SAN FRANCISCO
PLANNING DEPARTMENT

Letter of Determination

1650 Mission St.
Suite 400
San Francisco,
CA 94103-2479

Reception:
415.558.6378

Fax:
415.558.6409

Planning
Information:
415.558.6377

October 19, 2016

James A. Reuben
Reuben, Junius & Rose, LLP
One Bush Street, Suite 600
San Francisco, CA 94104

Name:	**Zymergen**
Site Address:	**No Address Specified**
Staff Contact:	**Corey Teague, (415) 575-9183 or corey.teague@sfgov.org**
Record No.:	**2016-006306ZAD**

Dear Mr. Reuben:

This letter is in response to your request for a Letter of Determination regarding the proper use classification for Zymergen, Inc. The request seeks a confirmation that the subject use is a "non-life science laboratory use" and does not seek a determination about whether the use would be allowed at a specific property.

Background

As noted in your letters (dated May 11, 2016 and August 6, 2016), Zymergen "is an analytics laboratory company that employs robotics, advanced manufacturing techniques, and proprietary software to traditional biochemistry methods." It is noted that the "advanced manufacturing techniques" relate to Zymergen's use of "advanced robotics machines to speed up its analytic process in its own laboratory" and "the information gleaned from this analysis is used by Zymergen's industrial clients to optimize production microbes in order to more efficiently manufacture commodity chemicals and carbon-based materials." Based upon your letters, while Zymergen uses propriety software and advanced robotics systems, it does not use advanced biological techniques. The biological techniques employed are "basic protocols developed in the 1970s and 1980s and applied broadly in the fields of fermentation and analytical chemistry" and are conducted in a laboratory with Biosafety level 1 controls. Zymergen does not manufacture products, but through its analytical services provides "its industrial clients with a roadmap for optimizing microbes for industrial fermentation at their own facilities." Further, it is emphasized that Zymergen "does not create anything or provide any service that would aid in the analysis or detection of illness."

Planning Code Definitions

As noted in your letters, the Planning Code contains similar definitions for Laboratory and Life Science uses, and both were added to the Planning Code by Ordinance No. 298-08 to implement the Eastern Neighborhoods Area Plan.

Planning Code Section 890.52 defines Laboratory as follows:

> *Laboratory shall mean space within any structure intended or primarily suitable for scientific research. The space requirements of uses within this category include specialized facilities and/or built accommodations that distinguish the space from office uses (as defined in Section 890.70), light manufacturing (as defined in Section 890.54(a)), or heavy manufacturing (including uses listed in 226(g) through 226(w)). Examples of laboratories include the following:*
>
> *(a) Chemistry, biochemistry, or analytical laboratory;*
>
> *(b) Engineering laboratory;*
>
> *(c) Development laboratory;*
>
> *(d) Biological laboratories including those classified by the Centers for Disease Control (CDC) and National Institutes of Health (NIH) as Biosafety level 1, Biosafety level 2, or Biosafety level 3;*
>
> *(e) Animal facility or vivarium, including laboratories classified by the CDC/NIH as Animal Biosafety level 1, Animal Biosafety level 2, or Animal Biosafety level 3;*
>
> *(f) Support laboratory;*
>
> *(g) Quality assurance/Quality control laboratory;*
>
> *(h) Core laboratory.*

Planning Code Section 890.53 defines Life Science use as follows:

> *Life Science is an industry that involves the integration of natural and engineering sciences and advanced biological techniques using organisms, cells, and parts thereof for products and services. This includes the creation of products and services used to analyze and detect various illnesses, the design of products that cure illnesses, and/or the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production. Life Science uses may utilize office, laboratory, light manufacturing, or other types of space. As a subset of Life Science uses, Life Science laboratories typically include biological laboratories and animal facilities or vivaria, as described in Section 890.52(d) and (e).*

Determination

Based upon the information provided in your request letters, it is my determination that Zymergen is a Laboratory use, and more specifically, an analytical/biochemistry/biological laboratory (with Biosafety level 1) use as defined in Planning Code Section 890.52. This is due to the focus on analytical work and the means and methods of research as described in your request. The subject use, as described in your request letters, is not consistent with the definition of Life Science Use in Planning Code Section 890.53.

Please note that a Letter of Determination is a determination regarding the classification of uses and interpretation and applicability of the provisions of the Planning Code. This Letter of Determination is not a permit to commence any work or change occupancy. Permits from appropriate Departments must be secured before work is started or occupancy is changed.

APPEAL: If you believe this determination represents an error in interpretation of the Planning Code or abuse in discretion by the Zoning Administrator, an appeal may be filed with the Board of Appeals within 15 days of the date of this letter. For information regarding the appeals process, please contact the Board of Appeals located at 1650 Mission Street, Room 304, San Francisco, or call (415) 575-6880.

Sincerely,

Scott F. Sanchez
Zoning Administrator

cc: Citywide Mailing List

REUBEN, JUNIUS & ROSE, LLP

May 11, 2016

R#2016-006306ZAD
CK # 26648 $645 -
C. TEAGUE

Via Hand Delivery

Mr. Scott Sanchez, Zoning Administrator
San Francisco Planning Department
1650 Mission Street, 4th Floor
San Francisco, CA 94103

RECEIVED
MAY 11 2016
CITY & COUNTY OF S.F.
PLANNING DEPARTMENT
ZA OFFICE

Re: Request for Written Determination
Subject: Zymergen Use Definition
Our File No.: 10178.01

Dear Mr. Sanchez:

This office represents Zymergen, Inc., an innovative technology and analytics company that utilizes advanced robotics and data analysis to improve upon how microbes are used to produce industrial materials and commodity chemicals.

Zymergen is currently headquartered in Emeryville, but is seeking to move its operations to San Francisco and employ 200-250 people by mid 2017, with consistent growth from this point forward. Zymergen is primarily looking at properties in the SALI and PDR zoning districts. In those districts, laboratory uses are principally permitted, while the subset of laboratory uses categorized as life sciences laboratory uses are not permitted.

Accordingly, pursuant to San Francisco Planning Code ("Planning Code") Section 307(a), we respectfully request a written determination confirming that Zymergen is a laboratory use as set forth in Planning Code Sections 102 and 890.52.

I. Description of Zymergen

Zymergen is an analytics laboratory company that employs robotics, advanced manufacturing techniques, and proprietary software to traditional biochemistry laboratory methods. Its proprietary software and advanced robotics manufacturing technologies allow it to analyze how microbes create products as diverse as vitamins, commodity chemicals and industrial materials including adhesives, fiberoptics, films, and polyesters. This process is called industrial fermentation.

The company's novel algorithms, advanced robotics manufacturing technology, and big data approach facilitate the study of microbial chemical interactions faster and on a much larger scale than would be possible with manual testing performed by individual scientists.

James A. Reuben | Andrew J. Junius | Kevin H. Rose | Daniel A. Frattin | John Kevlin
Jay F. Drake | Lindsay M. Petrone | Sheryl Reuben[1] | Tuija I. Catalano | Thomas Tunny
David Silverman | Melinda A. Sarjapur | Mark H. Loper | Jody Knight | Stephanie L. Haughey
Chloe V. Angelis | Louis J. Sarmiento | Jared Eigerman[2,3] | John McInerney III[2]
1. Also admitted in New York 2. Of Counsel 3. Also admitted in Massachusetts

One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

www.reubenlaw.com

The information gleaned from this analysis is used by Zymergen's industrial clients to optimize production microbes in order to more efficiently manufacture commodity chemicals and carbon-based materials. Over the long term, Zymergen plans to use its combinations of machine learning, automation, and data driven approaches to build a large chemical and materials business. Zymergen's clients are major industrial and chemical companies like BASF, Dow Chemical, Cargill, and DuPont.

By the end of 2017, Zymergen expects to employ a mix of 25% blue collar technicians and operators, 30% scientists, 25% software engineers, and 20% facilities and administrative personnel (including finance, legal, facilities and maintenance staff). As the company grows, it anticipates adjusting these ratios accordingly. By the end of 2019, Zymergen anticipates an employment mix of 35% blue collar technicians and operators, 25% scientists, 25% software engineers, and 15% facilities and administrative personnel.

A. Understanding Microbes

Zymergen employs its advanced manufacturing robotics and data analytics algorithms to study the process in which microbes create commodity chemicals and industrial materials. Microbes are a broad category of single cell organisms that include bacteria, algae, and fungi. Common examples include the strains of bacteria used to culture yogurt and cheese, and yeast, the fungus used to make bread and ferment beer and wine.

Microbes are ubiquitous. They exist on almost all surfaces, including human skin. They are critical for life and also form a major part of the global economy. In addition to being used to make alcohol, yogurt, and bread, they are also used as the building blocks for making vitamins, biodegradable plastics, MSG, flavors and fragrances such as patchouli, rose scent, citrus and vanilla flavoring.

B. Understanding Zymergen's Process

The day-to-day analytical process Zymergen conducts unfolds as follows:

- Zymergen first starts with a microbe—yeast, for example. A computer algorithm designs a set of approximately 1,000 experiments to run on the genetic makeup of that microbe. The goal of these experiments is to somehow make the microbe better—for example, alter the yeast so that when combined with the typical amount of sugar it produces twice the amount of alcohol. A scientist reviews the experiments designed by the algorithm and passes them on to the laboratory/factory.

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One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

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- Second, the experiments compiled by the computer algorithm are run in the Zymergen laboratory by mechanized robots, which are operated by laboratory technicians. The advanced robotics machines conduct the experiments in high throughput fashion, constantly collecting and recording data along the way, as well as mapping the flow of experiments and materials throughout the entire process.

- Third, Zymergen's mechanized robots then test each of the microbes. For example, a robot would take each altered microbe of yeast and test it by running a fermentation process to see which altered strands yield the desired results (for example, which yeast microbes produce double the alcohol when left to ferment with the same amount of sugar). All the data from these tests is gathered and stored in a large database.

- Fourth, Zymergen employs its data scientists and computer algorithms to analyze all the data collected. Based on that data and the multivariate results of the thousands of experiments conducted, a scientist works with proprietary computer algorithms to determine the best design for the next set of 1,000 experiments.

This cycle is run multiple times until Zymergen has a microbe that meets the aforementioned goal (for example, until Zymergen identifies a yeast which actually produces twice the amount of alcohol when fermented with the standard amount of sugar).

II. Distinction between Life Science and Biochemistry/Analytical Laboratories

A. Planning Code Definitions

The Planning Code confusingly sets forth two nearly identical sets of definitions for "laboratory" and "life science" uses. The PDR zoning districts refer to the definitions found in Planning Code Section 102, while the Article 8 mixed used districts refer to the definitions in Sections 890.52 and 890.53. The set of definitions found in Section 102 are included below. The set of definitions found in Sections 890.52 and 890.53 are not copied here, but the only difference between the two sets of definitions is that the definitions in Section 102 specify that laboratory and life science uses are non-retail sales and services uses; whereas the definitions found in Sections 890.52 and 890.53 lack that same specification. Planning Code Section 102 defines a laboratory use as:

> A Non-Retail Sales and Services Use intended or primarily suitable for scientific research. The space requirements of uses within this category include specialized facilities and/or built accommodations that distinguish the space from Office uses,

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One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

www.reubenlaw.com

Light Manufacturing, or Heavy Manufacturing. Examples of laboratories include the following:

(a) Chemistry, biochemistry, or analytical laboratory;
(b) Engineering laboratory;
(c) Development laboratory;
(d) Biological laboratories including those classified by the Centers for Disease Control (CDC) and National Institutes of Health (NIH) as Biosafety level 1, Biosafety level 2, or Biosafety level 3; [i]
(e) Animal facility or vivarium, including laboratories classified by the CDC/NIH as Animal Biosafety level 1, Animal Biosafety level 2, or Animal Biosafety level 3;
(f) Support laboratory;
(g) Quality assurance/Quality control laboratory; and
(h) Core laboratory.

Planning Code Section 102 then defines a life science use as a subset of the above laboratory use category, as follows:

> A Non-Retail Sales and Service Use that involves the integration of natural and engineering sciences and advanced biological techniques using organisms, cells, and parts thereof for products and services. This includes the creation of products and services used to analyze and detect various illnesses, the design of products that cure illnesses, and/or the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production. Life Science uses may utilize office, laboratory, light manufacturing, or other types of space. As a subset of Life Science uses, Life Science laboratories typically include biological laboratories and animal facilities or vivaria, as described in the Laboratory definition Subsections (d) and (e).

Although the definitions of laboratory and life science overlap, life science laboratories primarily involve the study of human illness and the production of products that are FDA regulated, neither of which Zymergen is engaged in.

B. Distinction between Life Science Laboratories and Biochemistry or Analytical Laboratories

The definition of life science includes a description of "life science laboratories." This subset of life science uses typically includes "biological laboratories and animal

[i] The Planning Code does not address biosafety level 4.

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One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

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facilities or vivaria, as described in the Laboratory definition *Subsections (d) and (e).*" Those subsections (d) and (e) refer specifically to biological laboratories and animal facilities or vivaria—leaving several categories of laboratory uses that are not considered life science laboratories. Among the laboratory uses that are not considered life science laboratories are chemistry, biochemistry, and analytical laboratories as set forth in subsection (a) of the laboratory use definition found at Planning Code Sections 102 and 890.52.

The Planning Code does not explain what constitutes a biochemistry or analytical laboratory. However, the Planning Code focuses on life science laboratories as those that study human illness and create products for human use that are FDA regulated. Accordingly, it is reasonable to conclude that the biochemistry and analytical laboratory categories cover laboratories whose work involves scientific analysis, but does not involve human or animal testing, the development of products or drugs to treat or prevent human illness, or FDA oversight. This distinction, and Zymergen's alignment with the biochemistry and analytical laboratory categories, is illustrated by the attached chart (Exhibit A).

The line between life science laboratories and biochemistry or analytical laboratories is supported by a July 18, 2015 Letter of Determination ("July 2015 LOD"; Exhibit B) in which the Planning Department concluded that a genetics testing company that works with human blood is not a life science use. According to the July 2015 LOD, "Invitae provides medical information using genetic data beginning with a blood draw . . . The blood sample is sent to Invitae where DNA is extracted from the blood sample and the requested genetic information is processed using genetic sequencing technology." The Planning Department concluded, and we agree, that Invitae's work analyzing DNA did not cause it to be categorized as a life science use pursuant to Planning Code Section 102, and the July 2015 LOD determined that Invitae is in fact a laboratory use that would be permitted to operate in the PDR-1-D district. Note that soon after the July 2015 LOD was issued, Invitae committed to landlord SKS to move into the McClintock building at 1400 16th Street, a building that is zoned PDR-1-D.

If the life science category was intended to capture every use that involved cells or DNA, then Invitae would have to be considered a life science use. The Planning Department's conclusion to the contrary affirms the position that not all uses that involve cells are life science uses. Rather, the life science laboratory category is much narrower—covering biological laboratories that create and design products and services used to analyze and detect illnesses (for example, Genentech, Roche and Bio-Rad) and classified by the Centers for Disease Control ("CDC") and National Institutes of Health ("NIH") as biosafety level 2 or 3 and/or which keep animal facilities or vivarium. Zymergen does not meet these life science laboratory criteria. There is no question that Zymergen's industrial business is much further removed from the "life science" definition than Invitae, which actually uses a human blood draw.

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One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

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The primary purpose of zoning laws is to separate incompatible property uses. As explained herein, Zymergen's development of software and advanced manufacturing robotics to analyze microbe strains for use in industrial manufacturing is consistent with the industrial development and production uses prioritized in PDR districts. Additionally, because Zymergen works only with biosafety level 1 microbes, the company's presence would pose no risk to any other uses in its vicinity.

The distinction between "research and development industrial activities" and "heavy/high impact manufacturing industrial activities" set forth in the Oakland Planning Code is informative here. The Oakland Planning Code defines "research and development industrial activities" as those that "include scientific research for the design, development, engineering, and testing of . . . industrial or scientific products," including biotechnology firms with a biosafety rating of 1, 2 or 3.[1] Research and development uses in Oakland are permitted in Regional Commercial zones,[2] Central Business District General Commercial and Mixed Commercial zones,[3] Housing and Business Mix zones,[4] and Industrial zones.[5] A separate category called "heavy/high impact manufacturing and industrial activities" includes "any biotechnology research, development or production activities involving material defined by the National Institute of Health as Risk Group 4 or Restricted Agents (commonly known as biosafety level 4)."[6] These high impact industrial uses are permitted only in a small handful of zoning districts. The distinction between types of laboratory uses drawn by the Oakland Planning Code, and the fact that Oakland permits a laboratory with a biosafety rating below level 4 to operate in most commercial and industrial districts, serves as further evidence that Zymergen's biosafety level 1 laboratory is compatible with the industrial and manufacturing uses prioritized in San Francisco's PDR districts.

III. Zymergen is a Biochemistry Analytical Laboratory

A. Biosafety Level 1 is not Determinative of Life Science Use

Zymergen maintains biosafety level 1 controls in its laboratory—which are the same as the biosafety controls implemented in high school chemistry labs, and are not comparable to the controls in life science biological facilities, which work with hazardous biological agents and are required to implement more stringent biosafety protective measures. The CDC explains on its website that every laboratory that works with microbes, "regardless of biosafety level, follows standard microbiological practices."[7] The biosafety levels range from biosafety level 1 (the most low-risk microbes) to level 4 (the high risk microbes) and each biosafety level builds on the safety procedure controls of the level before it.[8] The microbes present in a biosafety level 1 laboratory do not cause disease and do not present a hazard to laboratory employees or the environment—and indeed, can be ingested by humans without posing any risk or harm.[9] Work in these laboratories is performed on an open bench or table, and workers wear basic gear similar to the measures that one would expect to find in any

REUBEN, JUNIUS & ROSE, LLP

One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

www.reubenlaw.com

food or manufacturing facility (coats and gloves), which are meant to protect the integrity of the product more than for the protection of the worker. According to the Federation of American Scientists, biosafety level 1 laboratories are the type of laboratories generally found in high schools.[10] As high school laboratories are not considered life science uses, not all laboratories that abide by biosafety level 1 controls can be categorized as life science laboratories under the Planning Code based simply on their biosafety level 1 rating.

B. Starting Point in Lengthy Process is not Determinative

Just as the Planning Department concluded in its July 2015 LOD that Invitae's use of blood samples to analyze DNA did not qualify the company as a life science laboratory, Zymergen's study of microbial pathways to produce different products should likewise not qualify it as a life science laboratory. Zymergen's use of microbes is merely the initial piece in a long, heavily automated and analytical process that ultimately leads to the improvement of techniques to create industrial materials and commodity chemicals—and notably not therapeutics, drugs or any product that is intended to address illnesses or any product that requires compliance with FDA regulatory protocols before being made available to the public.

Its proprietary algorithms and advanced manufacturing robotics techniques are what make Zymergen unique. The company approaches microbial analysis as a high throughput data and computational problem rather than a biological one, and its results are the product of an automated manufacturing paradigm and computational algorithm that allow Zymergen to consider thousands of microbial strains in the amount of time it would take an individual scientist to test tens. Though microbes are the first piece of the process, the company's focus is on the technological innovations that allow it to analyze microbe strains on a mass scale, rather than the strains themselves.

For example, Zymergen's business relies on microbes in the same way that a baker, brewer, or dairy relies on microbes. Bacterial cultures are crucial to the production of yogurt and cheese, and yeast is required to make bread, beer and wine. But the bacteria and yeast relied on by those producers is simply the essential first step in a long process that requires a number of other ingredients and tools. The same is true of Zymergen. If every business that worked with microbes were classified as a life science use, then any kitchen, brewery, winery, or factory in which bread, yogurt, cheese, beer or wine is produced would have to be categorized as a life science use.

C. Zymergen is an Analytical or Biochemistry Laboratory

Zymergen is an analytical or biochemistry laboratory and not a life science laboratory. As explained in Section II, the Planning Code definitions of life science

REUBEN, JUNIUS & ROSE, LLP

One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

www.reubenlaw.com

laboratories (§ 102 and § 890.53) focus on those uses that involve the study and treatment of illness and the development and production of therapeutics and drugs that are regulated by the FDA. Further, Planning Code Sections 102 and 890.53 explicitly state that life science laboratories "typically include biological laboratories and animal facilities or vivaria." Zymergen does not produce therapeutics or drugs, and does not develop products that detect or treat illness. Nor are any of Zymergen's activities overseen by the FDA or any other regulatory agency.

What Zymergen offers its industrial clients is the technological ability to analyze large numbers of microbial strains in a relatively short period of time so that they can be optimized for the more efficient production of commodity chemicals and industrial materials. These activities are in line with those of a biochemistry or analytical laboratory as defined in Planning Code Sections 102 and 890.52(a).

IV. Zymergen's Website

We understand that representatives of the Planning Department have reviewed Zymergen's website. We address the website below, with copies of the relevant website pages attached as Exhibit C.

- Biology (Exhibit C:1) – Zymergen's website homepage includes the tagline "Technology. Biology. Automation. Computation." It goes on to state that Zymergen is "applying the latest in automation, data architecture and machine learning" to make "better microbes for use in industrial fermentation."

  As explained above, the biological aspect of Zymergen's business is its use of microbes as a starting point. Microbes are a living thing, but they are the most basic of all living things (single cell organisms) and include bacteria, fungi and algae. Further, the microbes that Zymergen works with pose no potential hazard to the environment or to human health. Considering that dairies, bakeries, wineries and breweries also work with microbes yet are not classified as life science uses, the mere presence of microbes in Zymergen's laboratory cannot on its own indicate a life science use.

- Engineering and Strain Optimization (Exhibit C:2) – These pages mention "strain optimization," "engineering biology," and "strain improvement and development."

  Zymergen utilizes its advanced manufacturing robotics and proprietary search algorithms to improve the economics of their clients' industrially fermented products by modifying clients' existing production microbe strains. As discussed,

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One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

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this process does involve the alteration of microbe strains. This process is comparable to a chemical company that improves upon a formula for glue by making it stronger and easier to manufacture, or a brewery that alters yeast so that it ferments more quickly. The improved microbes Zymergen creates allow its clients to produce their industrially fermented materials more efficiently—meaning savings in cost and time.

- Bio-Based Development (C:3) – On its "New Product Development" page, Zymergen discusses its work in "bio-based manufacturing." The page explains that "scientists have classified more than 200,000 naturally-occurring chemicals" which can be used to manufacturing cheaper raw materials.

  These references help to explain how the biological/microbial piece of Zymergen's business fits into the much larger, industrially-focused puzzle. The company is harnessing the manufacturing potential of chemical-producing microbes. In other words, Zymergen is using something that occurs naturally to improve upon the production of chemicals and materials used in industrial manufacturing. This work is directly in line with the activities encouraged in PDR districts, which according to Planning Code Section 102, include all industrial and agricultural uses.[ii]

- Technology (C:4) – On Zymergen's "Technology," "Biology," "Automation," and "Computation" pages, the company discusses its "design-build-test-analyze" approach to microbe engineering.

  Again, this set of web pages illustrates that Zymergen operates in a cross section between biochemistry, manufacturing automation, and computer technology. Its developments in automation and computation are the cornerstone of the business, and are the tools that allow Zymergen to analyze microbial strains at the speed and scale it does. Biochemistry is at play, but its advanced manufacturing robotics and data integration technologies are the core of what Zymergen has to offer its industrial clients. The company's focus on the design and development of these technologies make Zymergen an appropriate use for a PDR district.

If you have any further questions about Zymergen's website, we would be happy to answer them, or open Zymergen's current location to a Planning Department staff tour.

[ii] Note that any agricultural use in which plants are manipulated or genetically modified would also be considered a life science use if life sciences uses are considered to include any use involving cells or DNA.

REUBEN, JUNIUS & ROSE, LLP

One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

www.reubenlaw.com

V. Written Determination Request

Zymergen is a company that applies advanced manufacturing robotics, big data and analytics to traditional biochemistry laboratory techniques to analyze and collect data on how microbes create commodity chemicals and industrial materials via industrial fermentation. The first building block in this process is a microbe. But the mere presence of microbes in Zymergen's laboratory cannot on its own push the company into the life science use category. If so, every kitchen, brewery, and winery that works with bacteria cultures and yeast would be categorized as a life science use. Further, Zymergen does not study or treat human illness, does not develop therapeutics or create drugs or products for human consumption that are FDA regulated, and does not conduct human or animal testing or work with any agents that pose a potential hazard to human health or the environment.

Accordingly, and based on the foregoing, we respectfully request a written determination that Zymergen meets the Planning Code definition of a non-life science laboratory use pursuant to Sections 102 and 890.52.

Please contact me should you have any questions.

Very truly yours,

REUBEN, JUNIUS & ROSE, LLP

James A. Reuben

Enclosures

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[1] Oakland Plan. Code § 17.10.581.
[2] Oakland Plan. Table 17.37.01.
[3] Oakland Plan. Table 17.58.01.
[4] Oakland Plan. Table 17.65.030.
[5] Oakland Plan. Table 17.72.01.
[6] Oakland Plan. Code § 17.10.580.
[7] CDC "Recognizing the Biosafety Levels" < http://www.cdc.gov/training/QuickLearns/ biosafety/> (Mar. 13, 2016).
[8] *Id.*
[9] *Id.*
[10] Federation of American Scientists "Biosafety Levels Informations" < http://fas.org/ programs/bio/resource/biosafetylevels.html> (Mar. 13, 2016).

REUBEN, JUNIUS & ROSE, LLP

One Bush Street, Suite 600
San Francisco, CA 94104

tel: 415-567-9000
fax: 415-399-9480

www.reubenlaw.com

EXHIBIT A

Zymergen Activities	Laboratory Use	Life Science Use
• Zymergen studies the interaction between microbes and chemicals (industrial fermentation) to produce commodity chemicals and specialty chemicals on a contract basis • Its products never require FDA or other regulatory approvals	• The Planning Code broadly defines laboratory space as that used for scientific research in the service of the production of products other than biotech products or those that are FDA regulated.	• Life science laboratories are a type of laboratory space that involves the integration of natural and engineering sciences using organisms, cells and parts thereof for biotech products and services that are FDA regulated.
• Zymergen is a big data and software company—its primary technological innovation is the use of advanced robotics, software and data analysis to optimize microbes for industrial fermentation • Zymergen's industrial clients use the improved microbes to produce fragrances, amino acids, and other commercial products • Zymergen does not produce therapeutics or drugs, and does not develop products that detect or treat illness—none of its products require FDA approval or other regulatory oversight	• Examples of laboratory uses, as set forth in the Planning Code, include: ▪ Chemistry, biochemistry, or analytical laboratory ▪ Engineering laboratory ▪ Development laboratory ▪ Biological laboratory[1] • Planning Code distinguishes between "biochemistry laboratory" and "biological laboratory"[2] ▪ A biochemistry laboratory is non-life science laboratory, while a biological laboratory is a kind of laboratory that may be a life science laboratory[3] • Examples of non-life science laboratories: ▪ Invitae (DNA analytics) ▪ Anresco (Food testing) ▪ DOW Chemical (specialty chemicals) ▪ HTC (industrial design laboratory)	• Life science uses, as set forth in the Planning Code, include: ▪ Creation of products and services to analyze and detect illnesses ▪ Design of products to cure illnesses[4] • Focus on the creation of products and services used to detect and cure illness • Examples of life science companies: ▪ Genentech (pharmaceuticals) ▪ Pfizer (pharmaceuticals) ▪ Merck (pharmaceuticals) ▪ Gilead (biopharmaceuticals) ▪ Bio-Rad (research and development in fields of genomics, proteomics, drug discovery, food safety, medical diagnostics) ▪ Roche (diagnostics and pharmaceuticals, focus on medical solutions)

• Zymergen's approach abstracts away the "biology" of microbes—it treats strain engineering as a big data problem • The company works on "synthetic biology"—microbes are the first piece in a long process that focuses on data analytics and chemical reactions, not life processes	• The dictionary definition of chemistry is "a science that deals with the structure and properties of substances and with the changes that they go through"[5] • The dictionary definition of biochemistry is "chemistry that deals with the chemical compounds and processes occurring in organisms"[6]	• The dictionary definition of life science is "a branch of science (as biology, medicine, and sometimes anthropology or sociology) that deals with living organisms and life processes"[7]
• Zymergen is not required to post toxic materials warnings at its facilities—every substance in the laboratory could be safely ingested • Zymergen does not do any animal testing and no animals are kept at its facilities		• Life science facilities typically include biological laboratories (including those classified by the Centers for Disease Control and National Institutes of Health) and animal facilities or vivaria

- **Microbes are merely the initial step in a long process,** but are not a big enough piece of the puzzle to push Zymergen into the life science category. If every company that utilizes microbes is a life science use, then kitchens and breweries would be life science laboratories. For example breweries start with yeast (a type of microbe) in order to make beer and kitchens culture bacteria (another type of microbe) to make yogurt, but such uses are not considered biological laboratories because the life science is such a minimal part of the process. Zymergen's use of microbes is similarly de minimis—the microbes are a merely a starting point, just like yeast for bread and beer and bacteria for yogurt.

- **Zymergen is a big data analytics company.** Its advanced robotics and the software that runs them are what set Zymergen apart, rather than a biological discovery or breakthrough. Simply put, Zymergen is concerned with the mathematics of microbial processes rather than underlying biology.

- **Zymergen technicians run the robotics and are the crucial employees.** The big data that is at the center of the company's business is generated by technicians trained by Zymergen.

[1] Plan. Code §§ 102; 890.52.
[2] *Id.*

[3] *Id.* ["Life Science laboratories **typically include biological laboratories** and animal facilities or vivaria. . ." (emphasis added)].
[4] *Id.*
[5] "Chemistry." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. (Feb. 1 2016).
[6] "Biochemistry." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. (Feb. 1 2016.)
[7] "Life Science." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. (Feb. 1, 2016).

EXHIBIT B

SAN FRANCISCO
PLANNING DEPARTMENT

Letter of Determination

1650 Mission St.
Suite 400
San Francisco,
CA 94103-2479

Reception:
415.558.6378

Fax:
415.558.6409

Planning
Information:
415.558.6377

July 28, 2015

Lawrence Badiner
Badiner Urban Planning, Inc.
95 Brady Street
San Francisco, CA 94103

Site Address:	**1400 16th Street**
Assessor's Block/Lot:	**3938/001**
Zoning District:	**PDR-1-D (Production Distribution & Repair-Design)**
Staff Contact:	**Kimberly Durandet (415) 575-6816**
	kimberly.durandet@sfgov.org

Dear Mr Badiner:

This letter is in response to your request for a Letter of Determination regarding the property at 1400 16th Street. This parcel is located in the PDR-1-D (Production Distribution & Repair-Design) Zoning District, 58-X and 68-X Height and Bulk Districts, and Showplace Square/Potrero Plan Area. You have requested a determination of the proper land use classification for a proposed tenant (dba "Invitae") and have suggested that the proposed use is a Laboratory and not a Life Science use.

Based upon the description in your request, Invitae provides medical information using genetic data beginning with a blood draw at a remote location by a doctor or a service such as LabTech. The blood sample is sent to Invitae where DNA is extracted from the blood sample and the requested genetic information is processed using genetic sequencing technology. The information is shared with the medical professional or patient to identify a client's predisposition to disorders such as cancer, cardiology, hematology, neurology, and pediatrics.

Laboratory is defined in Planning Code Section 102 as follows:
A Non-Retail Sales and Services Use intended or primarily suitable for scientific research. The space requirements of uses within this category include specialized facilities and/or built accommodations that distinguish the space from Office uses, Light Manufacturing, or Heavy Manufacturing. Examples of laboratories include the following:

(a) Chemistry, biochemistry, or analytical laboratory;
(b) Engineering laboratory;
(c) Development laboratory;
(d) Biological laboratories including those classified by the Centers for Disease Control (CDC) and National Institutes of Health (NIH) as Biosafety level 1, Biosafety level 2, or Biosafety level 3;
(e) Animal facility or vivarium, including laboratories classified by the CDC/NIH as Animal Biosafety level 1, Animal Biosafety level 2, or Animal Biosafety level 3;
(f) Support laboratory;
(g) Quality assurance/Quality control laboratory; and
(h) Core laboratory.

Lawrence Badiner
Badiner Urban Planning, Inc.
95 Brady Street
San Francisco, CA 94103

July 28, 2015
Letter of Determination
1400 16th Street

Life Science is defined in Planning Code Section 102 as follows:
A Non-Retail Sales and Service Use that involves the integration of natural and engineering sciences and advanced biological techniques using organisms, cells, and parts thereof for products and services. This includes the creation of products and services used to analyze and detect various illnesses, the design of products that cure illnesses, and/or the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production. Life Science uses may utilize office, laboratory, light manufacturing, or other types of space. As a subset of Life Science uses, Life Science laboratories typically include biological laboratories and animal facilities or vivaria, as described in the Laboratory definition Subsections (d) and (e).

Your letter states that "While Invitae performs genetic testing on blood samples, it does not use '...organisms, cells and parts thereof for products and services...' which is the prerequisite for being a Life Science use."

Based upon your description of the proposed use, I would concur that Invitae operates consistent with the definition of a Laboratory use and would not be considered a Life Science use. Planning Code Section 210.3 lists Laboratory as a Permitted Use under Non-Retail Sales and Services in the PDR-1-D District.

APPEAL: If you believe this determination represents an error in interpretation of the Planning Code or abuse in discretion by the Zoning Administrator, an appeal may be filed with the Board of Appeals within 15 days of the date of this letter. For information regarding the appeals process, please contact the Board of Appeals located at 1650 Mission Street, Room 304, San Francisco, or call (415) 575-6880.

Sincerely,

Scott F. Sanchez
Zoning Administrator

cc: Kimberly Durandet, Planner
Property Owner
Neighborhood Groups

EXHIBIT C:1

zymergen

TECHNOLOGY. BIOLOGY. AUTOMATION. COMPUTATION.

We believe in harnessing the power of biology to make transformative products that are good for business, people and the environment. By applying the latest in automation, data architecture and machine learning, we're making better microbes for use in industrial fermentation.

LEARN MORE

A NEW APPROACH TO MAKING BETTER MICROBES

We engineer strains for partners, helping improve existing products and developing new ones. We work across microbes, products, and traits.

APPLYING AUTOMATION AND BIG DATA TO MICROBIAL ENGINEERING

Our integrated approach dramatically accelerates strain optimization and brings unprecedented scale, reliability and performance to an otherwise uncertain process.

JOIN ZYMERGEN

Here, you will work with diverse talent to transform an industry and the world.

ABOUT

WHAT WE DO

TECHNOLOGY

CAREERS

CONTACT

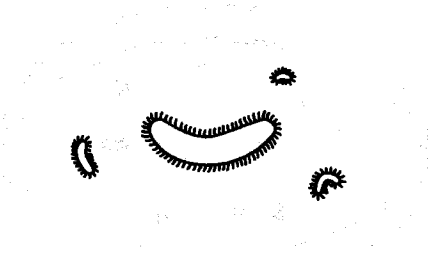
6121 Hollis St., Suite 700 Emeryville, CA 94608

EXHIBIT C:2

zymergen

STRAIN IMPROVEMENT & DEVELOPMENT

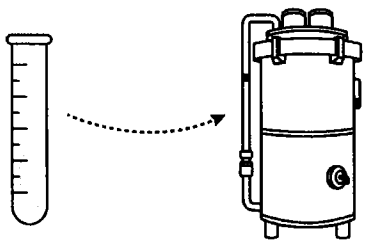
Zymergen has a flexible platform to engineer a wide variety of industrially-relevant microbes and improve the economics of new and existing products made via industrial fermentation.



IMPROVING EXISTING PROCESSES

We work with our partners to improve the economics of their industrially-fermented products by reducing manufacturing costs and/or increasing revenue. We typically begin with their

existing production strains and build upon improvements our partners have already made. Modifying the current production strain helps ensure that process modifications reduce cost and avoid additional capital infrastructure. Progress against process-improvement targets is steady, predictable and trackable. Strains that confer improved economics are shipped to our partners on a routine, agreed-upon schedule.



SCALING FERMENTATION

Historically, the transition from demonstration in lab to full-scale production is prone to fail. We have developed approaches to improve the correlation in performance between small-scale models and commercial manufacturing, enabling us to reduce risk and timelines. Our familiarity with large-scale fermentation means that we are sensitive to the challenges and opportunities available through strain optimization. Our commercial terms align our incentives with our partners such that we succeed when our strains scale successfully.

6121 Hollis St., Suite 700 Emeryville, CA 94608

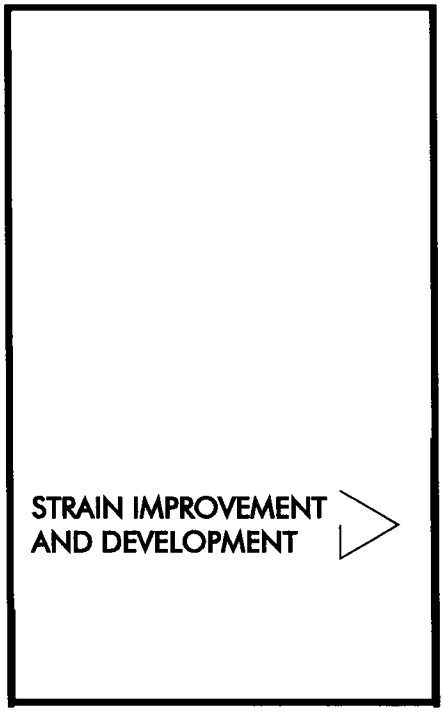
zymergen

WHAT WE DO

WHAT WE DO STRAIN IMPROVEMENT NEW PRODUCT DEVELOPMENT

WE'RE APPLYING AN ENGINEERING MINDSET TO THE CHALLENGE OF STRAIN OPTIMIZATION.

At Zymergen, we eschew traditional reductionist approaches to engineering biology. Instead, we take a data-driven approach, embrace the complexity of biology and treat strain optimization as a heuristically-guided search process. Our platform allows us both to improve the performance of nearly any strain used in existing commercial fermentation and to develop new products.



NEW PRODUCT DEVELOPMENT

6121 Hollis St., Suite 700 Emeryville, CA 94608

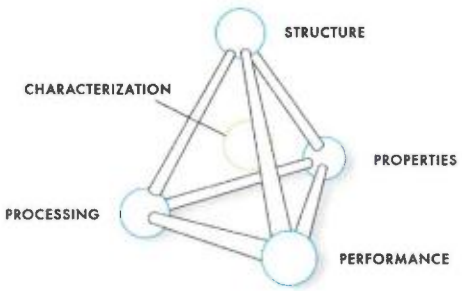
EXHIBIT C:3

zymergen

NEW PRODUCT DEVELOPMENT

New Product Development

At Zymergen, we are in awe of the incredible potential of biology as an innovation engine. We're already using biology to convert renewable feedstocks into valuable chemicals, but we know that's just the start. Our platform will allow us to leverage the power of biology to make entirely new products with inherently better properties to serve a range of industries and applications. The possibilities of bio-based manufacturing are endless – with potential applications we can't yet predict.



RATIONALE FOR BIO-BASED DEVELOPMENT

To date, scientists have classified more than 200,000 naturally-occurring chemicals—and millions more are likely to exist. These chemicals, with their diverse structures and properties, are the molecular origins of life's grandeur – and we're taking note. We look to nature for inspiration and are building capabilities for rapid prototyping and large-scale manufacture of any biological molecule to make new products to improve the world we live in. Bio-based manufacturing enables cheaper raw materials, cheaper operating costs, and cheaper capital expenditures than traditional manufacturing methods.

INDUSTRIES WE FOCUS ON

If scientists could harness the chemistries available in biology, we would spur a revolution, with innovation in a range of vital applications. Zymergen is partnering with proven innovators in a variety of industries to develop novel products derived from molecules made in nature. We know that innovation in materials can have phenomenal implications in a range of industries, including:

- Medical devices & Healthcare
- Electronics
- Food nutrition & Feed
- Home & Personal care, industrial cleaning
- Apparel and sporting goods
- Transportation
- Oil & Gas exploration

Construction

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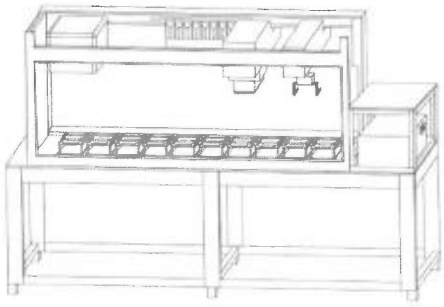
EXHIBIT C:4

zymergen

AUTOMATION

We are realizing the promise of synthetic biology through an efficient, cost-effective approach.



ROBOTICS FOR HIGH THROUGHPUT BIOLOGY

Key to our approach is the fact that we automate every step of the process, removing guesswork and human error that exists when scientists are left to do these experiments by hand. Zymergen's robots – and the protocols we created to control them – have enabled us to build and test thousands of strains with resources typically required to build and test tens of strains, fueling breakthroughs far more quickly and predictably

DATA-INTEGRATION IN THE LAB

With our automation layer, we're generating an immense amount of data, which feeds directly into our complementary data architecture and statistical analysis system. By integrating our automation and analysis, we are able to rapidly capture and analyze the information from all of our machines in order to direct improvement at each step of the process. In essence, our robots get smarter as we go collect more information.

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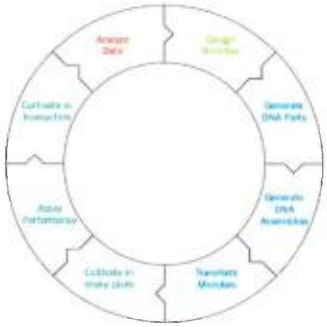
BIOLOGY

TECHNOLOGY BIOLOGY AUTOMATION COMPUTATION

We're taking a data-driven approach to biology, enabling our engineers to uncover solutions faster and more effectively than ever before.



AN INTEGRATED APPROACH

The Design-Build-Test-Analyze cycle guides our work as we improve the performance of the microbes we engineer. By bringing together the most advanced techniques in biology with the latest in automation and computation we work in high-throughput to engineer and evaluate

thousands of strains in parallel. Our results guide our next set of experiments.

A FLEXIBLE PLATFORM

Zymergen has proven capability to work on the full range of microbes currently used for industrial production. Modern microbial engineering has focused on S. cerevisiae and E. coli, but our platform doesn't limit us to these model microbes. We are host-agnostic and have worked with both gram-positive and gram-negative bacteria as well as a variety of fungi. This flexibility allows us to work with partners already committed to a particular microbe and to choose the right microbe to produce a certain product most effectively and efficiently.

ABOUT

WHAT WE DO

TECHNOLOGY

CAREERS

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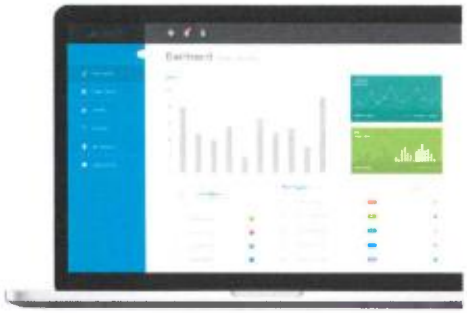
6121 Hollis St., Suite 700 Emeryville, CA 94608

zymergen

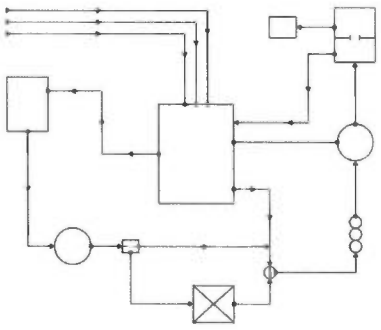
COMPUTATION

At Zymergen, we apply the latest in software tools, Big Data technology and machine learning techniques to challenges in biology and chemical manufacturing. Zymergen's software engineering team plays a critical role in distinguishing our products and systems from those developed by our competitors. We are building a state-of-the art laboratory information management system (LIMS) that supports our company's activities from data capture to analytics to execution. Data is automatically captured by our LIMS for every activity we perform on the factory floor. This data then drives all aspects of the genome design lifecycle.



INTEGRATED DATA COLLECTION SYSTEM

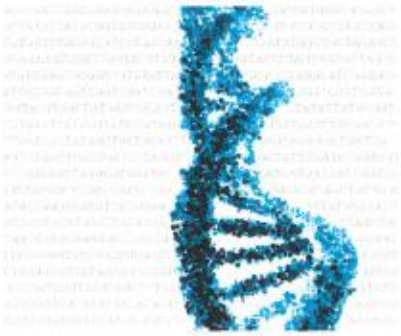
At Zymergen, the quality of our scientific efforts rests on a foundation of data collection capabilities. Instruments and sensors throughout our lab feed data to our LIMS where we catalog every assay, plate and strain on our factory floor. The ability to easily compare laboratory conditions from run to run of an experiment allows us to drive out errors and get to meaningful results more quickly. A historical record of data allows us to identify anomalous conditions, double-check results, and provides meaningful input to Helix, our DNA search platform.



ADVANCED AUTOMATION WORKFLOWS

Our automation platform combines repeatable genetic engineering workflows with a high-level description language for DNA and assembly routines that allows our research staff to specify what they need done, and for the automation system to choose the most effective way to accomplish our tasks. We support our automation engineering team in their efforts to build complex workflows, schedule resources, manage capacity constraints, and track the progress

of all processes running in our factory



DECODING BIOLOGY WITH MACHINE LEARNING

How do you design a thousand genomes a week? In the center of Zymergen's software stack is Helix, our advanced machine learning platform for biology. The space of DNA modifications is large, and prioritizing our exploration is the key to successfully engineering new strains efficiently. Helix combines captured data and human intuition in a central interface that helps propose and rank modifications to genomes of interest. These modifications can then be dispatched to our factory floor for assembly and testing.

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HOME

ABOUT

WHAT WE DO

TECHNOLOGY

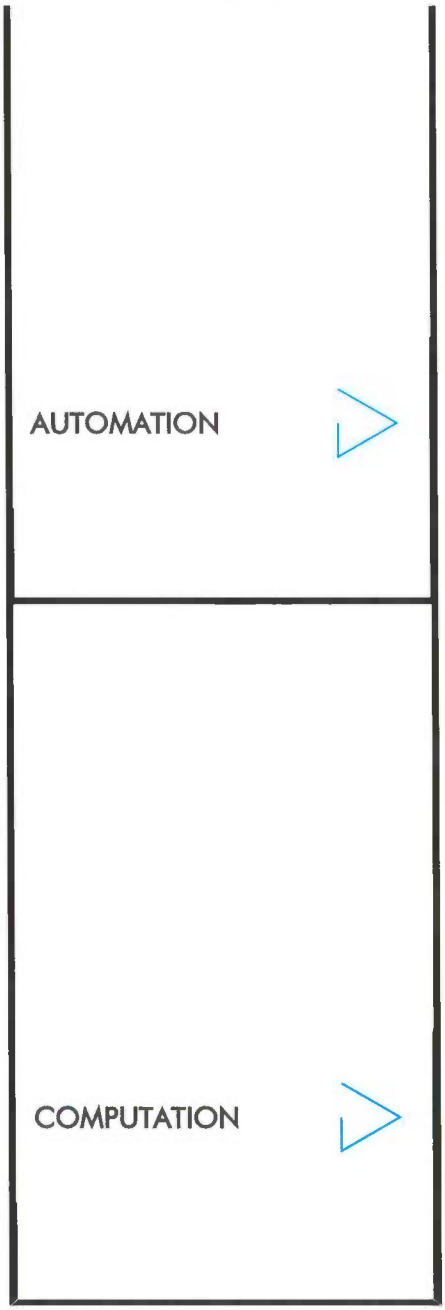
CAREERS

CONTACT

zymergen

A DATA-DRIVEN APPROACH TO BIOLOGY

Zymergen has a proven, computationally-driven method for optimizing production microbes. By integrating biology, automation, and computation approach drives improvements far more reliably and more efficiently than ever before.



6121 Hollis St., Suite 700 Emeryville, CA 94608

REUBEN, JUNIUS & ROSE, LLP

August 5, 2016

Via Hand Delivery

Mr. Scott Sanchez, Zoning Administrator
San Francisco Planning Department
1650 Mission Street, 4th Floor
San Francisco, CA 94103

Re: Request for Written Determination
Subject: Zymergen Use Definition
Our File No.: 10178.01

Dear Mr. Sanchez:

This letter serves to follow up on the request for Letter of Determination submitted by this office on May 11, 2016 (Record No. 2016-006306ZAD) ("**LOD Request**") regarding the use category applicable to Zymergen, Inc.

A. Planning Code Focuses on Life Science Uses as those that Primarily Involve the Study of Human Illness.

Planning Code Sections 102 and 890.53 state that a life science use "includes *(1)* the creation of products and services used to analyze and detect various illnesses, *(2)* the design of products that cure illnesses, and/or *(3)* the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production."

Of the three examples of life science uses that the definition provides, two of the three refer to the study and treatment of human illness. Planning Code Section 249.36 also states that "The Life Science and Medical Special Use District is intended to support uses that benefit from proximity to the University of California, San Francisco (UCSF) campus at Mission Bay"—further suggesting that life sciences uses are primarily those that involve medicine and the study of human illness. It is therefore reasonable to infer that the Planning Code focuses on life science uses as those that primarily involve the study of human illness. Zymergen does not do any work related to human health or illness.

James A. Reuben | Andrew J. Junius | Kevin H. Rose | Daniel A. Frattin | John Kevlin
Tuija I. Catalano | Jay F. Drake | Lindsay M. Petrone | Sheryl Reuben[1] | Thomas Tunny
David Silverman | Melinda A. Sarjapur | Mark H. Loper | Jody Knight | Stephanie L. Haughey
Chloe V. Angelis | Louis J. Sarmiento | Jared Eigerman[2,3] | John McInerney III[2]

1. Also admitted in New York 2. Of Counsel 3. Also admitted in Massachusetts

San Francisco Office
One Bush Street, Suite 600, San Francisco, CA 94104
tel: 415-567-9000 | fax: 415-399-9480

Oakland Office
827 Broadway, Suite 205, Oakland, CA 94607
tel: 510-257-5589

www.reubenlaw.com

B. Zymergen Falls Outside the Scope of Life Science Uses Based on a Careful Reading of the Life Science Definition.

Even if the Planning Department determines that the life science category merely includes (rather than focuses on) the study of human illness, Zymergen still falls outside the scope of life science uses based on a careful reading of the definition, as explained here.

Planning Code Section 102[i] defines a life science use as follows:

> A Non-Retail Sales and Service Use that involves the *(1)* integration of natural and engineering sciences and *(2)* advanced biological techniques *(3)* using organisms, cells, and parts thereof for products and services. This includes *(4)* the creation of products and services used to analyze and detect various illnesses, *(5)* the design of products that cure illnesses, and/or *(6)* the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production. Life Science uses may utilize office, laboratory, light manufacturing, or other types of space. As a subset of Life Science uses, Life Science laboratories typically include biological laboratories and animal facilities or vivaria, as described in the Laboratory definition Subsections (d) and (e).

(1) Integration of natural and engineering sciences. The first criteria needed to establish a life science use is the "integration of natural and engineering sciences." Neither the Planning Code, nor, to our knowledge, any other Zoning Administrator interpretation or Planning Department policy, defines either "natural sciences" or "engineering sciences." The Merriam-Webster Dictionary defines natural science as "a science (such as physics, chemistry, or biology) that studies the physical and natural world or the events that happen in nature."[1] Zymergen studies microbial chemical interactions. While algae and fungi are types of microbes, and do exist in nature, Zymergen's work is limited to how certain microbes can be used to create industrial products. Industrial fermentation is by definition an intentional process. And while certain kinds of fermentation can occur in nature, none of the chemical reactions that Zymergen creates in its laboratory would take place without human intervention.

"Engineering sciences" does not appear to be a dictionary-defined term, but the Merriam-Webster Dictionary defines engineering as "the application of science and mathematics by which the properties of matter and the sources of energy in nature are made useful to people."[2] As Zymergen is studying how microbes can be used in industrial

[i] The Section 890.53 definition is substantively the same, except without the distinction of "Non-Retail Sales and Service Use."

San Francisco Office
One Bush Street, Suite 600, San Francisco, CA 94104
tel: 415-567-9000 | fax: 415-399-9480

Oakland Office
827 Broadway, Suite 205, Oakland, CA 94607
tel: 510-257-5589

REUBEN, JUNIUS & ROSE, LLP
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fermentation to make industrial products more efficiently, its work could accurately be described as an engineering science.

However, because the industrial fermentation that occurs in Zymergen's laboratory cannot occur naturally, Zymergen is not integrating natural and engineering sciences, and thus cannot be categorized as a life science use.

(2) Advanced biological techniques. In order for a use to be a life science use under the Planning Code, it must integrate natural and engineering sciences *and* advanced biological techniques. Therefore, even if the Planning Department determines that Zymergen is integrating natural and engineering sciences, it must also find that the company uses advanced biological techniques. Advanced means "being beyond others in progress or ideas."[3] Zymergen's proprietary software and robotics systems are advanced technologies, but its biochemistry analytical techniques are not.

The company employs basic protocols developed in the 1970s and 1980s and applied broadly in the fields of fermentation and analytical chemistry. It runs microbe fermentations in vessels of varying sizes from Erlenmeyer flasks to bench-scale glass fermentation tanks. Zymergen then samples from these cultures, dilutes and cleans the material, and utilizes analytical chemistry techniques such as chromatography (separates materials by absorption) and optical readers (measures absorbance by the material at a specific wavelength) to determine concentrations of various compounds of interest. These techniques are foundational to the fields of fermentation and analytical chemistry and were developed well before 1970. In fact, the study of fermentation (and presumably the techniques used in that study) is so basic that is included in high school lab curriculums. Further, Zymergen runs all its workflows in throughput fashion using off-the-shelf automation components built by large vendors and developed in the 1980s and 1990s.

Advanced biological techniques are techniques developed in the 2000's and include work with stem cells, CAR T-Cell immunotherapy, and generating fabricated organisms with minimal synthetic genomes. Stem cells are the few progenitor cells of those fully differentiated cells that make up the body. Stem cells and techniques associated with stem cells are used to deliver therapeutic benefits in humans or other organisms. CAR T-cell immunotherapy is a new technique to use natural aspects of the immune system to attack unwanted or disruptive cells in the human body. Lastly, organisms with minimal synthetic genomes are organisms built from scratch, include as few genes as possible to support essential life functions, and represent an advanced technique to streamline cells to serve specific technology purposes such as amplifying synthetic DNA. Zymergen does not work with any of these cells or use any of these advanced biological techniques.

San Francisco Office
One Bush Street, Suite 600, San Francisco, CA 94104
tel: 415-567-9000 | fax: 415-399-9480

Oakland Office
827 Broadway, Suite 205, Oakland, CA 94607
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Given that the analytical techniques used by Zymergen have all been in existence for at least 20 years, these techniques cannot be considered advanced, and thus Zymergen cannot be described as a company that is integrating natural and engineering sciences *and advanced biological techniques*.

(3) Using organisms, cells, and parts thereof for products and services. Under the Planning Code, a life science use involves the integration of natural and engineering sciences and advanced biological techniques using organisms, cells, and parts thereof for products and services. Zymergen studies microbes and optimizes them for use in the industrial fermentation process. As explained in the LOD Request, microbes are a broad category of single cell organisms that include bacteria, algae, and fungi—such as the strains of bacteria used to culture yogurt and cheese, and yeast, which is the fungus used to make bread and ferment beer and wine.

While microbes are organisms, they are ubiquitous. If Zymergen were to be considered a life science use based on its use of microbes, then a brewery or bakery could just as easily be considered a life science use.

(4) The creation of products and services used to analyze and detect various illnesses. The Planning Code states that a life science use includes "the creation of products and services used to analyze and detect various illnesses." Zymergen analyzes how microbes can be modified to more efficiently ferment industrial materials and commodity chemicals. It does not create anything or provide any service that would aid in the analysis or detection of illness.

(5) The design of products that cure illnesses. Nor does Zymergen design products that are intended to cure or treat illness. Zymergen's analysis of microbes is limited to optimizing them for use in industrial fermentation.

code says and/or

(6) The provision of capital goods and services, machinery, instruments, software, and reagents related to research and production. The Planning Code states that a life science use "includes (a) the creation of products and services used to analyze and detect various illnesses, (b) the design of products that cure illnesses, and/or (c) the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production." Because Zymergen does not create or design products or services used to analyze, detect or cure illness, it would need to provide "capital goods and services, machinery, instruments, software, and reagents related to research and production" in order to qualify as a life science use under the Planning Code.

San Francisco Office
One Bush Street, Suite 600, San Francisco, CA 94104
tel: 415-567-9000 | fax: 415-399-9480

Oakland Office
827 Broadway, Suite 205, Oakland, CA 94607
tel: 510-257-5589

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A very technical reading of this clause would require finding that a life science use provides capital goods and services, *and* machinery, *and* instruments, *and* software, *and* reagents related to research and production. Even if we assume that the "and" in the clause "software, and reagents" was intended to be read as "or", Zymergen still cannot be considered a life science use. Based on the description of the company laid out in the LOD Request, it is clear that Zymergen does not qualify under this portion of the life science definition either:

- Capital Goods and Services. Capital goods are "products (such as factory equipment and tools) that are used to make other products,"[4] and capital services refers "to the flow of productive services provided by an asset that is employed in production . . . [and] are the appropriate measure of capital input in production analysis."[5] Even if the clause "capital goods and services" was intended to be read as "capital goods" and "services" rather than as "capital goods and capital services," it would still require a use to provide capital goods *and* services related to research and production in order to be considered a life science use. Zymergen provides its industrial clients a roadmap for optimizing microbes for industrial fermentation at their own facilities. While the company does provide services related to research and production, it does not provide capital goods, and thus does not provide capital goods *and* services.

- Machinery. Zymergen uses advanced robotics machines to speed up its analytic process in its own laboratory, but the company does not provide any machinery to its clients.

- Instruments. Zymergen does not design or create instruments.

- Software. Zymergen does create proprietary software, which it applies to more traditional biochemistry methods of study. But this software is for use entirely in-house and Zymergen does not sell or provide any software to its clients.

- Reagents. A reagent is defined as "a substance that is used to test for the presence of another substance by causing a chemical reaction with it."[6] Zymergen does not produce reagents. Rather, it analyzes how microbes can be optimized for more efficient industrial fermentation in order to create commodity chemicals and industrial materials (including adhesives, fiberoptics, films, and polyesters).

Accordingly, Zymergen does not provide capital goods and services, machinery, instruments, software, or reagents related to research and production, and thus, cannot be categorized as a life science use.

San Francisco Office
One Bush Street, Suite 600, San Francisco, CA 94104
tel: 415-567-9000 | fax: 415-399-9480

Oakland Office
827 Broadway, Suite 205, Oakland, CA 94607
tel: 510-257-5589

www.reubenlaw.com

C. Conclusion

Because Zymergen's work does not involve the integration of natural and engineering sciences and advanced biological techniques, it falls outside the scope of a life science use as defined in Planning Code Sections 102 and 890.53. Even if the Planning Department were to determine that Zymergen does integrate natural and engineering sciences and advanced biological techniques using organisms, cells, and parts thereof for products and services, it still could not classify Zymergen as a life science use. This is because the company does not create products and services used to analyze and detect various illnesses, does not design products that cure illnesses, and does not provide capital goods and services, machinery, instruments, software, or reagents related to research and production.

Please feel free to contact me if you have any questions or would like to discuss this matter further.

Very truly yours,

REUBEN, JUNIUS & ROSE, LLP

James A. Reuben

[1] "Natural Science." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. 20 July 2016.
[2] "Engineering." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. 20 July 2016.
[3] "Advanced." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. 20 July 2016.
[4] "Capital Goods." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. 21 July 2016.
[5] OECD Glossary of Statistical Terms, https://stats.oecd.org/glossary/detail.asp?ID=270 (last visited July 21, 2016).
[6] "Reagent." *Merriam-Webster.com*. Merriam-Webster, n.d. Web. 21 July 2016.

REUBEN, JUNIUS & ROSE, LLP

August 5, 2016

Via Hand Delivery

Mr. Scott Sanchez, Zoning Administrator
San Francisco Planning Department
1650 Mission Street, 4th Floor
San Francisco, CA 94103

Re: Request for Written Determination
Subject: Zymergen Use Definition
Our File No.: 10178.01

Dear Mr. Sanchez:

This letter serves to follow up on the request for Letter of Determination submitted by this office on May 11, 2016 (Record No. 2016-006306ZAD) ("**LOD Request**") regarding the use category applicable to Zymergen, Inc.

A. Planning Code Focuses on Life Science Uses as those that Primarily Involve the Study of Human Illness.

Planning Code Sections 102 and 890.53 state that a life science use "includes *(1)* the creation of products and services used to analyze and detect various illnesses, *(2)* the design of products that cure illnesses, and/or *(3)* the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production."

Of the three examples of life science uses that the definition provides, two of the three refer to the study and treatment of human illness. Planning Code Section 249.36 also states that "The Life Science and Medical Special Use District is intended to support uses that benefit from proximity to the University of California, San Francisco (UCSF) campus at Mission Bay"—further suggesting that life sciences uses are primarily those that involve medicine and the study of human illness. It is therefore reasonable to infer that the Planning Code focuses on life science uses as those that primarily involve the study of human illness. Zymergen does not do any work related to human health or illness.

James A. Reuben | Andrew J. Junius | Kevin H. Rose | Daniel A. Frattin | John Kevlin
Tuija I. Catalano | Jay F. Drake | Lindsay M. Petrone | Sheryl Reuben[1] | Thomas Tunny
David Silverman | Melinda A. Sarjapur | Mark H. Loper | Jody Knight | Stephanie L. Haughey
Chloe V. Angelis | Louis J. Sarmiento | Jared Eigerman[2,3] | John McInerney III[2]

1. Also admitted in New York 2. Of Counsel 3. Also admitted in Massachusetts

San Francisco Office
One Bush Street, Suite 600, San Francisco, CA 94104
tel: 415-567-9000 | fax: 415-399-9480

Oakland Office
827 Broadway, Suite 205, Oakland, CA 94607
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www.reubenlaw.com

B. Zymergen Falls Outside the Scope of Life Science Uses Based on a Careful Reading of the Life Science Definition.

Even if the Planning Department determines that the life science category merely includes (rather than focuses on) the study of human illness, Zymergen still falls outside the scope of life science uses based on a careful reading of the definition, as explained here.

Planning Code Section 102[i] defines a life science use as follows:

> A Non-Retail Sales and Service Use that involves the *(1)* integration of natural and engineering sciences and *(2)* advanced biological techniques *(3)* using organisms, cells, and parts thereof for products and services. This includes *(4)* the creation of products and services used to analyze and detect various illnesses, *(5)* the design of products that cure illnesses, and/or *(6)* the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production. Life Science uses may utilize office, laboratory, light manufacturing, or other types of space. As a subset of Life Science uses, Life Science laboratories typically include biological laboratories and animal facilities or vivaria, as described in the Laboratory definition Subsections (d) and (e).

(1) Integration of natural and engineering sciences. The first criteria needed to establish a life science use is the "integration of natural and engineering sciences." Neither the Planning Code, nor, to our knowledge, any other Zoning Administrator interpretation or Planning Department policy, defines either "natural sciences" or "engineering sciences." The Merriam-Webster Dictionary defines natural science as "a science (such as physics, chemistry, or biology) that studies the physical and natural world or the events that happen in nature."[1] Zymergen studies microbial chemical interactions. While algae and fungi are types of microbes, and do exist in nature, Zymergen's work is limited to how certain microbes can be used to create industrial products. Industrial fermentation is by definition an intentional process. And while certain kinds of fermentation can occur in nature, none of the chemical reactions that Zymergen creates in its laboratory would take place without human intervention.

"Engineering sciences" does not appear to be a dictionary-defined term, but the Merriam-Webster Dictionary defines engineering as "the application of science and mathematics by which the properties of matter and the sources of energy in nature are made useful to people."[2] As Zymergen is studying how microbes can be used in industrial

[i] The Section 890.53 definition is substantively the same, except without the distinction of "Non-Retail Sales and Service Use."

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REUBEN, JUNIUS & ROSE, LLP
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fermentation to make industrial products more efficiently, its work could accurately be described as an engineering science.

However, because the industrial fermentation that occurs in Zymergen's laboratory cannot occur naturally, Zymergen is not integrating natural and engineering sciences, and thus cannot be categorized as a life science use.

(2) Advanced biological techniques. In order for a use to be a life science use under the Planning Code, it must integrate natural and engineering sciences *and* advanced biological techniques. Therefore, even if the Planning Department determines that Zymergen is integrating natural and engineering sciences, it must also find that the company uses advanced biological techniques. Advanced means "being beyond others in progress or ideas."[3] Zymergen's proprietary software and robotics systems are advanced technologies, but its biochemistry analytical techniques are not.

The company employs basic protocols developed in the 1970s and 1980s and applied broadly in the fields of fermentation and analytical chemistry. It runs microbe fermentations in vessels of varying sizes from Erlenmeyer flasks to bench-scale glass fermentation tanks. Zymergen then samples from these cultures, dilutes and cleans the material, and utilizes analytical chemistry techniques such as chromatography (separates materials by absorption) and optical readers (measures absorbance by the material at a specific wavelength) to determine concentrations of various compounds of interest. These techniques are foundational to the fields of fermentation and analytical chemistry and were developed well before 1970. In fact, the study of fermentation (and presumably the techniques used in that study) is so basic that is included in high school lab curriculums. Further, Zymergen runs all its workflows in throughput fashion using off-the-shelf automation components built by large vendors and developed in the 1980s and 1990s.

Advanced biological techniques are techniques developed in the 2000's and include work with stem cells, CAR T-Cell immunotherapy, and generating fabricated organisms with minimal synthetic genomes. Stem cells are the few progenitor cells of those fully differentiated cells that make up the body. Stem cells and techniques associated with stem cells are used to deliver therapeutic benefits in humans or other organisms. CAR T-cell immunotherapy is a new technique to use natural aspects of the immune system to attack unwanted or disruptive cells in the human body. Lastly, organisms with minimal synthetic genomes are organisms built from scratch, include as few genes as possible to support essential life functions, and represent an advanced technique to streamline cells to serve specific technology purposes such as amplifying synthetic DNA. Zymergen does not work with any of these cells or use any of these advanced biological techniques.

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Given that the analytical techniques used by Zymergen have all been in existence for at least 20 years, these techniques cannot be considered advanced, and thus Zymergen cannot be described as a company that is integrating natural and engineering sciences *and advanced biological techniques*.

(3) Using organisms, cells, and parts thereof for products and services. Under the Planning Code, a life science use involves the integration of natural and engineering sciences and advanced biological techniques using organisms, cells, and parts thereof for products and services. Zymergen studies microbes and optimizes them for use in the industrial fermentation process. As explained in the LOD Request, microbes are a broad category of single cell organisms that include bacteria, algae, and fungi—such as the strains of bacteria used to culture yogurt and cheese, and yeast, which is the fungus used to make bread and ferment beer and wine.

While microbes are organisms, they are ubiquitous. If Zymergen were to be considered a life science use based on its use of microbes, then a brewery or bakery could just as easily be considered a life science use.

(4) The creation of products and services used to analyze and detect various illnesses. The Planning Code states that a life science use includes "the creation of products and services used to analyze and detect various illnesses." Zymergen analyzes how microbes can be modified to more efficiently ferment industrial materials and commodity chemicals. It does not create anything or provide any service that would aid in the analysis or detection of illness.

(5) The design of products that cure illnesses. Nor does Zymergen design products that are intended to cure or treat illness. Zymergen's analysis of microbes is limited to optimizing them for use in industrial fermentation.

code says and/or

(6) The provision of capital goods and services, machinery, instruments, software, and reagents related to research and production. The Planning Code states that a life science use "includes (a) the creation of products and services used to analyze and detect various illnesses, (b) the design of products that cure illnesses, and/or (c) the provision of capital goods and services, machinery, instruments, software, and reagents related to research and production." Because Zymergen does not create or design products or services used to analyze, detect or cure illness, it would need to provide "capital goods and services, machinery, instruments, software, and reagents related to research and production" in order to qualify as a life science use under the Planning Code.

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A very technical reading of this clause would require finding that a life science use provides capital goods and services, *and* machinery, *and* instruments, *and* software, *and* reagents related to research and production. Even if we assume that the "and" in the clause "software, and reagents" was intended to be read as "or", Zymergen still cannot be considered a life science use. Based on the description of the company laid out in the LOD Request, it is clear that Zymergen does not qualify under this portion of the life science definition either:

- Capital Goods and Services. Capital goods are "products (such as factory equipment and tools) that are used to make other products,"[4] and capital services refers "to the flow of productive services provided by an asset that is employed in production . . . [and] are the appropriate measure of capital input in production analysis."[5] Even if the clause "capital goods and services" was intended to be read as "capital goods" and "services" rather than as "capital goods and capital services," it would still require a use to provide capital goods *and* services related to research and production in order to be considered a life science use. Zymergen provides its industrial clients a roadmap for optimizing microbes for industrial fermentation at their own facilities. While the company does provide services related to research and production, it does not provide capital goods, and thus does not provide capital goods *and* services.

- Machinery. Zymergen uses advanced robotics machines to speed up its analytic process in its own laboratory, but the company does not provide any machinery to its clients.

- Instruments. Zymergen does not design or create instruments.

- Software. Zymergen does create proprietary software, which it applies to more traditional biochemistry methods of study. But this software is for use entirely in-house and Zymergen does not sell or provide any software to its clients.

- Reagents. A reagent is defined as "a substance that is used to test for the presence of another substance by causing a chemical reaction with it."[6] Zymergen does not produce reagents. Rather, it analyzes how microbes can be optimized for more efficient industrial fermentation in order to create commodity chemicals and industrial materials (including adhesives, fiberoptics, films, and polyesters).

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C. Conclusion

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