flongle
[451] *Ibid.*
[452] https://nanoporetech.com/about-us/news/clive-g-brown-nanopore-community-meeting-2018-talk.
[453] *Ibid.*

Product	Date of commercial release
MinION	May 2015[454]
GridION X5	May 2017[455]
PromethION (beta)	May 2018[456]
PromethION 24	Estimated Q2 2019 - pre-orders now available.[457]
PromethION 48	Estimated Q2 2019 - pre-orders now available.[458]
MinION Mk1c	Expected mid 2019[459]
SmidgION	No commercial release date provided. ONT's website states the SmidgION is "coming soon".
Other devices	
MinIT	October 2018[460]
VolTRAX v1	Only available in early access from November 2017.
VolTRAX v2	2018
Flongle	Released into early-access in late 2018. Broader release stated to follow in 2019.[461]
Ubik[462]	Unknown

390. [redacted]

391. [redacted]

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[454] The MinION was introduced into early access in Spring 2014; See https://nanoporetech.com/about-us/history
[455] https://nanoporetech.com/about-us/history; https://twitter.com/clive_g_brown/status/864122363868315649?lang=en
[456] https://nanoporetech.com/about-us/news/promethion-24-and-promethion-48-now-available
[457] https://nanoporetech.com/about-us/news/promethion-24-and-promethion-48-now-available
[458] https://nanoporetech.com/about-us/news/promethion-24-and-promethion-48-now-available
[459] https://nanoporetech.com/about-us/news/clive-g-brown-nanopore-community-meeting-2018-talk
[460] https://nanoporetech.com/about-us/news/minit-launch
[461] https://nanoporetech.com/products/flongle
[462] Ubik is a low cost, portable, sample preparation device. Please see https://nanoporetech.com/about-us
[463] Please see pages 24-28 of **Annex** 2 submitted on 27 February 2019. [redacted]
[464] https://www.genomeweb.com/sequencing/grandomics-raises-nearly-rmb-100m-series-b-financing#.XIqY7ChKiUk.

392. [redacted]

393. [redacted]

III. Potential entry

394. As illustrated by the chart below, there are numerous companies planning to launch sequencing systems. Most of these potential entrants have received significant funding from investors, and many have been acquired by large life science companies.

Figure 22: Potential entrants

[redacted]

395. The table below reflects the Parties' best current understanding of whether each company is expected to enter the potential market for short read or native long read systems, respectively. Limited information is currently available regarding certain potential entrants' sequencing technologies. At this stage, the Parties do not have sufficient information about the technologies under development by [redacted],[465]

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465 [redacted]

[redacted][466] to definitively identify them as working on short read or native long read systems, respectively.

[redacted]

396. The table above lists numerous potential entrants in the potential markets for short read and native long read systems, reflecting the well-appreciated opportunities in both potential markets. As discussed below, of the potential entrants listed, a greater number of those poised to enter within the [redacted] are expected to supply short read systems [redacted], rather than native long read systems (*i.e.*, [redacted]).[468]

397. There are various reasons why a particular entrant might select either of short read or native long read technology over the other. Entrants generally seek to offer an

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[redacted]

466 [redacted]

467 [redacted].

468 [redacted]

innovative sequencing technology. The underlying sequencing technology innovations available to an entrant may partially be a function of circumstance (*e.g.*, a new sensing method is discovered and subsequently commercialised). Certain innovations may be better suited for short reads or native long reads. For instance, nanopores tend to lend themselves to native long read technologies, and many of the native long read technologies being developed by potential entrants (*e.g.*, [redacted]) are nanopore-based.

398. There are no companies which currently supply both short read and native long read systems. Illumina, [redacted] only supply short read systems.[469] PacBio and [redacted] only supply native long read systems. [redacted].[470] The Parties are not aware of any supplier which is likely to start supplying both short read and native long read systems in the near future.

399. Of the many companies currently developing sequencing technologies, [redacted] are expected to announce, or have announced, the intention to enter in the next [redacted]. A description of these [redacted] companies and their anticipated sequencing technologies is provided below.

400. [redacted][473]

401. [redacted]

469 [redacted].
470 [redacted]
471 [redacted]
472 [redacted].
473 [redacted]
474 [redacted]
475 [redacted].
476 [redacted].
477 [redacted]

[redacted]

402. [redacted]

403. [redacted]

404. [redacted]

---

478 [redacted]
479
480 [redacted]
481
482
483
484
485

[redacted]

405. [redacted]

406. [redacted]

407. [redacted]

408. [redacted]

409. [redacted]

[redacted]

[redacted]

410. [redacted]

411. [redacted]

412. [redacted]

- [redacted]

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500 [redacted]

501 [redacted].

502 [redacted]

503 [redacted]

504 [redacted]

505 [redacted]

Countervailing buyer power

23. Where notifying parties would like the CMA to consider whether or not the merged entity will be subject to countervailing buyer power, explain, with evidence where available, how the merged entity will be subject to this constraint.

413. Sequencing adoption is still at a very early stage and is only used in a small number of applications with regularity and at scale. However, the Notifying Parties believe that there is significant potential for materially broader adoption of existing applications and the development of a whole range of new applications that could, among other things, transform the diagnosis and treatment of certain diseases.

414. Illumina's commercial strategy reflects this. It is based on long-term, rather than short term, considerations. Illumina takes the view that the expansion of the use of sequencing will only occur if research customers are able to conduct the large scale

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507 [redacted]

508 [redacted]

509 [redacted]

510 [redacted]

511 [redacted]

512 [redacted]

projects that will demonstrate the utility of, and pave the way for, the use of sequencing in new fields and applications.

415. As a result, customers who conduct these often large scale novel research projects establish the utility of sequencing in new fields and applications. This makes these customers, and their projects, critical to Illumina and other sequencing system suppliers. In practical terms, this means that these customers must be able to conduct their research at the necessary scale, without their ability to do so being impeded by cost, and over often extended timeframes.

416. Translational and clinical customers also fill important roles in the ongoing growth of sequencing, developing the tests and assays that will enable the routine clinical and diagnostic adoption of new tests that can be used in developing new diagnostic tools and new personalised treatments for customers with diseases.

417. As a result of these dynamics, Illumina seeks to build long-term relationships with its customers, to encourage and facilitate broadening the understanding, utility, and adoption of sequencing.

418. The following paragraphs provide some examples of customers that are important to Illumina, for the reasons described above, and whose ability to negotiate with Illumina will not be impaired as a result of the Transaction.

I. There are customers with the ability to negotiate for highly favourable terms in the UK and globally

419. Within the various customer groups described in Section 15, there are customers (both in the UK and globally) that are particularly well placed to negotiate with the Notifying Parties. These customers include:

- [redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]
- [redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]

420. [redacted]

[redacted]

[redacted]

421. [redacted]

422. [redacted]

II. The Transaction will not reduce customers' negotiating strength

423. Post-Transaction, large customers that pave the way for the use of sequencing in new fields and applications will remain critical for Illumina. The acquisition of PacBio will not change Illumina's commercial strategy based on building long-term relationships with customers and enabling them to undertake pioneering projects.

[redacted]

424. As explained in Section 13, the Notifying Parties submit that short read and native long read systems fall into distinct product markets, such that the activities of Illumina and PacBio do not overlap. As a result, the Transaction will not give rise to horizontal concerns. Further, as explained in Sections 19 and 20, the Transaction will not raise either vertical or conglomerate concerns.

425. As a result, the Transaction will not give rise to a SLC in the potential markets for short read and native long read systems in which Illumina and PacBio, respectively, are active, that could reduce the ability of customers to negotiate. In essence, since the Notifying Parties are not competitors, the competitive landscape after the Transaction will remain the same in both potential markets.

Efficiencies and customer benefits

24. Where notifying parties would like the CMA specifically to consider at phase 1 any efficiencies or relevant customer benefits that the notifying parties believe will arise from the merger, describe such efficiencies and provide any documents prepared internally or by external consultants that discuss such expected efficiencies or relevant customer benefits.

426. As explained in Sections 13 and 15, the Transaction will not give rise to a SLC because the Notifying Parties do not compete. Rather, their technologies are used either for different applications or for the same applications in a complementary fashion. The Notifying Parties take the view that the Transaction will generate significant merger-specific efficiencies and customer benefits in both the short-term and long-term.

427. The Notifying Parties submit that in its assessment the CMA should consider the following efficiencies and customer benefits which form the core of the Transaction's strategic and economic rationale:

- facilitate wider distribution of/access to PacBio's products and technology by enabling PacBio to benefit from Illumina's global production, and support and service infrastructure;
- increase adoption of PacBio's systems by clinical and diagnostic customers by enhancing PacBio system quality with Illumina's quality systems and system management processes;
- improve PacBio's systems using Illumina's proprietary technologies;
- enable Illumina to develop coordinated solutions (including bioinformatics) to enable customers to harness the complementary nature of the technologies; and
- accelerate innovation.

I. Facilitate distribution of PacBio's systems and technology by enabling PacBio to benefit from Illumina's global production, and support and service infrastructure

428. [redacted]

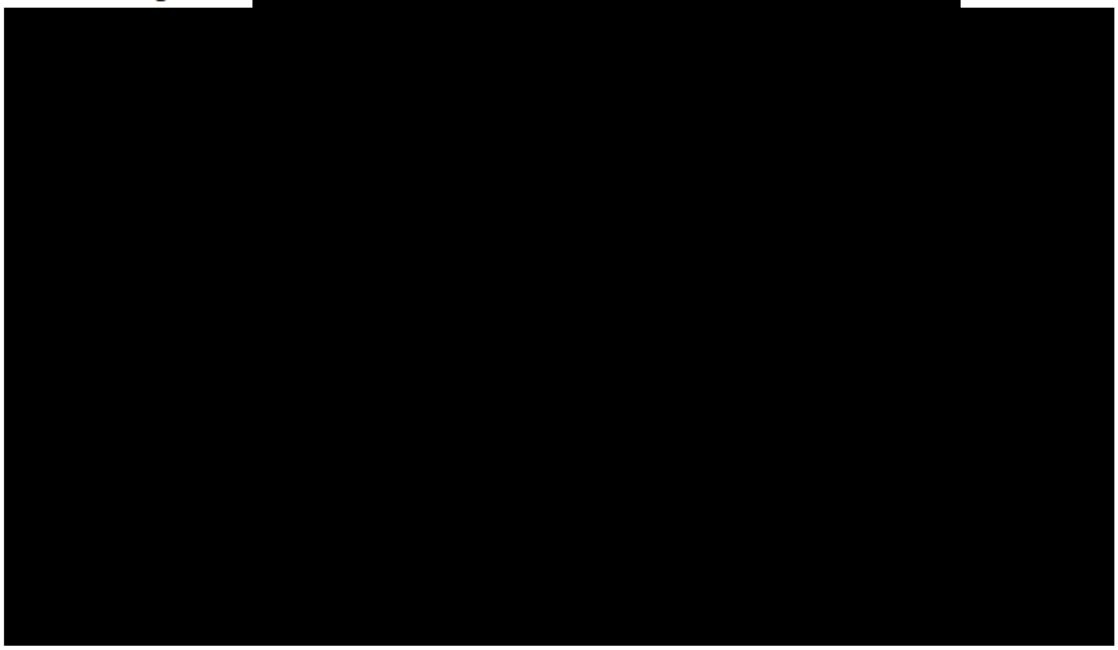
429. Illumina is uniquely positioned to significantly enhance PacBio's ability to commercialise its native long read systems in the short-term, as a result of its:

- high volume manufacturing infrastructure and engineering capabilities. [redacted]
- extensive specialist commercial teams. [redacted]
- extensive customer base, with Illumina's customer reach being [redacted] that of PacBio's;
- experience and expertise in developing reproducible workflows and processes for use in clinical settings [redacted]); and
- brand recognition and quality of customer service. [redacted].

430. After closing, PacBio will gain access to Illumina's global distribution and commercialisation infrastructure, teams, and customer base, thereby broadening its access to customers more than [redacted].[535] Reflecting this, Illumina predicts that, [redacted]

[535] [redacted].

Figure 24: [redacted]



431. Illumina has a track record in prior sequencing acquisitions of driving development of acquired technology and reducing costs, thereby accelerating customer adoption of that technology. For example, in 2006, Illumina bought Solexa. Prior to the acquisition, Illumina was a gene-testing technology company using genotyping arrays, not sequencing, and Solexa had just launched its first sequencer (the Genome Analyzer). Illumina took the view that Solexa had a promising, nascent technology that could become commercially viable with significant additional development. [redacted] Solexa's sequencing technology forms the basis for [redacted] of Illumina's total revenue (2018).

432. Other instances where Illumina acquired companies and accelerated their growth, further reducing the cost of sequencing, include:

- *Avantome*: a company with an early-stage technology for detection and sequencing of DNA on a CMOS chip. After Illumina acquired Avantome in 2008, [redacted].
- *Epicentre*: a provider of library preparation technology and specialty enzymes. Epicentre developed a technology called "Nextera", a transformative library preparation technology, simplifying and improving the sequencing workflow. [redacted].

- *Edico*: an informatics and data-analysis company whose technology accelerates and simplifies the real-time analysis of genomic information at the time of sequencing. Illumina acquired Edico in 2018 and [redacted]

433. Illumina believes that, through continued R&D investment and innovation, it can further develop PacBio's technology to increase output and lower the native long read sequencing cost per Gb.

A. Supply-side efficiency: cost reductions

434. The Transaction will enable PacBio to benefit from significant economies of scale through access to Illumina's distribution infrastructure and commercial organisation, thereby reducing its distribution costs. In addition, PacBio's products will benefit from the more efficient production processes that Illumina has developed and which PacBio would otherwise be unable to replicate in the short-to-medium-term. All funds that PacBio would have spent to develop its commercial organisation if it remained a stand-alone company could then be invested in R&D efforts to improve the quality of its existing, and to develop new, systems.

435. In addition to lower costs, the Transaction will bring a number of other short-term benefits to PacBio, including additional resources for customer service and support, increased brand recognition, and more efficient manufacturing and distribution.

B. Illumina does not have the ability or incentive to facilitate distribution of/access to PacBio's technology in the absence of the Transaction

436. Absent the Transaction, Illumina would have neither the ability nor the incentive to generate these efficiencies at PacBio. To generate the benefits contemplated by Illumina, PacBio must have direct access to Illumina's manufacturing, distribution and other service and support infrastructure. In the longer term, Illumina would also lack the ability and incentive to drive technical development, including new solutions and coordinated workflows.

II. Enhance adoption of PacBio's systems by clinical and diagnostic customers by enhancing system quality

437. As explained in response to Section 12, PacBio's native long read technology is not widely adopted in the clinical and diagnostic context, and [redacted].

438. Developing and obtaining regulatory approval for clinical and diagnostic applications is difficult, expensive, and time-consuming, and requires:

- significant resources to design and carry out studies for regulatory approval;

- significant experience and expertise working with regulatory agencies to obtain relevant approvals;
- the ability to develop and reproducibly manufacture robust systems and assays;
- reproducibility and process scalability in clinical or diagnostic settings;
- informatics able to produce actionable results for clinical diagnosis or treatment; and
- customer service and support.

439. [redacted]

440. In contrast, Illumina has successfully developed and obtained regulatory approval for clinical sequencing, with the MiSeqDX system being the first FDA-approved NGS system in the US, and end-to-end solutions for particular applications. In addition to expertise and experience, Illumina has the R&D and financial resources to develop such regulated systems and applications.

441. Illumina [redacted] a clinical-grade infrastructure and an organisation to support the creation of regulatory approved products, such as the MiSeqDx, which in 2013 became the first NGS system to receive FDA clearance. Subsequently, Illumina has received FDA clearance for its NextSeq 550Dx sequencing system and has received regulatory approvals in China and CE-IVD marking in Europe (for NIPT). [redacted]

442. Building a clinical-grade infrastructure and an organisation to obtain regulatory approvals and markings of sequencing products has required significant and ongoing investment into, among other things: building and maintaining robust, complex, and ISO-certified quality and control systems, manufacturing, and operations; and a large number of personnel with highly specialised expertise, including acquiring a company that focused on bringing regulatory-cleared products to market.

A. <u>Demand-side efficiency: Introduction of new products for clinical and diagnostic customers</u>

443. The Transaction will enable Illumina to develop PacBio's native long read systems for clinical and diagnostic applications. PacBio will benefit from Illumina's experience and expertise in developing and reproducibly manufacturing robust systems and assays for use in clinical and diagnostic applications.

444. As explained above in Section 13, there are certain applications for which customers can use both short read and native long read technologies to take advantage of their

complementary strengths. The complementary nature of Illumina's short read systems and PacBio's native long read systems could be used in clinical and diagnostic settings to resolve SVs, HLA, haplotype phasing (*e.g.*, CFTR), and RUGD, for example:

- **HLA**: as explained earlier, short read systems are well-suited for screening a typically large number of potential donors and identifying the incompatible ones. Native long read systems can then be used to provide additional information about potentially compatible donors. Illumina can use PacBio's native long read systems to develop a clinical diagnostic test, which will be used as a "reflex" test to provide additional information about compatibility to potential recipients;

- **CFTR Haplotype phasing**: where less costly short read sequencing can be used to screen whether certain variants that can cause diseases only when both gene copies of the allele are defective in a given sample, for example. If such variants are present, native long-read sequencing can then be used to determine whether or not such disease-causing variants exist on both the maternal and paternal gene copies, to elucidate the presence and severity of the disease, or if such variants exist only on one gene copy, to indicate the absence of the disease. This ability of native long read systems could form the basis of clinical applications where PacBio's native long read data are used as a "reflex test" to confirm or augment the results produced by short read systems;

- **RUGD**: where short read systems, such as Illumina's, are the first line sequencing technology used due to their lower cost, high accuracy and throughput, and ability to sequence the most known actionable variants (*e.g.*, SNVs). When testing beyond first line short read sequencing is appropriate, clinical tests using native long read systems could be developed to:

    - "phase" variants with the aim of identifying an allele causing the disease; or

    - to potentially elucidate whether the disease is caused by a larger variant such as a larger SV.

445. Illumina anticipates that it can materially accelerate the introduction of PacBio's systems into clinical and diagnostic applications.

III. Improve PacBio's systems using Illumina's proprietary technologies

446. Illumina envisions many opportunities to use its existing proprietary technologies and know-how to improve PacBio's systems. [redacted]

447. [redacted]

[redacted]

448. [redacted]

449. [redacted]

IV. Enabling Illumina to develop coordinated solutions

450. The Transaction would enable Illumina to develop coordinated, complementary solutions for "reflex" testing, initial discovery, and coordinated sequencing applications.[536]

451. [redacted]

- [redacted]

[536] Please see Section 13 above.

[537] [redacted]

[redacted]

- [redacted]

- [redacted]

- [redacted]

- [redacted]

[redacted].

452. [redacted]

[redacted]

453. The development of coordinated workflows cannot be achieved in the absence of the Transaction.

454. The Notifying Parties have not had the ability nor incentive to collaborate in the manner enabled by the Transaction.

455. In addition, replicating the incentives to develop solutions to co-ordinate and analyse datasets in the dynamic sequencing sector, where there are different technical solutions (in the face of different proprietary solutions today), would be difficult absent the Transaction. In a dynamic environment of this nature, the value of undertaking such an initiative through collaboration, and the uncertainty associated with making such investments, impose contracting and monitoring costs that are avoided through common ownership of the two technologies.

V. The Transaction will accelerate innovation

456. Illumina's strong incentives to innovate will not be reduced by the Transaction. Because the Notifying Parties are not competitors today, the Transaction will not reduce Illumina's ability and incentives to innovate including using PacBio's technology.[538]

457. [redacted]

458. [redacted]

459. [redacted]

[538] Please see Section 18, regarding how Illumina has been the driving force in constantly reducing sequencing costs.

Other information

25. Provide any other information that the notifying parties consider may be relevant to the CMA's Phase 1 investigation.

Not applicable.

PART V – THIRD PARTY CONTACT DETAILS

26. Provide contact details for the relevant competitors and customers of the merger parties for (where applicable):

(a) **each of the Candidate Markets in which they overlap;**

(b) **each of the Candidate Markets in which the merger parties have a vertical relationship (providing contact details for the relevant competitors and customers of the merger parties on the upstream and downstream markets on which each merger party is active); and**

(c) **each of the Candidate Markets in which each of the merger parties provides related products/services.**

460. Please see [redacted]

27. To the extent applicable, provide contact details for relevant suppliers providing an estimate of the annual value and/or volume of purchases.

461. Please see [redacted].

28. To the extent applicable, provide contact details for each of the companies that the notifying parties consider are likely to enter and expand into any of the Candidates Markets.

462. Please see [redacted].

29. Provide the name and contact details, including address, and email address and telephone number, of:

(a) **any relevant regulatory authorities covering the industry in which the merger parties overlap, have a vertical relationship, or supply related product(s)/service(s).**

(b) **any trade associations which cover the industry in which the merger parties overlap, have a vertical relationship, or supply related product(s)/service(s).**

463. Please see [redacted].