EN

Case No COMP/M.5264 - INVITROGEN / APPLIED BIOSYSTEMS

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REGULATION (EC) No 139/2004
MERGER PROCEDURE

Article 6(1)(b) NON-OPPOSITION
Date: 11/11/2008

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PUBLIC VERSION

MERGER PROCEDURE
ARTICLE 6(1)(b) DECISION

In the published version of this decision, some information has been omitted pursuant to Article 17(2) of Council Regulation (EC) No 139/2004 concerning non-disclosure of business secrets and other confidential information. The omissions are shown thus […]. Where possible the information omitted has been replaced by ranges of figures or a general description.

To the notifying party

Dear Sir/Madam,

Subject: Case No COMP/M.5264 - Invitrogen/ Applied Biosystems
Notification of 7 October 2008 pursuant to Article 4 of Council Regulation No 139/2004[1]

1. On 7 October 2008, the Commission received notification of a proposed concentration pursuant to Article 4 of Council Regulation (EC) No 139/2004 ('the EC Merger Regulation') by which the undertaking Invitrogen Corporation ('Invitrogen', United States of America) acquires within the meaning of Article 3(1)(b) of the Council Regulation control of the undertaking Applied Biosystems Inc. ('Applied Biosystems', United States of America) by way of purchase of shares.

2. After examination of the notification, the Commission has concluded that the notified operation falls within the scope of the Merger Regulation and does not raise serious doubts as to its compatibility with the common market and the functioning of the EEA Agreement.

I. THE PARTIES

3. Invitrogen is a US-based life science company. It is organised in two principal business segments: BioDiscovery and Cell Systems. The BioDiscovery unit encompasses molecular biology, cell biology and drug discovery product lines that are used *inter alia* to purify and copy nucleic acid (DNA and RNA) and improve gene cloning, gene expression and gene analysis techniques. The Cell Systems unit supplies products such as sera, cell and tissue culture media and reagents used in life sciences research, as well as in processes to grow cells in the laboratory and produce pharmaceuticals and other highly valued proteins.

[1] OJ L 24, 29.1.2004, p. 1.

4. Applied Biosystems Inc. ('Applied Biosystems') is also a US-based life science company. It is a global supplier of instrument-based systems, consumables,[2] software, and services to academic research, the life science industry and commercial markets.

II. THE OPERATION

5. On 11 June 2008, Applera Corporation (now known as Applied Biosystems Inc.[3]) entered into an Agreement and Plan of Merger with Invitrogen and Atom Acquisition LLC, a wholly-owned subsidiary of Invitrogen, whereby Applied Biosystems will merge with and into Atom Acquisition LLC. Atom Acquisition LLC will continue as the surviving company and a direct wholly-owned subsidiary of Invitrogen.

6. Invitrogen will therefore acquire sole control of Applied Biosystems and the proposed transaction constitutes a concentration within the meaning of Article 3(1)(b) of the EC Merger Regulation.

III. COMMUNITY DIMENSION

7. The undertakings concerned have a combined aggregate world-wide turnover of more than EUR 2 500 million (Invitrogen: EUR 935 million, Applied Biosystems: EUR 1 603 million). The aggregate Community-wide turnover of each undertaking concerned is more than EUR 100 million (Invitrogen: EUR […], Applied Biosystems: EUR […]. In […], the combined turnover of all the undertakings concerned is more than EUR 100 million. In each of the aforementioned Member States the aggregate turnover of each undertaking concerned is more than EUR 25 million while neither undertaking concerned achieves more than two-thirds of its aggregate Community-wide turnover within one and the same Member State.

8. The notified operation therefore has a Community dimension pursuant to Article 1(3) of the EC Merger Regulation.

IV. COMPETITIVE ASSESSMENT

9. The proposed transaction will combine two major suppliers of products and services to the life sciences research industry. Invitrogen is predominantly a reagents supplier with *de minimis* sales of instruments. Applied Biosystems on the other hand, in addition to its supply of reagents, also makes significant sales of instruments that are used in life sciences research and related areas.

10. A reagent is a substance or compound used during a chemical or biochemical reaction in an artificial model system used to facilitate experimentation in the laboratory. Reagents are the components which are added together with biological samples in an experimental system in the laboratory in order to bring about or facilitate a reaction or to see whether a reaction occurs. Reagents in life science include buffers, enzymes, salts, dyes and stains.

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2 Consumables being defined as products customers buy recurrently, i.e. items that get used up.

3 At the time of the signing of the Merger Agreement, Applera Corporation consisted of two business divisions: the Applied Biosystems Group and the Celera Group. On 1 July 2008, Applera Corporation separated from Celera Corporation, which became an independent publicly traded company. Applera Corporation changed its name to Applied Biosystems Inc. on the same day.

11. The parties' activities overlap in the supply of reagents for: (i) nucleic acid purification; (ii) nucleic acid amplification; (iii) gene silencing; (iv) DNA microarrays and (v) mass spectrometry. The parties' activities also overlap to a limited extent in the supply of DNA ladders and markers.

Relevant product markets

1. Nucleic acid purification

12. Nucleic acid purification is the process of extracting pure DNA (including plasmids) or RNA[4] material from a variety of sample types (blood, mammalian tissue, plant tissue, bacteria, etc.). Nucleic acid purification is the first step in many nucleic acid analyses, where DNA or RNA is extracted from the collected sample and prepared for downstream applications, including amplification and DNA sequencing.

13. The notifying party submits there are several methods of nucleic acid purification including: (i) column-based; (ii) liquid-based; (iii) magnetic bead-based; and (iv) a combination of these methods although the most commonly used methods for the purification of both DNA and RNA in standard academic research are the column- and liquid-based methods. The notifying party submits that these two methods are generally used to purify both DNA and RNA with the selection of a particular purification technology being determined by the researcher based on his experience with the sample and the type of analysis that will be required.

14. According to the notifying party, the same reagents are generally used for both DNA and RNA purification processes[5] and the same core nucleic acid purification methods described above (i.e. column- and liquid-based) are generally offered by all the leading suppliers for purification of both DNA and RNA. In view of these considerations, the notifying party submits that the relevant product market should be defined as nucleic acid purification without any distinction by purification method or reagent.

15. The Commission's market investigation has confirmed that both column- and liquid-based methods can be used to purify both DNA and RNA. However, many respondents indicated that the same reagents cannot be used for both DNA and RNA purification processes. Despite these indications that a distinction should be drawn between reagents for DNA purification and reagents for RNA purification, the precise market definition can be left open in the present case as it would not alter the competitive assessment.

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4 DNA (deoxyribonucleic acid) is a chemical (composed of two complementary strands) inside the nucleus of a cell that carries the genetic instructions for making living organisms. RNA (ribonucleic acid) is a chemical similar to a single strand of DNA. RNA delivers DNA's genetic message to the cytoplasm of a cell where proteins are made. A plasmid is an extra-chromosomal ring of DNA which occurs naturally in bacteria. It is capable of replicating autonomously within a cell.

5 According to the notifying party, the chemistries of the reagents are very similar with only the proportions differing slightly to ensure the sample is 'RNase free'. As RNA degrades more easily than DNA, chemistries for RNA purification must ensure that the buffer and consumables used (plastic tubes, pipette tips, glassware etc) are sterilised.

2. Nucleic acid amplification

Introduction

16. The notifying party submits that in order to properly assess the effects of the operation on the markets for reagents used in nucleic acid amplification, a distinction should be drawn between the research market and the commercial human diagnostic market in the light of patent restrictions and other differences in the competitive landscape between the two fields. In nucleic acid amplification, Applied Biosystems' activities are limited to research applications […]. Moreover, the activities of all of Applied Biosystems' sub-licensees, […], are similarly […] to the extent they are based on the same […].[6]

17. Nucleic acid amplification is a technology for copying a segment of a nucleic acid (DNA or RNA) to enable further analysis of the sample. This is most commonly achieved through the use of the Polymerase Chain Reaction ('PCR'). There are four basic PCR processes each of which is described in more detail below at section A.

18. According to the notifying party there are two main groups of reagents used in PCR processes: (a) standard reagents that are common to all PCR processes and (b) differentiated reagents that are largely specific to one or more particular PCR processes. A description of these two groups of reagents follows the explanation of the four PCR processes at section B.

19. The Commission will then address the issue of product market definition in nucleic acid amplification at section C.

A. The Polymerase Chain Reaction

(i) Conventional Polymerase Chain Reaction (PCR)

20. The PCR reaction derives its name from one of its key components, a DNA polymerase, that is used to amplify a short strand of DNA (a template)[7] by *in vitro* enzymatic replication. As PCR progresses, the DNA generated is itself used as a template for subsequent rounds of amplification. Thus, what is set in motion is a chain reaction, in which the DNA template is exponentially amplified. With PCR it is possible to amplify a piece of DNA by several orders of magnitude thereby generating millions of copies of the DNA template. PCR requires an instrument known as a thermocycler which maintains the appropriate temperature for the three steps of each PCR cycle.[8]

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6 Roche and Applied Biosystems were the legal successors of the two companies that first developed PCR, Perkins Elmer and Cetus. […]. In […], Roche and Applied Biosystems signed an agreement […]

7 Templates are often obtained from a tissue or blood sample through purification.

8 These steps are: denaturation, primer annealing and primer extension. In the denaturation step, the DNA template is heated to a high temperature which breaks the bonds holding together the two complementary strands of the DNA's double helix. This results in two single stranded DNA molecules. In the next step, (primer annealing) the temperature is reduced so that oligonucleotides called primers can bind (or anneal) with their complementary sequences in the now single stranded DNA. Finally, in primer extension, the temperature is increased to the point at which the DNA polymerase enzyme functions optimally and synthesises the new DNA strand. It attaches to the primers and extends them by adding on nucleotides

(ii) Quantitative PCR (qPCR)

21. Although conventional PCR (or 'end-point PCR') can be used to accurately detect the presence of the target sequence in the specimen, it does not allow for the precise determination of its quantity. In order to do attain both these objectives (i.e. amplification and quantification), customers must use a process known as real-time PCR or quantitative PCR ('qPCR'). The procedure follows the general principle of PCR but in contrast to the conventional PCR technique, the qPCR technique allows users to accurately measure the amount of a target sequence that has been reproduced after each cycle using a qPCR thermocycler.

22. This quantification of the amplified sequences is possible through the use of a detection chemistry, which typically fluoresces with greater intensity as more of the target sequence is replicated. Greater accuracy is achieved using qPCR than using conventional PCR because measuring the rate of signal increase is a more accurate indicator of the initial target number than measuring the final yield after many cycles.[9] A qPCR thermocycler regulates the temperatures at which the PCR occurs but it is also equipped with a special camera that measures the phosphorescence of the detection chemistry.

23. According to the notifying party, there are two main types of detection chemistry used in qPCR: dyes and probes[10]. Dyes (or nucleic acid stains) are molecules that become fluorescent (glow) when they bind to any double-stranded DNA. Probes, which are oligonucleotides that contain fluorescent labels attached to them, bind to a specific sequence of DNA and release a fluorescent signal or increase in fluorescence when that sequence is replicated.

(iii) Reverse Transcriptase PCR (RT-PCR)

24. Nucleic acid amplification can also be performed using RNA templates. In this case, the process is known as reverse transcriptase PCR (or 'RT-PCR'). In the first step of RT-PCR, the RNA template is combined with a reverse transcriptase enzyme ('RT enzyme') that synthesizes a strand of complementary DNA ('cDNA'). This cDNA is then used as the template for amplification (i.e. PCR).

(iv) Quantitative Reverse Transcriptase PCR (qRT-PCR)

25. qRT-PCR follows the same steps as RT-PCR, with the addition of a detection chemistry, which allows the user to quantify the target RNA sequence during the course of the experiment.

B. Reagents for PCR

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that are complementary to the single stranded templates. This process results in two copies of each piece of DNA that was present in step one.

9 The difference between conventional PCR and qPCR is that any enzymatic activity measurement is more accurate if it is made kinetically, that is to say, during the course of the enzymatic reaction rather than at its end.

10 The notifying party notes that in addition to these two detection chemistries, there is a third, primer-based detection chemistry that is less commonly used by customers. Primer-based detection products are more specific than dyes but less specific than probes. As Applied Biosystems is not active in primer-based detection and Invitrogen made negligible sales of these products in the EEA in 2007, this type of detection chemistry is not considered further.

(i) Standard reagents

26. The notifying party submits there are three main types of standard PCR reagents that are common to all four PCR processes (i.e. conventional PCR, qPCR, RT-PCR and qRT-PCR). These standard reagents are (i) primers / oligonucleotides; (ii) dNTPs (nucleotides); and (iii) ancillary reagents such as buffers, salts and distilled water. It is argued that these are standard, commodity products that customers can purchase from a variety of different suppliers on either a stand-alone basis or in 'mastermixes' that typically include all of the PCR reagents needed for the desired PCR process to be performed. However, in particular for dNTPs and buffers, the vast majority of product sold is in the form of a mastermix.

27. Primers are individually customised oligonucleotides that serve as the starting point for DNA amplification. Oligonucleotides used as primers for PCR techniques are customized to recognize a specific gene sequence. A pair of two primers flanking the gene region of interest is required for any PCR process (for this reason, PCR primers are often referred to as "gene-specific" or "target-specific" primers). During the PCR process, the primer binds to a single stranded piece of DNA and subsequently, the primer becomes the starting point at which the polymerase adds the new nucleotides.

28. dNTPs are the structural components, or building blocks of DNA. A nucleotide consists of a base (one of four chemicals: adenine, thymine, guanine and cytosine) plus sugar and phosphate.

29. Ancillary reagents such as buffers and distilled water are commodity, non-differentiated components that enable the PCR applications. Buffers ensure optimal reaction conditions by maintaining a constant pH. According to the notifying party, there is no difference in the buffer type based on the process. Rather the choice of buffer is made in relation to the enzymes and sample used.

(ii) Differentiated reagents

30. The notifying party submits that three main groups of differentiated reagents can be distinguished for PCR. These are: (i) thermostable DNA polymerase; (ii) detection chemistries (dyes and probes); and (iii) reverse transcriptase enzymes. Differentiated reagents are sold on a stand alone basis or as part of a mastermix.

31. Thermostable DNA polymerases are naturally occurring enzymes that are used in all PCR processes. According to the notifying party, the common feature of all DNA polymerase enzymes that are used in PCR which distinguishes them from all other DNA polymerases (such as those used in DNA sequencing) is their stability at the relatively high temperature at which PCR elongation occurs. According to the notifying party, there is no industry standard temperature at which a DNA polymerase is considered thermostable. However, if a DNA polymerase can be active and functional at temperatures greater than 90°C which are used for denaturation of DNA during the first step of a PCR cycle, it will generally be considered thermostable.

32. The most commonly used thermostable polymerase in PCR is Taq polymerase (which is licensed by Applied Biosystems for use in the research field). There are a number of alternative thermostable DNA polymerase including Tfi, Tth, Pfu and Pfx. The notifying party submits that thermostable DNA polymerases can be divided into two groups: those

with a proofreading activity and those without (including Taq).[11] In spite of this distinction, the notifying party submits that each thermostable DNA polymerase could be substituted for Taq DNA polymerase in virtually any application as they are all capable of synthesising DNA and are, by definition, able to withstand high temperatures. Consequently, the notifying party submits that all thermostable DNA polymerases form part of the same product market.

33. Detection chemistries enable scientists to monitor the amplification of individual molecules during qPCR and qRT-PCR. There are two main types of detection methods used in quantitative PCR processes: dye-based and probe-based. In dye-based detection chemistry, the dye basically binds to any double stranded DNA and emits light when excited. The fluorescence increases as the amount of PCR product increases and is quantified after each completed PCR cycle. Dye-based detection chemistries are normally sold as part of a mastermix and not on a stand alone basis.

34. Probe-based detection chemistry is more specific than dye-based detection chemistry in that the probe is gene-specific and will only bind to a specific piece of the DNA template rather than to any double stranded DNA. The light given off in each PCR cycle is quantified using a fluorescence detector instrument coupled to a computer. Probes can be supplied in one of two ways: pre-designed or custom made. Pre-designed probes are offered by suppliers which have developed 'libraries' of probes for pre-defined target sequences. If a researcher's particular gene target of interest is not available from one of these libraries, he can submit a design of his gene target sequence of interest to a custom oligonucleotide manufacturer. The manufacturer then synthesises and delivers the target specific 'assay' (a set of primers and probe) to the customer on a one-time, custom basis. In addition, probes can be labelled with different reporter dyes allowing amplification of several distinct sequences in one reaction tube (multiplexing) and quantification.[12] Probes, whether pre-designed or custom made are normally sold on a stand alone basis rather than as part of a mastermix.[13]

35. The notifying party submits that a significant number of customers use both dyes and probes for detection, depending on the specific experimental design, and may switch from one technology to the other within a single project or experiment based on scale or costs of reagents or detection chemistries.

36. Reverse transcriptase enzyme is required in all reverse transcriptase PCR processes (i.e. RT-PCR and qRT-PCR). In the first step of reverse transcriptase PCR, the RNA template is combined with the RT enzyme which synthesises a strand of complementary DNA ('cDNA'). This cDNA is much more stable than RNA and is then used as the template for

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[11] Proofreading thermostable DNA polymerase are more accurate than non-proofreading polymerase, according to the notifying party, as they can remove an incorrectly incorporated nucleotide from a growing chain of DNA.

[12] The notifying party submits that a distinction should be made between an intercalating dye used in dye-based detection chemistries, on the one hand, and reporter or tagging dyes used *inter alia* for probe labelling, on the other hand.

[13] Applied Biosystems offers a few qRT-PCR kits that include a qRT-PCR mastermix together with a specific Taqman (pre-designed) probe. The price of this combination offering is higher than the sum of the price of the mastermix and probe when purchased separately, representing a 'convenience premium'.

amplification either immediately or at a later stage.[14] RT enzymes can be divided into two groups: 'native' and 'engineered.' Native (or naturally occurring) RT enzymes are not patented. Engineered RT enzymes on the other hand, which have been genetically modified within the laboratory, may be protected by patents. Engineered enzymes typically have some performance advantages over native RT enzymes such as an ability to function at higher temperatures.

C. Market definition in nucleic acid amplification

(i) Submission of the notifying party

37. According to the notifying party, customers typically select reagents for nucleic acid amplification on the basis of the specific needs of their research project, including specificity and time requirements as well as cost. A selection of the appropriate reagents therefore generally depends on (i) the type of PCR process required for the experiment (e.g. requiring exact specificity in quantification necessitating quantitative PCR processes that include detection chemistries); (ii) the available sample (a DNA sample, or an RNA sample, which would require a reverse transcriptase PCR process); and (iii) the cost and scale requirements of their experiment.

38. In view of the above considerations, the notifying party submits that for the purpose of defining relevant product markets, a distinction should be drawn between conventional PCR reagents, quantitative PCR reagents, conventional RT-PCR reagents and quantitative RT-PCR reagents.

39. The notifying party further submits that a distinction should be drawn between 'standard' and 'differentiated' reagents whether these are sold on a stand alone basis or as part of a mastermix.[15]

40. In the case of differentiated reagents, the notifying party submits that all thermostable DNA polymerase form part of one product market as they are substitutable from the demand side in virtually any application. In a similar fashion, the notifying party submits that it would not be appropriate for the purposes of market definition to distinguish between RT enzymes (i.e. on the basis of whether they are native or genetically engineered) as all types of RT enzyme can be used in virtually all reverse transcriptase applications. In the case of detection chemistries, although the notifying party notes that many researchers may use both dye-based and probe-based methods in their work, it acknowledges that a distinction should be drawn between the two as dyes are less specific than probes and generally less expensive.

41. The notifying party submits that the relevant markets in the present case, which primarily concern the research field, should not include both instruments and reagents. In support of this statement, the notifying party notes that instruments for PCR-based

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[14] According to the notifying party, unlike RNA samples, cDNA samples can be stored without risk of denaturation and therefore many researchers run the amplification process on the cDNA sample – that was obtained using the RT enzyme – at a later point in time.

[15] As the parties' sale of standard reagents on a stand alone basis would not result in an affected market regardless of the definition retained, the question whether the sale of each standard reagent on a stand alone basis constitutes a distinct relevant product market can be left open in the present case and such standard stand alone reagents are not discussed further in the present decision.

amplification are open systems and customers can use a wide variety of reagents on any supplier's instruments. It further notes that a number of leading reagent suppliers do not market instruments which has not affected their ability and incentives to compete forcefully and develop and market 'best of breed' reagents.

(ii) Results of the market investigation

42. The market investigation has broadly confirmed the appropriateness of the four PCR processes identified by the notifying party (i.e. conventional PCR, qPCR, RT-PCR and qRT-PCR).[16] A limited number of respondents identified alternative amplification technologies such as NASBA (Nucleic Acid Sequence Based Amplification) but none of these was generally perceived as offering a viable alternative to PCR at the present time.

43. In terms of demand-side substitution between the four PCR processes, the market investigation demonstrated that each technique has particular attributes for the end user and are generally not perceived as substitutes. For example, whilst conventional (or end point) PCR and RT-PCR enable a user to detect the presence of a target sequence, its quantification is only possible using quantitative methods. In addition, a number of respondents indicated that a distinction should be made between conventional PCR and qPCR on the one hand and RT-PCR and qRT-PCR on the other in terms of the initial sample as the reverse transcriptase processes use RNA as the starting point rather than DNA.

44. At the same time, however, a number of respondents indicated a certain degree of demand-side substitution could exist in terms of the instruments used in the four PRC processes. In this regard, it was noted that quantitative thermocyclers (used in qPCR and qRT-PCR) could theoretically be used to perform conventional PCR (i.e. end point and RT-PCR) although it was also acknowledged that this would not be cost effective and substitution would only be in one direction (i.e. conventional thermocyclers could not be used to perform quantitative PCR processes). The market investigation also confirmed that software used to analyse the results of PCR processes is typically integrated in the instrument and supplied by the instrument manufacturer.

45. The market investigation tended to support the notifying party's submission that instruments used in PCR in the research field at this stage of market development are 'open' in the sense that the reagents used on a particular instrument do not necessarily have to be supplied by the manufacturer of that instrument.[17] This contrasts with instruments used in human diagnostic applications which were generally perceived to be 'closed.'

46. In terms of reagents, although a majority of competitors considered that the same reagents could be used in more than one PCR process, the market investigation revealed that customers tend to purchase reagents that are designed or optimised for a particular PCR process.

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16 A number of respondents also identified additional PCR processes such as the Sanger method, multiplex PCR, mutagenesis and emulsion PCR. The notifying party submits that these do not constitute separate product markets. Moreover, the merging parties' activities to the extent they may overlap in these additional PCR processes are reflected in the sales of stand alone reagents, such as thermostable DNA polymerase, that can be used in these other methods.

17 Question 21 of the Commission's questionnaire to customers and question 24 of the Commission's questionnaire to competitors dated 10 October 2008.

47. The market investigation was somewhat less clear as regards the manner in which customers purchase reagents (i.e. on a stand alone basis or as part of a mastermix). Whilst many customers indicated a preference for mastermixes in view of their convenience and the consistency of results they could achieve, others indicated a preference for stand alone reagents because of their cheaper cost and the flexibility they could afford the user.[18] This was reflected in the views of many reagent suppliers which indicated they supply reagents both on a stand alone basis and as part of a mastermix so as to respond to differing customer preferences.[19] When specifically asked about switching, a number of customers indicated that they would not switch from mastermixes to stand alone products if the former were to increase by 5-10% on a non-transitory basis (the 'SNNIP test').[20] This would indicate that mastermixes and stand alone products do not form part of the same relevant product market.

48. As far as differentiated reagents are concerned, a majority of customers in the market investigation highlighted differences between the various thermostable DNA polymerase (i.e. Taq, Tfi, Tth, Pfu) in terms of functionality and suitability for certain PCR processes.[21]

49. Likewise, a majority of customers indicated that a distinction should be made between genetically engineered and native RT enzymes given their differing properties and that they would not switch from genetically engineered to native enzymes if the former were subject to a small but significant and non-transitory increase in price.[22]

50. In terms of detection chemistries, the market investigation has to a large extent confirmed the relevance of a distinction between dye-based and probe-based detection chemistries from the demand-side perspective with many respondents highlighting the specificity that can be achieved with probe-based methods. Moreover, if the price dye-based detection chemistries were to increase by 5-10% on a non-transitory basis, a majority of customers indicated that they would not switch to using probe-based detection chemistries.[23] In terms of supply-side substitutability, however, a majority of competitors indicated that suppliers usually offer both dye-based and probe-based detection chemistries.

(iii) Conclusion on the relevant product markets in nucleic acid amplification

51. In light of the above, the Commission considers that for the purposes of assessing the competitive effects of the proposed transaction on nucleic acid amplification, a distinction should be made in the first instance between standard and differentiated reagents. Taking into account the results of the market investigation, further segmentation within differentiated reagents appears warranted as follows: between Taq DNA polymerase and other thermostable DNA polymerase; between native and genetically engineered RT

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18 Question 29 of the Commission's questionnaire to customers dated 10 October 2008.

19 Question 29 of the Commission's questionnaire to competitors dated 10 October 2008.

20 Additional request for information addressed to certain users of PCR mastermixes on 31 October 2008.

21 Questions 36 and 37 of the Commission's questionnaire to customers dated 10 October 2008.

22 Questions 41 and 42 of the Commission's questionnaire to customers and question 40 of the Commission's questionnaire to competitors dated 10 October 2008.

23 Questions 33 of the Commission's questionnaire to customers dated 10 October 2008.

enzymes; and between dye-based and probe-based detection chemistries.[24] Furthermore, in view of the results of the market investigation, a differentiation between reagents that are sold as part of mastermix and those that are sold on a stand alone basis appears justified for the competitive assessment of the proposed transaction. In the context of mastermixes, it is appropriate to distinguish between each of the four main PCR processes (i.e. conventional PCR, qPCR, RT-PCR and qRT-PCR) given the distinction between conventional (end point) PCR and quantitative PCR processes as well as the difference in sample choice (i.e. DNA for PCR and qPCR, RNA for RT-PCR and qRT-PCR). Moreover, given the focus of the proposed transaction on research applications, instruments and reagents used in PCR should not be considered as forming part of the same product market, in contrast to human diagnostics markets.

3. Gene silencing

52. Gene silencing is the process by which the expression of a particular gene is inhibited (i.e. the gene is 'switched off'). The most common downstream application for gene silencing products is gene function studies (e.g. to study what happens when a gene is switched off). Gene silencing applications are also being developed for therapeutic uses (e.g. to stop or prevent the expression of a gene associated with disease or biological process) but by companies other than Invitrogen or Applied Biosystems.

53. The process is brought about by the introduction of 'effectors' into the cell by means of 'delivery systems.' Commonly used effectors include synthetic small interfering RNA (siRNA) and vector-based short hairpin RNA (shRNA). The effect on gene expression with vector-based RNAi is longer lasting than with siRNA (i.e. the gene is switched off for longer).

54. According to the notifying party, delivery systems can use either electrical or chemical means with the choice of delivery system depending on the researcher's preferences and the on the receptiveness of the target cell to each method[25].

55. The notifying party submits that the relevant product market is for gene silencing products, that is to say effectors and delivery systems combined (excluding instruments), as suppliers of gene silencing products are typically active in effectors and delivery systems.

56. Responses to the market investigation concerning the question of product market definition were not conclusive. However, as the proposed transaction does not give rise to any affected market regardless of the definition retained (i.e. whether effectors and delivery systems are considered together or separately and even in the case of a narrower segmentation within effectors and delivery systems), the product market can be left open in the present case and gene silencing is not discussed further in the present decision.

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[24] This differentiation between dye-based and probe-based detection chemistries is relevant in the context of mastermixes given the fact that there would be no affected market for these detection chemistries on a stand alone basis.

[25] With electrical means (‘electroporation’) an instrument is used to pass an electrical current through the cell to open up the pores in the cell membrane through which the effector can be introduced. The primary method for chemical effector introduction is commonly called lipofection and is commonly achieved using lipids which fuse with the cell membrane to introduce the effector. Delivery is also possible through viral delivery.

4. DNA microarrays

57. According to the notifying party, DNA microarrays are a research tool used by molecular biologists to study genetic variation, gene expression, and other aspects of a cell's genetic composition. A DNA microarray consists of series of thousands of microscopic spots of DNA oligonucleotides each containing picomoles[26] of a specific DNA sequence. This sequence can be a short section of a gene or other DNA element. These can be either spotted on the microarray, or they can be synthesized directly on the microarray. By overlaying fluorescently labelled nucleic acid on to the microarray, researchers can observe (via a microarray scanner) the binding between their sample and the DNA attached to the microarray.

58. The notifying party submits that the relevant product market consists of consumables for DNA microarray analysis, which include arrays and related products used in the microarray analysis such as amplification and labelling chemistries and basic reagents used in the process. It submits that suppliers generally supply both the arrays and other related reagents and customers generally purchase arrays together with reagents. Consequently, in the notifying party's view, a distinction between arrays and reagents for microarray analysis would be highly artificial.

59. The market investigation has shown a diverse range of opinions concerning DNA microarrays and consequently does not allow for firm conclusions to be drawn regarding the scope of the product markets. In particular, it is not evident that suppliers offer arrays and other related reagents together or indeed that customers have a clear preference to purchase them concurrently. Moreover, there were indications that the regents used in DNA microarrays could be used in other applications.

60. For the purposes of the present investigation, however, it is not necessary to determine the precise scope of the relevant product markets in DNA sequencing as no competition concerns would arise under any alternative definition and consequently DNA sequencing is not discussed further in this decision.

5. Mass spectrometry

61. Mass spectrometry is used to identify the chemical composition of a sample on the basis of the mass-to-charge ratio of charged particles. According to the notifying party, the two primary applications of mass spectrometry in the life science research field are chemical analysis and protein quantification.

62. The three essential functions of a mass spectrometer are: (i) a small sample of compound is ionized, usually to cations (positively charged ions) by loss of an electron (the ion source); (ii) the ions are sorted and separated according to their mass and charge (the mass analyzer); and (iii) the separated ions are then detected and tallied, and the results are displayed on a chart (the detector). According to the notifying party, the use of reagents in mass spectrometry is limited in comparison to other processes in the life science field such as gene expression and gene sequencing. Although alternative methods can be used to identify proteins, such as ELISA (Enzyme-Linked ImmunoSorbent Assay) or

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26 One millionth of a millionth of one mole; a mole being the SI unit of amount of substance equal to the quantity containing as many elementary units as there are atoms in 0.012 kg of carbon-12.

Western blotting, the notifying party submits that mass spectrometry should be distinguished from these methods in view of its high degree of specificity.

63. The notifying party further submits that instruments for mass spectrometry are 'open' and customers that purchase consumables for these instruments can choose between products from a number of competing suppliers. Consequently, it considers that mass spectrometry instruments and reagents constitute separate product markets. In the case of reagents, it considers only reagents that are specific to mass spectrometry and are not used in other applications should be considered.

64. For the purposes of the present case, however, it is not necessary to reach a conclusion on the definition of the relevant product market as the proposed transaction would not give rise to any competition concerns whatever the product market definition considered.

6. DNA ladders and markers

65. DNA ladders and markers are commoditised products used as internal markers to determine the length of PCR products (i.e. the resultant DNA molecules that are products of the PCR reaction). The notifying party submits that they are optional products used in connection with conventional PCR after the process is concluded and are therefore always sold as stand alone products. It further submits that both ladders and markets are substitutable from a demand-side perspective.

66. In the present case, however, the product market definition can be left open as it would not alter the competitive assessment.

Relevant geographic markets

67. The notifying party submits that the relevant geographic markets in the present case are at least EEA-wide. In this regard, it notes that suppliers are generally active globally and typically offer, from centralised production facilities, identical products regardless of the customer's location. In addition, it submits that transport costs are not significant and there are no significant price differences between member states. As many customers order the products under consideration via the internet, phone or fax, the necessity of having a local infrastructure in each member state is not seen as a key determinant of success. Finally, it submits there are no regulatory or other barriers to trade that would indicate narrower geographic markets.

68. In the market investigation, the overwhelming majority of respondents expressed the view that the markets are at least EEA-wide.[27] Even though many respondents remarked that is important for suppliers to be represented in each member state to promote effective sales relationships and product service, the market investigation demonstrated that in the main there are no differences in the type of products supplied or their price between member states. It is therefore concluded that the relevant geographic markets in the present case are at least EEA-wide.

Competitive assessment

Introduction

[27] Question 55 of the Commission's questionnaire to customers and question 65 of the Commission's questionnaire to competitors dated 10 October 2008.

69. The notifying party submits that the research market for life science technology is characterised by a number of features that would ensure that post-merger no supplier (including the merged entity) could maintain a sustained leadership position without competing intensely to generate constant innovation, product development and customer satisfaction. These features include: (i) dynamic and rapid growth with opportunities for product extension by existing suppliers and entry by new firms; (ii) a high rate of product innovation; (iii) a lack of capacity constraints on suppliers; and (iv) the expertise and sophistication of customers. To this list, the notifying party adds that key patents relating to PCR have expired and others will expire in future. Taken together with the widespread licensing of technologies in life sciences, this means that any 'first mover' advantage in a new market which may result in an initial strong market position is unlikely to be sustainable over time. Any anti-competitive unilateral effects of the proposed merger can also be excluded according to the notifying party because life science research has further characteristics, namely: (i) the presence of numerous competing suppliers including Roche, BioRad, Qiagen, Promega, ThermoFisher; (ii) competition from home brewed products (that is, reagents produced by customers themselves in house); (iii) low barriers to entry; and (iv) lack of barriers to switching, which would exclude the possibility of sustained non-coordinated effects post merger. These same industry characteristics are also said to rule out the possibility of coordinated effects.

70. The market investigation has confirmed a number of the characteristics described above. In particular, a majority of respondents agreed that the competitive landscape of the overall life science market is constantly evolving. At the same time, however, a number of respondents pointed to the ongoing consolidation in the sector. Despite indications of this consolidation process, the majority of respondents confirmed a high level of innovation in the development of new reagents and instruments.[28] In this regard, it should be noted that competitors confirmed that there are also in general no capacity constraints on the production side, in particular in the area of reagents.[29]

71. The Commission's market investigation showed that the customer's choice is in general driven by the suitability and quality of the product for their specific research interest rather than its price. There are indications that certain customers, in particular in academia, make use of 'home-brew' products as a cheaper alternative for certain reagents. However, as the market investigation did not show that home-brew reagents are a valid alternative for the majority of customers, their impact on the commercial reagent markets appears limited.[30]

72. The market investigation also found out that a number of customers have to a certain extent buyer power due to their individual size or by way of collaborating with other customers.[31] Although a certain lock-in effect was observed by some customers, as a change of reagent could involve certain product testing and validation costs, the

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28 Question 7 of the Commission's questionnaire to customers and question 6 of the Commission's questionnaire to competitors dated 10 October 2008.

29 Question 85 of the Commission's questionnaire to competitors dated 10 October 2008.

30 Question 27 of the Commission's questionnaire to customers dated 10 October 2008.

31 Minutes of telephone conversations conducted with certain customers on 28 and 29 October 2008.

investigation showed that research customers are more likely able to switch to other suppliers than would be the case for customers in the neighbouring diagnostic market (where the parties are to a large extent not active). In addition, the majority of customers indicated they have alternative suppliers to whom they could switch.[32]

73. Overall, the market investigation indicated that the competitive landscape of life science research has many of the characteristics listed above. These characteristics were taken into account when assessing the competitive effects of the proposed transaction in an area which might be considerably different in the future given the overall constantly evolving character of these scientific markets.

Horizontal Relationships

1. Nucleic acid purification

74. The merged entity's share of an overall market for nucleic acid purification reagents is only [5-10] % at an EEA-wide level. As such the transaction would not result in an affected market.

75. If however, narrower segments for DNA and RNA purification reagents are considered, the market for RNA purification would be technically affected with a combined market share of [10-20] % as shown in the following table.

Invitrogen	Applied Biosystems	Combined	Qiagen	Roche	Sigma	Promega	Others
[5-10] %	[10-20] %	[10-20] %	[40-50] %	[5-10] %	[5-10] %	[0-5] %	[20-30] %

Market shares for the EEA in 2007 based on the notifying party's best estimates. Source: Form CO Annex 7.3(b)(i). Market shares are rounded

76. In this regard, it should be noted that the parties are not each other's closest competitor on the market for RNA purification as Invitrogen focuses more on liquid-based purification technology while Applied Biosystems focuses predominantly on column-based purification products.

77. The market investigation has shown that there are many other competitors active in the supply of products for nucleic acid purification (including RNA purification) such as the market leader Qiagen, Roche, Sigma, Promega, GE and Agilent.

78. It is therefore concluded in light of the merged entity's market position and the presence of numerous, credible competitors that the proposed transaction does not give rise to concerns in nucleic acid purification in general or on the basis of the type of sample being analysed.

2. Nucleic acid amplification

(i) Conventional PCR and RT-PCR mastermixes

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[32] Question 70 concerning PCR reagents and instruments of the Commission's questionnaire to customers dated 10 October 2008.

79. The notifying party estimates that the merged entity will hold a market share of [5-10]% on a market for conventional PCR mastermixes. Its combined market share on a market for conventional RT-PCR mastermixes would be [10-20]% meaning that neither of these hypothetical product markets would be affected. The proposed transaction would however give rise to affected markets in the supply of qPCR and qRT-PCR mastermixes.

(ii) Quantitative PCR mastermixes

80. The notifying party estimates that the merged entity will hold a market share of approximately [50-60]% on an overall market for qPCR mastermixes, i.e. probe-based and dye based (intercalating dye) mastermixes (Invitrogen [0-5]%, Applied Biosystems [40-50]%).[33] The notifying party submits that the combined market share overstates the competitive impact of the proposed concentration in that Invitrogen and Applied Biosystems are not each other's closest competitor since the majority of Applied Biosystems' qPCR sales stem from mastermixes that comprise qPCR mastermixes adjusted for probe-based detection chemistry whereas the majority of Invitrogen's sales of qPCR mastermixes use dye-based detection chemistries.

81. Although the notifying party submits that mastermixes with an intercalating dye and mastermixes that can be used with probe-based detection chemistry should be considered within the same product market, the market investigation has to a large extent indicated the relevance of a distinction between dye-based and probe-based detection chemistries with many respondents highlighting the specificity that can be achieved with probe-based methods and the price differences between these methods.

82. The notifying party estimates that the merged entity will hold a market share of approximately [30-40]% on an EEA market for qPCR mastermixes including an intercalating dye (Invitrogen [5-10]%, Applied Biosystems [20-30]%) as shown in the following table.

Invitrogen	Applied Biosystems	Combined	Roche	Biorad	Qiagen	Others
[5-10]%	[20-30] %	[30-40] %	[10-20] %	[10-20] %	[10-20] %	[20-30] %

Market shares for the EEA in 2007 based on the notifying party's best estimates. Source: Form CO Annex 7.3 (f)(i). Market shares are rounded.

83. The market investigation revealed that most customers and competitors consider that different dyes have different properties and most customers would not switch from one dye to another. Even if the main intercalating dye offered by Invitrogen (SYBR Green) is deemed by certain respondents to have different properties to other dyes, it is widely licensed to competitors (around 35 companies which are active in the EEA hold a license from Invitrogen, including Applied Biosystems). […] Applied Biosystems does not own any intercalating dye technology and its sales of qPCR mastermixes including an intercalating dye are based on the SYBR Green technology licensed from Invitrogen. Notwithstanding the removal of Applied Biosystems as a licensee of Invitrogen SYBR Green technology, a number of competitors using this licensed product (such as Roche, Biorad and Qiagen holding market shares of [10-20]%, [10-20]% and [10-20]%

33 Form CO annex 7.3(a)(i).

respectively), are present on the market for qPCR mastermixes and may be expected to continue to exercise a competitive constraint on the merged entity.

84. The notifying party estimates that the merged entity will hold a market share of [60-70]% on a market for qPCR mastermixes for use with probes as shown in the table below.

Invitrogen	Applied Biosystems	Combined	Roche	Biorad	Qiagen	Others
[0-5]%	[60-70]%	[60-70]%	[10-20]%	[5-10]%	[5-10]%	[10-20]%

Market shares for the EEA in 2007 based on the notifying party's best estimates. Source: Form CO Annex 7.3 (f)(i). Market shares are rounded.

85. The notifying party submits that Applied Biosystems' position on the market can be largely attributed to the fact that Applied Biosystems was the first to develop and market probe-based detection chemistry for PCR for research applications. The notifying party indicates that it expects Applied Biosystems' market share […] competition for detection chemistries which will impact competition for mastermixes for probe-based qPCR. In this regard, the notifying party submits that a number of competitors have recently entered the market and have gained market shares equivalent to Invitrogen.

86. The proposed transaction will only bring about a minimal increment of [0-5]% in the market share of the merged entity on the market for qPCR mastermixes for use with probes. Moreover, the Commission has in particular considered that it is unlikely from the evidence brought forward by the notifying party that the proposed transaction will remove a leading or unique competitive constraint on Applied Biosystems. There are a number of other competitors on the market with higher market shares than Invitrogen, such as Roche, Bio-Rad and Qiagen. In addition, a number of other competitors have recently entered the market.

87. Applied Biosystems holds [80-90]% of the market for standalone probes whereas Invitrogen is not active there.[34] Although no customer or competitor complained about the possibility of the merged entity tying its qPCR mastermixes to a particular probe, it should be stated that mastermixes are not normally optimised for use with a particular probe and therefore it is unlikely that the merged entity will seek to tie its qPCR mastermixes to a particular probe.

88. In the light of the above, it is unlikely that the transaction will have significant anti-competitive effects on: (i) a market for qPCR mastermixes; (ii) a market for qPCR mastermixes with an intercalating dye; and (iii) a market for qPCR mastermixes for use with a probe.

(iii) Quantitative RT-PCR mastermixes

34 Invitrogen is not active in the market for standalone probes and therefore this market is not affected by the proposed transaction.

89. The notifying party estimates that the combined market share of the parties on the EEA market for qRT-PCR mastermixes will be [30-40]% (Invitrogen [20-30]% and Applied Biosystems [10-20]%).[35]

Invitrogen	Applied Biosystems	Combined	Roche	Qiagen	Bio-Rad	Others
[20-30] %	[10-20] %	[30-40] %	[10-20] %	[10-20] %	[5-10] %	[30-40] %

Market shares for the EEA in 2007 based on the notifying party's best estimates. Source: Form CO Annex 7.3(c)(ii). Market shares are rounded.

90. The notifying party submits that the transaction will not result a reduction of competition in the supply of qRT-PCR mastermixes as there are numerous suppliers of qRT-PCR mastermixes, with underlying technologies widely available.

91. As the market investigation has confirmed the relevance of a distinction between dye-based and probe-based detection chemistries, as many respondents highlighted the specificity that can be achieved with probe-based methods and indicated that they would not switch from dyes to probes if the former were to increase in price, a narrower segmentation within qRT-PCR mastermixes according to detection chemistry appears justified. The notifying party estimates that on an EEA market for qRT-PCR mastermixes with an intercalating dye, the merged entity would hold only an insignificant market share of [0-5]% (Invitrogen [0-5]% and Applied Biosystems [0-5]%).[36] As such, the proposed transaction would not raise serious doubts in the supply of qRT-PCR mastermixes using dye-based detection chemistry.

92. The notifying party estimates that the merged entity would have a share of approximately [50-60]% on an EEA market for qRT-PCR mastermixes for use with probe-based detection chemistry (Invitrogen [30-40]%, Applied Biosystems [20-30]%).[37] However, even in this sub-segment of the market for qRT-PCR mastermixes, the merging parties' products are not necessarily the closest substitutes as Invitrogen's mastermixes contain a genetically engineered RT enzyme whereas Applied Biosystems' mastermixes contain native RT enzymes.

93. In this respect it should be noted that in the market investigation, a majority of customers and competitors indicated that a distinction should be made between native and genetically engineered RT enzymes and most customers indicated they would not switch from genetically engineered to native enzymes if the former were subject to a small but significant and non-transitory increase in price.

94. In the light of the above, it is unlikely that the transaction will have significant anti-competitive effects on the market for qRT-PCR mastermixes as a whole or on any narrower segmentation (i.e. if qRT-PCR mastermixes are distinguished on the basis of detection chemistry and the nature of the RT enzyme.

(iv) Stand alone thermostable DNA polymerase enzymes

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35 Form CO Annex 7.3(c)(ii).

36 Form CO, Annex 7.3(f)(ii).

37 Form CO, Annex 7.3(f)(ii).

95. The proposed transaction would bring together two of the leading suppliers of thermostable DNA polymerase enzymes. Although the merged entity would have a market share of [30-40] % in 2007, as shown in the following table, this share has been in decline in recent years from a figure of [40-50] % in 2005.

Invitrogen	Applied Biosystems	Combined	Promega	Stratagene	Roche	Others
[10-20] %	[20-30] %	[30-40] %	[10-20] %	[5-10] %	[5-10] %	[30-40] %

Market shares for the EEA in 2007 based on the notifying party's best estimates Source: Form CO Annex 7.3(c)(iii). Market shares are rounded.

96. According to the notifying party, more than [90-100] % of sales of thermostable DNA polymerases in the EEA consist of sales of Taq polymerase enzymes. As such, it estimates that a market limited to Taq DNA polymerase enzyme sales would be substantially similar to the estimated shares on the broader market. In any event, the proposed transaction would not bring about any significant change in the supply of thermostable DNA polymerase enzymes other than Taq as Applied Biosystems has no sales of Pfu, Pfx, Tfi or any other thermostable DNA polymerase in the EEA.

97. Sales of Taq DNA polymerase result from the application of a technology originally patented by Roche. Applied Biosystems holds a non-exclusive worldwide license for the manufacturing and selling of Taq DNA polymerase from Roche. Invitrogen as well as many other competitors, is one of the sub-licensees of Applied Biosystems. The Roche PCR foundational patents (also known as 'method' patents) expired in Europe in 2006. Other patents on basic Taq DNA polymerase products will expire in January 2009. The merging parties, as well as a number of other competitors, have developed enhanced versions of Taq polymerase. Applied Biosystems holds certain patents relating to its enhancement of Taq polymerase for so-called hot start/cold stop methods, but these methods have according to the notifying party […] by customers.

98. The notifying party submits that the transaction will not lead to a material reduction of competition in the supply of thermostable DNA polymerase since: (i) Applied Biosystems has licensed this enzyme to more than […] suppliers throughout the industry […] and the merged entity will […] existing licensees; (ii) the Roche PCR foundational patents have expired in Europe and other key patents will expire in 2009 thereby further reducing barriers; (iii) there are no significant capacity constraints on suppliers and raw materials are readily available; (iv) Invitrogen does not exert a significant competitive constraint on Applied Biosystems in the supply of polymerase enzymes given that it is just one a number of Applied Biosystems' sub-licensees.

99. The market investigation has confirmed that there are many competitors to the merging parties offering thermostable DNA polymerase (principally Taq polymerase) on a stand alone basis. None of these competitors has indicated that they constrained in terms of capacity. The majority of customers in the market investigation indicated that the transaction would not lead to any competition concern in the market for thermostable DNA polymerase enzymes. A limited number of respondents raised general concerns over the patent license behaviour of Applied Biosystems. However, as the merged entity will […] position of the parties to the transaction will not change with the transaction, these concerns are not considered specific to the merger.

100. In light of the above, it is concluded that the transaction does not raise significant competition concerns in the supply of thermostable DNA polymerase nor in a narrower market for Taq polymerase

(v) RT enzymes

101. The notifying party estimates that the merged entity will hold a market share of approximately [40-50]% on a market for all standalone RT enzymes, i.e. including native and genetically engineered RT enzymes (Invitrogen [30-40]%, Applied Biosystems [10-20]%). The main competitors on this market are Promega, Qiagen and Roche with [10-20]%, [10-20]% and [5-10]% respectively as can be seen in the table below.

Invitrogen	Applied Biosystems	Combined	Promega	Qiagen	Roche	Others
[30-40] %	[10-20] %	[40-50] %	[10-20] %	[10-20] %	[5-10] %	[20-30] %

Market shares for the EEA in 2007 based on the notifying party's best estimates. Source: Annex 2 of the notifying party's reply to the Commission's article 11 letter 29 October 2008. Market shares are rounded.

102. The notifying party submits that Applied Biosystems' 2007 shares overstate its competitive significance in the supply of all RT enzymes in the EEA due to the fact that almost all of its sales in the EEA comprise [...].[38]

103. Although a limited number of customers and competitors raised concerns about the merged entity's position on the market for RT enzymes, the market investigation confirmed the presence of a number of alternative suppliers on the market for RT enzymes that are not subject to capacity constraints. These competitors are likely to be able to continue to place competitive constraints on the merged entity.

104. Invitrogen and Applied Biosystems are not each other's closest competitors on the market for RT enzymes. Invitrogen is mainly active in the sale of genetically engineered RT enzymes, whereas Applied Biosystems is mainly active in the resale of native RT enzymes. The market investigation revealed that genetically engineered and native RT enzymes have differing properties. In fact, a majority of customers and competitors indicated that a distinction should be made between native and genetically engineered RT enzymes and most customers indicated they would not switch from genetically engineered to native enzymes if the former were subject to a small but significant and non-transitory increase in price.

105. The notifying party estimates that the merged entity will hold a market share of [50-60]% on the EEA market for genetically engineered RT enzymes.

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38 According to the notifying party, more than […]% of Applied Biosystems' sales are attributable to native RT enzymes […] which Applied Biosystems sells on a […]. […]% of its sales are attributable to engineered RT enzymes […].

Invitrogen	Applied Biosystems	Combined	Promega	Roche	Sigma, Stratgene and Fermentas	Others
[50-60]%	[0-5]%	[50-60]%	[20-30]%	[10-20]%	[0-5]% each	0-5]%

Market shares for the EEA in 2007 based on the notifying party's best estimates. Source: Annex 2 of the notifying party's reply to the Commission's article 11 letter dated 29 October 2008, Market shares are rounded.

106. Strong competitors, including Promega (with a market share of [20-30]%), are present of the market for genetically engineered enzymes and a number of competitors do not currently face capacity constraints. The increment in market shares brought about by the merger is minimal ([0-5]%). Applied Biosystems' market share for 2007 is based on […] an enzyme […]. Roche itself is a leading competitor on the market with a market share of [10-20]%.

107. On the market for native RT enzymes, the notifying party estimates that the merged entity would have a market share of [30-40]% (Invitrogen [5-10]%, Applied Biosystems 23%) on an EEA-wide market.

Invitrogen	Applied Biosystems	Combined	Qiagen	Sigma	Promega and Biorad	Roche	Others
[5-10]%	[20-30]%	[30-40]%	[20-30]%	[5-10]%	[5-10]% each	[0-5]%	[20-30]%

Market shares for the EEA in 2007 based on the notifying party's best estimates. Source: Annex 3 of the notifying party's reply to the Commission's article 11 letter dated 29 October 2008

108. According to the notifying party, native RT enzymes are not patented[39] and post-merger, the merged entity will continue to face competition from a number of competitors present on the market including Qiagen ([20-30]%), Sigma ([5-10]%), Promega and Biorad ([5-10]% each) and Roche ([0-5]%).

109. In light of the above, it is unlikely that the transaction will have significant anti-competitive effects on the market for standalone RT enzymes both at an overall level and more narrowly distinguishing between native and genetically engineered RT enzymes.

3. DNA Microarrays

110. On a hypothetical market for DNA microarray consumables (i.e. arrays and related reagents together), Invitrogen and Applied Biosystems have approximately [0-5] % market shares, and therefore only a combined market share of [5-10] %. The market for microarray consumables would therefore not be affected market by the proposed transaction.

111. On a narrower market for reagents used in microarray analysis, (i.e. excluding arrays), Applied Biosystems and Invitrogen each have a market share of [5-10] % which would give the merged entity a market share of [20-30] % as shown in the following table.

Invitrogen	Applied	Combined	Affymetrix	Agilent	Roche	Qiagen	Others

[39] Annex 3 of the notifying party's presentation to the Commission, 29 October 2008.

	Biosystems						
[10-20] %	[10-20] %	[20-30] %	[20-30] %	[20-30] %	[5-10] %	[5-10] %	[10-20] %

Market shares for the EEA in 2007 based on the notifying party's best estimates Source: Form CO Annex 7.3(l). Market shares are rounded.

112. According to the notifying party, there are over 30 other suppliers intensely competing for microarray reagents, including the market leader, Affymetrix as well as other credible suppliers such as Agilent, Roche and Qiagen. Also, it was submitted, that the market is still continuously evolving resulting in a high degree of competition among suppliers.

113. The market investigation confirmed the presence of alternative suppliers of DNA microarray products. In addition, the majority of respondents confirmed that the transaction would have little or no impact on this area.

114. It is therefore considered that the proposed transaction would not give rise to any anti-competitive effects in the area of DNA microarrays.

4. Mass Spectrometry

115. The merged entity would have a market share of [20-30] % in a hypothetical market of reagents for mass spectrometry with an increment of [5-10] %.

Invitrogen	Applied Biosystems	Combined	ThermoFisher/ Pierce	Sigma Aldrich	Cambridge Isotope Laboratories	Others
[5-10] %	[20-30] %	[20-30] %	[5-10] %	[20-30] %	[20-30] %	[10-20] %

Source: Notifying party's reply to the Commission's Article 11 request of 21 October 2008

116. The notifying party submits that the use of reagents in mass spectrometry is limited and that the reagents supplied by the merging parties are not close substitutes. Applied Biosystems, but not Invitrogen, is also active in the supply of mass spectrometry instruments where it has an estimated market share of less than 25%. According to the parties, mass spectrometry instruments are open systems and that customers can choose between a numbers of suppliers' products. Therefore, it is unlikely that the merged entity would have an incentive or the ability for tying or bundling instruments and reagents in this market.

117. In view of the relatively small increment brought about by the proposed combination and the existence of a sufficient number of credible, alternative suppliers, the Commission concludes that the notified transaction is unlikely to have significant anti-competitive effects on the market for reagents for mass spectrometry.

5. DNA ladders and markers

118. In the hypothetical market of DNA ladders and marker, the merged entity would have a market share of approximately [20-30]% (Invitrogen [20-30]%, Applied Biosystems [0-5]%). The increment brought about by the proposed transaction is therefore limited even if a distinction were to be made between ladders and markers.

119. In view of the negligible increment arising from the notified operation and in the absence of concerns in the market investigation, the Commission considers that the proposed transaction is unlikely to have significant anti-competitive effects on the market for DNA ladders and markers.

V. CONCLUSION

120. For the above reasons, the Commission has decided not to oppose the notified operation and to declare it compatible with the common market and with the EEA Agreement. This decision is adopted in application of Article 6(1)(b) of Council Regulation (EC) No 139/2004.

For the Commission
(*signed)*
Janez POTOČNIK
Member of the Commission