

1 Dan Lawton (State Bar No. 127342)
2 Joseph C. Kracht (State Bar No. 228507)
3 LAWTON LAW FIRM
4 402 West Broadway, Suite 1860
5 San Diego, CA 92101
6 (619) 595-1370 (Telephone)
7 (619) 595-1520 (Facsimile)

8 Attorneys for Plaintiff AntiCancer, Inc.

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CLERK, U.S. DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

BY

DEPUTY

9 UNITED STATES DISTRICT COURT
10 SOUTHERN DISTRICT OF CALIFORNIA

11 ANTICANCER, INC., a California
12 corporation,

13 Plaintiff,

14 v.

15 BERTHOLD TECHNOLOGIES U.S.A.,
16 LLC, a Tennessee limited liability company;
17 BERTHOLD TECHNOLOGIES GMBH &
18 CO., KG, a German corporation; and DOES
19 1-100,

20 Defendants.

Case No.

'10 CV 2343 JAH

JMA

PLAINTIFF ANTICANCER, INC.'S
COMPLAINT FOR DAMAGES AND
PRELIMINARY AND PERMANENT
INJUNCTIONS FOR INFRINGEMENT OF
U.S. PATENTS NOS. 6,649,159 AND
6,759,038; DEMAND FOR TRIAL BY
JURY AND FOR SPEEDY HEARING

JURY TRIAL DEMANDED

21
22 Pursuant to Fed. R. Civ. P. 8 and 84 and Form 18 thereto, Plaintiff AntiCancer, Inc.
23 ("AntiCancer") alleges as follows:

24 JURISDICTION AND VENUE

- 25 1. This action for patent infringement arises under the patent laws of the United
26 States, Title 35 of the United States Code, and under 28 U.S.C. § 2201 and Fed. R. Civ. P. 57.
27 2. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331, 1338(a), and
28

1 2201.

2 3. Venue is proper in this judicial district under pertinent law, including, *inter alia*,
3 28 U.S.C. §§ 1391(b), (c).

4 THE PARTIES

5 4. AntiCancer is a corporation organized and existing under the laws of the State of
6 California and having as its principal place of business San Diego, California. Via years of
7 research and innovation (and large investments of time, capital, and effort by its scientists and
8 researchers), AntiCancer has developed patented techniques which allow researchers to

- 9 • track metastasis of tumor cells in live lab animals through the use of
10 fluorescent proteins, including green fluorescent protein (“GFP”), a
11 protein which occurs naturally in a species of jellyfish, *Aequorea victoria*
12 (known as the crystal jelly);
- 13 • do whole-body external optical imaging of gene expression in live
14 animals; and
- 15 • evaluate candidate protocols or drugs for treating disease using
16 fluorophores, *i.e.*, proteins which self-fluoresce (so that no other factor is
17 needed to cause them to glow).

18 5. GFP is understood by those skilled in the art to mean a protein which
19 fluoresces green or any other color and includes fluorophores such as RFP, YFP, and/or
20 DsRed.

21 6. AntiCancer engineers tumor cells encoded with GFP and other fluorophores,
22 which glow when excited by blue light. Afterward, AntiCancer implants the tumor cells into
23 laboratory animals (such as live mice) via such means as subcutaneous injection and surgical
24 orthotopic implantation. When the cells fluoresce, they glow green (or other colors, depending
25 on the fluorescent protein used), enabling scientists to track their growth and spread in the
26 living animal in real time by fluorescence imaging (or afterward under a microscope). These
27 methods are highly useful to researchers seeking to learn whether a given drug or treatment
28 regimen is slowing, stopping, or having no effect on the tumor cells being looked at. The

1 National Cancer Institute (the United States government's principal agency for cancer research,
2 and administrator of the Small Business Innovation Research and Small Business Technology
3 Transfer programs) has recognized AntiCancer's success by, *inter alia*, awarding AntiCancer
4 multiple Phase I and Phase II SBIR grants and contracts to help advance cancer research
5 technologies. These have included three research tools: MetaMouse, AngioMouse, and
6 OncoBrite. NCI has recognized AntiCancer in its print publications as "a leader in small-
7 animal imaging technology and mouse models" and the developer of "leading mouse models
8 for cancer research . . ." In these same publications NCI has noted that AntiCancer's mouse
9 models "are now used in contract research with pharmaceutical and biotechnology companies
10 to support novel cancer drug discovery and evaluation."

11 7. The discoverer of GFP, Osamu Shimomura of Boston University and
12 two of the scientists who developed its initial applications, Roger Tsien of UCSD and Martin
13 Chalfie of Columbia University, recently won the Nobel Prize for chemistry (awarded in
14 2008). In announcing the award of the Nobel Prize, the Nobel committee cited AntiCancer's
15 inventions of using GFP to watch cancer cells spread by stating:
16

17 The remarkable brightly glowing green fluorescent protein, GFP,
18 was first observed in the beautiful jellyfish, *Aequorea victoria*, in
19 1962. Since then, this protein has become one of the most
20 important tools used in contemporary bioscience. With the aid of
21 GFP, researchers have developed ways to watch processes that
22 were previously invisible, such as the development of nerve cells in
23 the brain **or how cancer cells spread**.

24 (Emphasis added.)

25 8. Defendant Berthold Technologies U.S.A., LLC ("Berthold USA") is a
26 limited liability company organized and existing under the laws of the State of Tennessee and
27 having as its principal place of business various places, including without limitation Oak
28 Ridge, TN. Via its bioanalytical division, Berthold U.S.A. designs, manufactures and
distributes instruments for life science research, biotechnology and drug discovery. Berthold

1 USA markets, offers for sale, and sells the Berthold image analyzers (defined hereinbelow at
2 paragraph 20) in the United States and is responsible for sales, service, and support of the
3 Berthold image analyzers in North America. Its customers are engaged in research,
4 biotechnology and the pharmaceutical industry. The stock of Berthold USA is wholly-owned
5 by its parent, defendant Berthold Technologies GmbH & Co., KG ("Berthold Germany"),
6 described further hereinbelow.

7 9. Berthold Germany is a corporation organized and existing under the
8 laws of the Federal Republic of Germany and having as its principal place of business
9 various places, including without limitation Bad Wilbad, Germany. Berthold Germany
10 designs, manufactures and distributes sensors, detection systems, and instruments for
11 customers in the biosciences and medicine industries. Under the "Detect and Identify"
12 banner, its instruments and systems include those designed to measure light. Berthold
13 Germany owns all shares of stock in its subsidiary, Berthold USA. Sometimes hereinafter
14 Berthold USA and Berthold Germany are referred to collectively as "Berthold."

15 10. The true names and capacities, whether individual, corporate, associate,
16 representative or otherwise, of Does 1 through 100, inclusive, are unknown to AntiCancer,
17 who therefore sues them by such fictitious names. AntiCancer will seek leave to amend this
18 complaint to show the true names and capacities of said defendants when they are ascertained.
19 AntiCancer is informed and believes, and thereupon alleges, that each of the defendants named
20 as a Doe, along with the named defendants, is responsible in some manner for the occurrences
21 herein alleged, and that AntiCancer's injuries herein alleged were legally or proximately
22 caused by said defendants. Wherever it is alleged that any act or omission was also done or
23 committed by any specifically named defendant, or by defendants generally, AntiCancer
24 intends thereby to allege, and does allege, that the same act or omission was also done and
25 committed by each and every defendant named as a Doe, and each named defendant, both
26 separately and in concert or conspiracy with the named defendants. Many defendants named
27 as Does are Berthold customers who have purchased (and/or who will purchase) Berthold
28

1 image analyzers (as defined further hereinbelow at ¶ 20) and use them to infringe claims of the
2 patents-in-suit.

3 11. At all times mentioned herein, defendants, and each of them, were the agents,
4 servants, co-conspirators, or employees of one another, and the acts and omissions herein
5 alleged were done or suffered by them, acting individually and through or by their alleged
6 capacity, within the scope of their authority. Each of the defendants aided and abetted and
7 rendered substantial assistance in the accomplishment of the acts complained of herein. In
8 taking the actions, as particularized herein, to aid and abet and substantially assist in the
9 commission of the misconduct complained of, each defendant acted with an awareness of his,
10 her or its primary wrongdoing and realized that his, her or its conduct would substantially
11 assist in the accomplishment of that misconduct and was aware of his, her or its overall
12 contribution to, and furtherance of the conspiracy, common enterprise, and common course of
13 conduct. Defendants' acts of aiding and abetting included, *inter alia*, all of the acts each
14 defendant is alleged to have committed in furtherance of the conspiracy, common enterprise,
15 and common course of conduct complained of herein.

16 THE PATENTS-IN-SUIT

17 12. '038 patent. Metastasis constitutes a major portion of the life-threatening aspects
18 of cancer. Metastasis is the spread of cancer in the body. It includes the growth of secondary
19 tumors at sites different from the primary tumor. Metastasis can defy surgical removal of the
20 primary tumor and make it impossible to arrest cancer's spread. In order to understand
21 metastasis, a real-time model which permits identification of small numbers of tumor cells
22 against a background of many host cells (so that secondary tumor emboli and micrometastases
23 can be observed over the course of real time) is needed.

24 13. Key terms in the '038 patent include GFP, *i.e.*, green fluorescent protein. The
25 '038 patent defines GFP as a fluorescent protein of any color. For example, the specification
26 of the '038 patent teaches:

27 By suitable modification, the spectrum of light emitted by the GFP
28 can be altered. Thus, although the term "GFP" is used in the
present application, the proteins included within this definition are

1 not necessarily green in appearance. Various forms of GFP exhibit
2 colors other than green and these, too, are included within the
3 definition of "GFP" and are useful in the methods and materials of
4 the invention. In addition, it is noted that green fluorescent proteins
5 falling within the definition of "GFP" herein have been isolated
6 from other organisms, such as the sea pansy, *Renilla reriformis*.
Any suitable and convenient form of the GFP gene can be used to
modify the tumor cells useful in the models of the invention, and
for retroviral transformation of endogenous tumors.

7
8 14. The '038 patent (Ex. 1 hereto) relates to the study of tumor progression.
9 Specifically, it concerns model systems for studying tumor metastasis in vertebrates and
10 evaluating candidate drugs for treating the tumors. It claims methods for following metastasis
11 by looking at GFP-expressing tumor cells in vertebrate animal organ tissues.

12 15. The priority date of the '038 patent is March 27, 1998.

13 16. '159 patent. The '159 patent (Ex. 2 hereto) relates to the whole-body external
14 optical imaging of gene expression. It claims methods for such imaging (as well as methods
15 for evaluating candidate protocols or drugs for treating disease) using fluorophores linked to
16 the endogenous promoters of genes. These methods offer simple, noninvasive, highly selective
17 and real-time means for recording and analyzing gene expression in animals. The '159 patent
18 does not limit the methods by which the images produced by fluorescence optical tumor
19 imaging can be monitored or captured. Instead, any suitable methods are encompassed by the
20 claims of the '159 patent. For example, Example 1 to the specification of the '159 patent
21 provides that high resolution images can be captured by computer, or continuously through
22 video output onto videotape. The '159 patent's more limited definition of GFP is in contrast to
23 the definitions set forth in the patent family that includes the '038 patent (which defines the
24 term GFP explicitly as including all colors, not just green). However, the claims use the term
25 "fluorophore," which can include any color (not just green). Claim 5 of the '159 patent
26 identifies as a claim limitation that the fluorophore used be selected from a group of
27 fluorescent proteins consisting of GFP, BFP (blue fluorescent protein), and RFP (red
28

1 fluorescent protein).

2 17. The priority date of the '159 patent is March 17, 2000.

3 18. AntiCancer licenses the use of its patented methods to others – both commercial
4 users (such as pharmaceutical companies) and non-commercial users (such as universities).

5 19. When a user uses AntiCancer's methods to image GFP-expressing tumor cells
6 and/or gene expression in a live, intact lab animal, it infringes AntiCancer's patents (unless
7 done pursuant to a license with AntiCancer).

8 DEFENDANTS' WRONGFUL COURSE OF CONDUCT

9 20. Berthold designs, manufactures, and sells imaging systems to customers. These
10 imaging systems include the following: the NightOWL LB 981 NC 100 and accessories
11 thereto (shown in Ex. 9 hereto); the NightOWL II LB 983 and accessories thereto (shown in
12 Ex. 3 and 5 hereto); and the NightOWL II LB 983 NC 320 and accessories thereto, including
13 indiGO TM software (shown in Ex. 8 hereto) and the NightOWLcam NC 320 (shown in Ex. 11
14 hereto). Together, these products are referred to collectively sometimes hereinafter as the
15 "Berthold image analyzers."

16 21. Published scientific articles, when read by persons of skill in the art together with
17 Berthold's publications, the '038 and '159 patents and AntiCancer's published applications, (a)
18 show that such persons can practice certain methods claimed in the patents-in-suit using the
19 Berthold image analyzers, and (b) make clear that Berthold encourages the use of its image
20 analyzers to practice those claimed methods. These articles include some of those listed in
21 Berthold's publication, "Literature about Imaging with NightOWL" (Ex. 12 hereto), and also
22 include the following:

23 • Y. Hattori, *et al.*, *Non-viral delivery of the connexin 43 gene with histone*
24 *deacetylase inhibitor to human nasopharyngeal tumor cells enhances gene expression and*
25 *inhibits in vivo tumor growth*, 30 International Journal of Oncology 1427-1439 (Institute of
26 Medicinal Chemistry, Hoshi University 2007), which describes detection of GFP expression in
27 tumor cells in nude mice using the NightOWL LB981 NC100 system (Ex.13);

28 • X. Li, *et al.*, *Gene Therapy for Prostate Cancer by Controlling Adenovirus E1a*

1 *and E4 Gene Expression with PSES Enhancer*, 65 Cancer Research 1941 (American Assn. for
2 Cancer Research 2004), which describes observation of GFP-expressing tumor cells in mice
3 via fluorescence microscopy using the Berthold LB981 NightOWL system (Ex. 14);

4 • M. Morille, *et al.*, *Long-circulating DNA lipid nanocapsules as new vector for*
5 *passive tumor targeting*, 31 Biomaterials 321-9 (Biomaterials 2009), which describes non-
6 invasive fluorescent imaging of glioma cell lines labeled with DiD, a near-infrared
7 fluorophore, in mice using the LB 983 NightOWL II; (Ex. 15);

8 • Caceres, G., *et al.*, *Imaging of luciferase and GFP-transfected human tumours in*
9 *nude mice*, 18 Luminescence 218-223 (John Wiley & Sons, Ltd., 2010), which describes *in*
10 *vivo* studies of GFP-transfected human breast tumor cells injected into nude mice using the
11 Berthold NightOWL LB981 Molecular Light Imager (Ex. 16);

12 • S. Emmrich, *et al.*, *Antisense gapmers selectively suppress individual oncogenic*
13 *p73 splice isoforms and inhibit tumor growth in vivo*, 8 Molecular Cancer 61 (Emmrich, *et al.*,
14 2009), which describes *in vivo* imaging of Oregon green 488 protein-expressing tumor cells in
15 nude mice using the NightOWL LB981 imaging system (Ex. 17); and

16 • H. Jiang, *et al.*, *The combined status of ATM and p53 link tumor development*
17 *with therapeutic response*, 23 Genes Dev. 1895-1909 (Cold Spring Harbor Laboratory Press
18 2009), which describes *in vivo* observation of response of GFP-expressing mouse lymphoma
19 cells to chemotherapy using a NightOWL imaging system (Ex. 18).

20 22. These papers, read in conjunction with Berthold's own bibliography which touts
21 them (Ex. 12), prove both (a) the suitability of the Berthold image analyzers for performing the
22 methods claimed in claims 1-2, 5-6 of the '038 patent and claims 1, 5, and 7-11 of the '159
23 patent and (b) Berthold's overt attempts to induce actual and potential customers to use the
24 Berthold image analyzers for that purpose.

25 23. Berthold has been marketing the Berthold image analyzers for sale in the United
26 States via its website (www.berthold.com) and paper marketing materials, wherein actual
27 and/or potential customers have found the following statements:

28 • "BFI [biofluorescence imaging] utilizes proteins, which fluoresce under

1 illumination . . . BFI ha[s] contributed to the understanding of disease mechanisms and the
2 development of new treatments” (Ex. 3, 8);

3 • “Whole animals . . . can be imaged . . . regardless [of whether] luminescent or
4 fluorescent markers are used” (*id.*);

5 • “Gene expression can be monitored in living organisms with ultra sensitive
6 imaging systems”; using the NightOWL, “a lot of special applications can be done easily like .
7 . . animal imaging”; NightOWL II “offers quantitative autofluorescence” (Ex. 4);

8 • “In vivo imaging in general allows a non-invasive insight into living organisms
9 and helps to understand metabolic processes and disease related changes. Especially . . . BFI
10 enable[s] monitoring of gene expression or disease progression in living organisms due to
11 outstanding sensitivity” (describing methods capable of usage with the NightOWL II LB 983)
12 (Ex. 5);

13 • NightOWL LB 981 NC 100 system “enables non-invasive visualization of gene
14 expression in intact animals”; including diagram of mice holder component of system (Ex. 6);

15 • “In biofluorescence imaging (BFI) proteins and their derivatives are utilized
16 In most cases GFP and its derivatives, YFP and dsRED are used”; “[N]ear infrared NIR)
17 fluorescence is a promising technique to get better signals from deep inside the animal” (Ex.
18 9); and

19 • description of an induction box for the NightOWL II LB 983 NC 100 which “can
20 be used for both mice and rats” and describing use of GFP and derivatives YFP and dsRED in
21 performing biofluorescence imaging using the instrument (Ex. 10).

22 24. Berthold’s publications clearly list the proper filters, excitation and emission
23 recommendations, reagents to use for imaging with GFP, and a glossary of terms (including
24 “fluorescence reflectance imaging”) (Ex. 7) useful in practicing the methods claimed in claims
25 1-2 and 5-6 of the ‘038 patent and claims 1, 5, and 7-11 of the ‘159 patent. The materials also
26 contain general, boilerplate notices to actual and would-be customers regarding use of the
27 Berthold image analyzers and potential liability for patent infringement, warnings its customers
28 as follows: “Some techniques for generating and/or detecting light in biological subjects are

1 patented and may require licences from third parties. Users are advised to independently
2 determine [sic] for themselves whether their activities infringe any valid patent." *See, e.g., Ex.*
3 *6, p. 45.*

4 25. At all relevant times, Berthold has actively encouraged its actual and prospective
5 customers to practice methods claimed in the patents-in-suit in the United States by using the
6 Berthold image analyzers for fluorophore-based imaging of tumor cells and gene expression in
7 live animals, without AntiCancer's consent. Berthold has sold multiple Berthold image
8 analyzers to its customers in the United States, and is continuing to do so. Berthold openly
9 advertises the fluorescent imaging capabilities of the Berthold image analyzers in direct
10 marketing pieces and on its website. It provides its customers with detailed user manuals
11 which provide filter settings and lens configurations necessary to use Berthold image analyzers
12 to do fluorescent imaging. In so doing, Berthold actively has induced and (unless enjoined by
13 the Court) will continue to induce infringement of AntiCancer's patents by knowingly causing
14 its customers (including *Does 1 et seq.*) to infringe those patents directly by using the Berthold
15 image analyzers to perform methods claimed in those patents.

16 FIRST CLAIM FOR RELIEF

17 (For Infringement of '038 Patent)

18 (Against all Defendants)

19 26. AntiCancer realleges and incorporates by reference as though fully set forth
20 preceding paragraphs 1 through 25.

21 27. The '038 patent issued on July 6, 2004. A true and correct copy of the '038
22 Patent is attached hereto as Exhibit 1 and incorporated herein by this reference.

23 28. AntiCancer is the sole owner of the '038 patent.

24 29. Defendants Berthold U.S.A. and Berthold Germany have infringed, and still are
25 infringing, the '038 patent by making, using, selling, and offering for sale the Berthold image
26 analyzers, *i.e.*, devices which can and are be used to infringe one or more claims of the '038
27 Patent by defendants' customers without AntiCancer's authorization or consent.

28 30. Defendants have infringed claims 1, 5, and/or 7-11 of the '038 patent and

1 encouraged others to do so, and will continue to do so unless enjoined by this Court.

2 31. Defendants are, and at all material times have been, aware of the '038 patent and
3 their infringement has been willful.

4 32. Defendants Berthold USA and Berthold Germany are actively inducing
5 infringement of the '038 patent by others, all of whom are sued herein as Does 1 through 100.
6 AntiCancer will seek leave to amend this complaint to show the true names and capacities of
7 said defendants when they are ascertained.

8 33. By reason of the foregoing, AntiCancer has suffered damages in an amount to be
9 proven at trial and, in addition, has suffered irreparable loss and injury.

10 34. The acts of infringement described above are willful, deliberate and in reckless
11 disregard of AntiCancer's patent rights.

12 SECOND CLAIM FOR RELIEF

13 (Infringement of '159 Patent)

14 (Against all Defendants)

15 35. AntiCancer realleges and incorporates by reference as though fully set forth
16 preceding paragraphs 1 through 34.

17 36. The '159 patent issued on November 18, 2003. A true and correct copy of the
18 '159 Patent is attached hereto as Exhibit 2 and incorporated herein by this reference.

19 37. AntiCancer is the sole owner of the '159 patent.

20 38. Defendants Berthold USA and Berthold Germany have infringed, and still are
21 infringing, the '159 patent by making, using, selling, and offering for sale the Berthold image
22 analyzers, *i.e.*, devices which can and are be used to infringe one or more claims of the '159
23 patent by defendants' customers without AntiCancer's authorization or consent.

24 39. Defendants Berthold USA and Berthold Germany have infringed claims 1-2 and
25 5-6 of the '159 patent and encouraged others (including Does 1 *et seq.*) to do so, and will
26 continue to do so unless enjoined by this Court.

27 40. Defendants are, and at all material times have been, aware of the '159 patent and
28 their infringement has been willful.

1 41. Defendants Berthold USA and Berthold Germany are actively inducing
2 infringement of the '159 patent by others, all of whom are sued herein as Does 1 through 100.
3 AntiCancer will seek leave to amend this complaint to show the true names and capacities of
4 said defendants when they are ascertained.

5 42. By reason of the foregoing, AntiCancer has suffered damages in an amount to be
6 proven at trial and, in addition, has suffered irreparable loss and injury.

7 43. The acts of infringement described above are willful, deliberate and in reckless
8 disregard of AntiCancer's patent rights.

9 PRAYER FOR RELIEF

10 WHEREFORE, AntiCancer prays for relief as follows:

11 A. That defendants, and each of them, be adjudged to have infringed '038 and/or
12 '159 patent(s), under 35 U.S.C. § 271(a), (b), (c), and (g);

13 B. That all defendants, and each of them, be adjudged to have willfully infringed the
14 '038 and/or '159 patent(s) under 35 U.S.C. § 271(a), (b), (c), and (g);

15 C. That defendants, and each of them, as well as their respective officers, agents,
16 servants, employees and attorneys, and those persons in active concert or participation with
17 them be preliminarily and permanently restrained and enjoined under 35 U.S.C. § 283 from
18 directly or indirectly infringing the '038 and /159 patent(s);

19 D. That the Court award damages to compensate AntiCancer for the defendants'
20 infringement of the '038 and '159 patent(s), as well as enhanced damages pursuant to 35
21 U.S.C. § 284;

22 E. That the Court award AntiCancer its attorney's fees pursuant to 35 U.S.C.
23 § 285;

24 F. That the Court assess against defendants and in favor of AntiCancer pre-
25 judgment and post-judgment interest and costs of suit; and
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27
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1 G. That AntiCancer have such other and further relief as this Court may deem just
2 and proper.


3
4 Dated: November 12, 2010

Respectfully submitted,

LAWTON LAW FIRM

5 By:


Dan Lawton


Joseph C. Kracht

Attorney for Plaintiff AntiCancer, Inc.

1 DEMAND FOR TRIAL BY JURY AND FOR SPEEDY HEARING

2 AntiCancer hereby demands a trial by jury as to all issues triable by jury, specifically
3 including, but not limited to, the infringement of United States Patent Nos. 6,649,159 and
4 6,759,038. AntiCancer also requests a speedy hearing pursuant to Fed. R. Civ. P. 57.

5 Respectfully submitted,

6 Dated: November 12, 2010

LAWTON LAW FIRM

7 By: 

8 Dan Lawton

9 Joseph C. Kracht

10 Attorneys for Plaintiff AntiCancer, Inc.

