

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

SYNAFFIX B.V.

Petitioner

v.

HANGZHOU DAC BIOTECH CO., LTD.,

Patent Owner

Patent No. 10,131,682

Ex Parte Reexamination Certificate Issued: January 4, 2021

Title: HYDROPHILIC LINKERS AND THEIR USES FOR CONJUGATION OF
DRUGS TO A CELL BINDING MOLECULES

Inter Partes Review No. IPR2022-01531

DECLARATION OF JAMES L. MULLINS, Ph.D.

TABLE OF CONTENTS

I.	INTRODUCTION	4
II.	BACKGROUND AND QUALIFICATIONS	5
III.	PRELIMINARIES	6
	1. Periodicals	11
	2. Cataloging/Indexing	11
IV.	OPINION REGARDING INDIVIDUAL DOCUMENTS	14
A.	EX1005. Morales-Sanfrutos, Julia, Francisco Javier Lopez-Jaramillo, Fernando Hernandez-Mateo, and Francisco Santoyo-Gonzalez, "Vinyl sulfone bifunctional tag reagents for single-point modification of proteins," <i>The Journal of Organic Chemistry</i> 75, no. 12 (2010): 4039-4047 ("Morales-Sanfrutos").	14
	1. Authentication	14
	2. Public Accessibility	17
	3. Conclusion	19
B.	EX1006. Straus, W. and J.M. Keller, "Unusual Binding Sites for Horseradish Peroxidase on the Surface of Cultured and Isolated Mammalian Cells," <i>Histochemistry</i> 85, September 1986, pages 277-285 ("Straus").	19
	1. Authentication	19
	2. Public Accessibility	22
	3. Conclusion	24
C.	EX1014. Joshua D. Thomas, et.al., "Application of Strain-Promoted Azide-Alkyne Cycloaddition and Tetrazine Ligation to Targeted Fc-Drug Conjugates," <i>Bioconjugate Chemistry</i> , Volume 23, Number 10, October 2012, pages 2007–2013 ("Thomas")	24
	1. Authentication	24
	2. Public Accessibility	27
	3. Conclusion	30

D.	EX1015. Kathrin-Maria Roy, <i>et al</i> , "Sulfones and Sulfoxides," <i>Ullmann's Encyclopedia of Industrial Chemistry</i> , Sixth, Completely Revised Edition, Volume. 34, 2003. pages 571-587. ("Roy")	31
	1. Authentication	31
	2. Public Accessibility	34
	3. Conclusion	36
E.	EX1016. Robert Y. Zhao, et al., "Synthesis and Evaluation of Hydrophilic Linkers for Antibody–Maytansinoid Conjugates." <i>Journal of Medicinal Chemistry</i> , Volume 54, Number 10, May 26, 2011: pages 3606-3623. ("Zhao")	36
	1. Authentication	36
	2. Public Accessibility	39
	3. Conclusion	42
V.	AVAILABILITY FOR CROSS-EXAMINATION	42
VI.	RIGHT TO SUPPLEMENT	43
VII.	JURAT	43

I, James L. Mullins, hereby declare under penalty of perjury:

1. My name is Dr. James L. Mullins.

2. I have been retained by Synaffix B.V., Petitioner, in the above-captioned *inter partes* review relating to U.S. Patent No. 10,131,682 and its Ex Parte Reexamination Certificate, issued January 4, 2021, to provide opinions on various documents.

I. INTRODUCTION

3. I have personal knowledge of the facts and opinions set forth in this declaration, I believe them to be true, and if called upon to do so, I would testify competently to them. I have been warned that willful false statements and the like are punishable by fine or imprisonment, or both.

4. I am a retired academic librarian working as the Founder and Owner of the firm Prior Art Documentation Librarian Services, LLC at 205 St Cuthbert, Williamsburg, VA 23188. Attached as exhibit EX1013 is a true and correct copy of my Curriculum Vitae describing my background and experience. Further information about my firm, Prior Art Documentation Librarian Services, LLC (PADLS), is available at www.priorartdoclib.com.

5. I have been retained by Petitioner to authenticate and establish the dates of public accessibility of certain documents for use in one or more *inter partes* review proceedings. For this service, I am being paid my usual hourly fee of

\$275/hour. My compensation in no way depends on the substance of my testimony or the outcome of the proceedings.

II. BACKGROUND AND QUALIFICATIONS

6. I am presently Dean Emeritus of Libraries and Esther Ellis Norton Professor Emeritus, Purdue University, 2018 – present.

Previously employed as follows:

- Dean of Libraries and Professor & Esther Ellis Norton Professor, Purdue University, West Lafayette, IN, 2004-2017;
- Assistant/Associate Director for Administration, Massachusetts Institute of Technology (MIT), Cambridge, MA, 2000-2004;
- University Librarian and Director, Falvey Memorial Library, Villanova University, Villanova, PA, 1996-2000;
- Director of Library Services, Indiana University South Bend, South Bend, IN, 1978-1996. Part-time instructor, School of Library and Information Science, Indiana University, Bloomington, IN, 1979-1996;
- Associate Law Librarian, and associated titles, Indiana University School of Law, Bloomington, IN, 1974-1978;
- Catalog Librarian, Assistant Professor, Georgia Southern College (now University), Statesboro, GA, 1973-1974.

7. Over the course of my career as a librarian, instructor of library science, author of scholarly publications, and presenter at national and international conferences, I have had experience with catalog records and online library management systems built around Machine-Readable Cataloging (MARC) standards.

8. In the course of more than forty-four years as an academic librarian and scholar, I have been an active researcher. In my years as a librarian, I have facilitated the research of faculty colleagues either directly or through the provision of and access to the requisite print and/or digital materials and services at the universities I worked. I have kept current on the professional library science literature and served on the editorial board of the most prominent library journal, *College and Research Libraries*. This followed service as the chair of the Research Committee of the Association of College and Research Libraries (ACRL), a division of the American Library Association (ALA). As an academic library administrator, I have had responsibility to ensure that students were educated to identify, locate, assess and integrate information garnered from library resources.

III. PRELIMINARIES

9. *Scope of this declaration.* I am not a lawyer, and I am not rendering an opinion on the legal question of whether a particular document is, or is not, a “printed publication” under the law.

10. I am, however, rendering my expert opinion on the authenticity of the document referenced herein and on when and how this document was disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, could have located the document by at least by November 24, 2012.

11. I am informed by counsel that an item is considered authentic if there is sufficient evidence to support a finding that the item is what it is claimed to be. I am also informed that authenticity can be established based on the contents of the documents themselves, such as the appearance, content, substance, internal patterns, or other distinctive characteristics of the item, taken together with all of the circumstances.

12. I am informed by counsel that a given reference is publicly accessible upon a satisfactory showing that such a document has been disseminated or otherwise made available to the extent that persons interested and ordinarily skilled in the subject matter or art exercising reasonable diligence, can locate it. I have also been informed by counsel that materials available in a library constitute printed publications if they are cataloged and indexed according to general library practices that make the references available to members of the interested public.

13. *Materials considered.* In forming the opinions expressed in this declaration I have reviewed the documents and exhibits referenced herein. These materials are records created in the ordinary course of business by publishers, libraries, indexing services, and others. From my years of experience, I am familiar with the process for creating many of these records, and I know these records are created by people with knowledge of the information in the record. Further, these records are created with the expectation that researchers and other members of the

public will use them. All materials cited in this declaration and its exhibits relied upon to establish authenticity and/or the dates of public accessibility are of a type that experts in my field would reasonably rely upon and refer to in forming their opinions.

14. *Persons of ordinary skill in the art.* I am told by counsel that the subject matter of this proceeding relates to antibody-drug conjugates, also known as ADCs.

15. I have been informed by counsel that a “person of ordinary skill in the art at the time of the inventions” (POSA) is a hypothetical person who is presumed to be familiar with the relevant field and its literature at the time of the inventions. This hypothetical person is also a person of ordinary creativity, capable of understanding the scientific principles applicable to the pertinent field.

16. I am told by counsel that persons of ordinary skill in this subject matter or art would have had a Ph.D. degree in organic chemistry, biochemistry, immunology and/or cell biology, along with at least several years of relevant applied research and/or industry experience in the same fields. Alternatively, I understand from counsel that a POSA would have had a Masters or Bachelors degree in one of the same fields with at least 5-10 year work experience.

17. It is my opinion that such a person would also have been engaged in research, learning through study and practice in the field and possibly through formal instruction the bibliographic resources relevant to his or her research. Such a person

would have had access to a vast array of print resources in content-delivery and interface design in interactive computer networks as well as to a fast-changing set of online resources.

18. *Library catalog records.* Some background on MARC formatted records, OCLC, WorldCat, and OCLC's Connexion is needed to understand the library catalog records discussed in this declaration.

19. Libraries world-wide use the MARC format for catalog records; this machine-readable format was developed by the Library of Congress in the 1960s.

20. MARC formatted records provide a variety of subject access points based on the content of the document being cataloged. All subject headings may be found in the MARC fields 6XX. For example, MARC Field 600 identifies personal names used as subjects and MARC Field 650 identifies topical terms. A researcher might discover material relevant to his or her topic by a search using the terms employed in MARC Fields 6XX.

21. The MARC Field 040, subfield a, identifies the library or other entity that created the original catalog record for a given document and transcribed it into machine readable form. The MARC Field 008 identifies the date when this first catalog record was entered on the file. This date persists in all subsequent uses of the first catalog record, although newly-created records for the same document, separate

from the original record will show a new date. It is not unusual to find multiple catalog records for the same document

22. *WorldCat* is the world's largest public online catalog, maintained by the Online Computer Library Center, Inc., or OCLC, and built with the records created by the thousands of libraries that are members of OCLC. *WorldCat* provides a user-friendly interface for the public to use MARC records; it requires no knowledge of MARC tags and codes. *WorldCat* is easily accessible through the World Wide Web to all who wish to search it; there are no restrictions to be a member of a particular community, etc. The date a given catalog record was created (corresponding to the MARC Field 008) appears in some detailed *WorldCat* records as the Date of Entry but not necessarily all.

23. Whereas *WorldCat* records are widely available, the availability of MARC formatted records varies from library to library.

24. When an OCLC participating institution acquires a document for which it finds no previously created record in OCLC, or when the institution chooses not to use an existing record, it creates a record for the document using OCLC's Connexion, the bibliographic system used by catalogers to create MARC records. Connexion automatically supplies the date of record creation in MARC Field 008.

25. Once the MARC record is created by a cataloger at an OCLC participating member institution, it becomes available to other OCLC participating

members in Connexion and also in *WorldCat*, where persons interested and ordinarily skilled in the subject matter or art, exercising reasonable diligence, can locate it.

1. Periodicals

26. A library typically creates a catalog record for a periodical publication when the library receives its first issue. When the institution receives subsequent issues/volumes of the periodical, the issues/volumes are checked in (often using a date stamp), added to the institution's holding records, and made available very soon thereafter – normally within a few days of receipt or (at most) within a few weeks of receipt.

27. The initial periodicals record will sometimes not reflect all subsequent changes in publication details (including minor variations in title, frequency, etc.).

2. Cataloging/Indexing

28. A researcher may discover material relevant to his or her topic in a variety of ways. One common means of discovery is to search for relevant information in an index of periodical and other publications. Having found relevant material, the researcher will then normally obtain it online, look for it in libraries, or purchase it from a publisher, a bookstore, a document delivery service, or other provider. Sometimes, the date of a document's public accessibility will involve both

indexing and library date information. Date information for indexing entries is, however, often unavailable. This is especially true for online indices.

29. Indexing services use a wide variety of controlled vocabularies to provide subject access and other means of discovering the content of documents. The formats in which these access terms are presented vary from service to service.

30. Online indexing services commonly provide bibliographic information, abstracts, and full-text copies of the indexed publications, along with a list of the documents cited in the indexed publication. These services also often provide lists of publications that cite a given document. A citation of a document is evidence that the document was publicly available and in use by researchers no later than the publication date of the citing document.

31. **ACS InfoCentral:** provides the latest information for prospective and current subscribers to ACS (American Chemical Society) Publications. <https://pubs.acs.org/page/4librarians/index.html>

32. **Springer Link** - Providing researchers with access to millions of scientific documents from journals, books, series, protocols, reference works and proceedings. <https://link.springer.com/>

33. **Wayback Machine/Internet Archive** -The Internet Archive is a digital archive/library that began in 1996 to ‘scrape’ publicly accessible webpages. The Internet Archive created a service called the *Wayback*

Machine that enables public access to surf more than 746 billion web pages (August, 2022) stored in the Internet Archive. Searches on the *Wayback Machine* can be undertaken by URL or name of entity. If an archive record for a URL is available, it will be shown. Through the *Wayback Machine* it is possible to view a specific webpage at a URL and see that page on that date as it then appeared. It is more or less a ‘snapshot’ of the website on that date <https://archive.org>.

34. **Wiley Online Library** - a full range of unrivaled journals, books, major reference works, and databases. Multidisciplinary collection of online resources covering life, health, and physical sciences; social science; and the humanities—850 scientific and scholarly societies around the world, and access to over 7.5 million articles from over 1,600 journals, over 21,000 online books, and hundreds of multi-volume reference works, databases, and other resources online. <https://onlinelibrary.wiley.com/researchers>

35. **Wisconsin TechSearch (WTS)** - WTS offers an array of article delivery and research services to individuals and organizations not affiliated with the University of Wisconsin or who need the specialized skills of WTS staff in locating and retrieving information. It is the policy of WTS to keep confidential all material submitted by clients with respect to searches as well as search results. WTS

will not disclose material pertaining to searches to third parties except as required by law. <https://wts.wisc.edu/>.

IV. OPINION REGARDING INDIVIDUAL DOCUMENTS

- A. EX1005. Morales-Sanfrutos, Julia, Francisco Javier Lopez-Jaramillo, Fernando Hernandez-Mateo, and Francisco Santoyo-Gonzalez, "Vinyl sulfone bifunctional tag reagents for single-point modification of proteins," *The Journal of Organic Chemistry* 75, no. 12 (2010): 4039-4047 ("Morales-Sanfrutos").**

1. Authentication

36. I have been asked to opine on the authenticity and public access of an article authored by Julia Morales-Sanfrutos *et al.*, titled "Vinyl Sulfone Bifunctional Tag Reagents for Single-Point Modification of Proteins," published in *The Journal of Organic Chemistry*, in volume 75, number 12, the June 18, 2010 issue on pages 4039-4047. (EX1005, "Morales-Sanfrutos" or "Morales" for short)

37. For consistency and clarification, Morales-Sanfrutos, when used in this declaration, refers not only to the Morales-Sanfrutos article but also the journal volume and issue in which it was published: *The Journal of Organic Chemistry*, Volume 75, Number 12, June 18, 2010.

38. I have evaluated the Morales-Sanfrutos reference in three ways: (1) by assessing scans of a copy of Morales-Sanfrutos (EX1005) provided to me by counsel; (2) accessing and assessing a scan of Morales-Sanfrutos, EX1020, I obtained through Wisconsin TechSearch (WTS) from the print copy owned by the

Linda Hall Library, Kansas City, Missouri, a pre-eminent research library in the areas of science, engineering and technology on September 27, 2022; and (3) by retrieving and reviewing a download, EX1021, I made on September 27, 2022 through Purdue University Libraries by my emeritus faculty status from *ACS Info Central*, a proprietary database of the American Chemical Society through this URL: <https://pubs-acrs-org.ezproxy.lib.purdue.edu/doi/pdf/10.1021/bc300052u>. It is available for a fee at this URL: <https://pubs.acs.org/doi/abs/10.1021/bc300052u>.

39. EX1020 is a scan of Morales-Sanfrutos that includes the issue cover of *The Journal of Organic Chemistry*, Volume 75, Number 12, June 18, 2010 with a stamp that reads “LINDA HALL LIBRARY JUN 16 2010”, as shown below, that indicates ownership and date of receipt by the Linda Hall Library, Kansas City, Missouri. The date indicates it was received and “checked-in” to the collections of the Linda Hall Library, on June 16, 2010; journal information pages; and the Morales-Sanfrutos article, pages 4039-4047.



40. All identifying characteristics, such as the stamp on EX1020, are consistent with library practice and procedure that I have observed during my career as a professional librarian. I have no cause for concern about the authenticity or accuracy of these identifying attributes. Exhibit 1018 was found within the custody of a library, the Linda Hall Library, one of the most likely locations for an authentic publication.

41. Exhibit 1019/21 is a copy of Morales-Sanfrutos that I retrieved on October 3, 2022, from the Purdue University Libraries by my emeritus faculty status through the *ACS InfoCentral* database, a proprietary database of the American Chemical Society as described above at this URL: <https://pubs-acsoe.org.ezproxy.lib.purdue.edu/doi/pdf/10.1021/jo100324pdf>.

It is available for a fee at this URL:

<https://pubs.acs.org/doi/pdf/10.1021/jo100324pdf>.

42. After comparing Morales-Sanfrutos as it appeared in EX1020 and EX1021, I conclude, based on finding Morales-Sanfrutos in print in a library – Linda Hall - and online through a reputable publisher database, *ACS InfoCentral*, that Morales-Sanfrutos is an authentic document, and that EX1020 and EX1021 are authentic and accurate copies of Morales-Sanfrutos. I then compared EX1020 and EX1021 with EX1005, provided by counsel, and I found no differences between any of the three documents.

43. Therefore, I conclude and affirm Morales-Sanfrutos (EX1005) is an authentic document.

2. Public Accessibility

44. EX1022 is a true and correct copy of the *WorldCat* entry for Morales-Sanfrutos. Morales-Sanfrutos was included among the articles published in *The Journal of Organic Chemistry*, Volume 75, Number 12, June 18, 2010, on pages 4039-4047. I obtained EX1022 by completing a search on *WorldCat* on October 4, 2022. The document cataloged in this record is a periodical record for *The Journal of Organic Chemistry* as verified by title: *Journal of Organic Chemistry*; publisher and publication date: American Chemical Society, 1936 -. The 1936 - indicates an ‘open entry’, that is, a serial that started in 1936 and will continue until some point in the future.

45. When undertaking the search of *WorldCat* as described above using the geographical location of Missouri, the Linda Hall Library was among the 1,515 libraries that hold *The Journal of Organic Chemistry* worldwide.

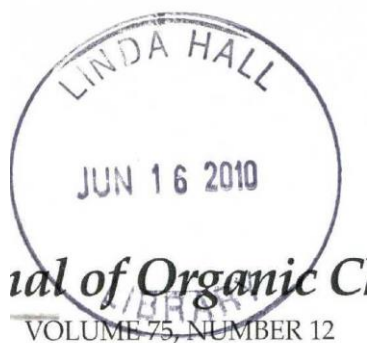
46. *The Journal of Organic Chemistry*, Morales-Sanfrutos, could have been identified and located in a library in print by searching title: *The Journal of Organic Chemistry*; and/or by subject headings: *Chemistry, Organic – Periodicals*.

47. EX1023 is a download I made from the Linda Hall Library OPAC (online catalog) on October 4, 2022. The document cataloged in this record is a

periodical record for: *The Journal of Organic Chemistry*, publisher and publication date: American Chemical Society, 1936- . The 1936- indicates an ‘open entry’, that is, a serial that started in 1936 and will continue in the future. Under “Item in Place” it reads as follows: “v.75:pgs 2767-4336 (2010)”, this string indicates that the Linda Hall Library holds the issue that includes the article by Morales-Sanfrutos.

48. Morales-Sanfrutos could have been located by searching on the Linda Hall Library OPAC (online catalog) for the title: *The Journal of Organic Chemistry*; and/or by searching the subject heading: *Chemistry, Organic – Periodicals*.

49. On EX1020 is the ownership and date stamp on the cover that reads “LINDA HALL JUN 16 2010 LIBRARY”, as shown below. The date of June 16, 2010 would be when receipt and the processing began on *The Journal of Organic Chemistry, Volume 75, Number 12, June 18, 2010* by the Linda Hall Library.



50. Consistent with standard library policy and practice, this issue would have been accessible on the shelf in the Linda Hall Library within a week to ten days

after receipt by the library, that is, no later than June 26, 2010, well before November 24, 2012.

51. Furthermore, and consistent with the availability of a physical copy of Morales-Sanfrutos as described above, the publisher's website, ACS Publications (<https://pubs.acs.org/doi/10.1021/jo100324p>), discloses that Morales-Sanfrutos was electronically published on May 24, 2010 as shown in EX1024. In my experience such dates typically reflect the date on which the article is available to licensed users (e.g., subscribers to *The Journal of Organic Chemistry*) of the publisher's website.

3. Conclusion

52. I conclude that Morales-Sanfrutos is an authentic document and would have been publicly accessible through the Linda Hall Library, more likely than not, at least by June 26, 2010, well before November 24, 2012.

B. EX1006. Straus, W. and J.M. Keller, "Unusual Binding Sites for Horseradish Peroxidase on the Surface of Cultured and Isolated Mammalian Cells," *Histochemistry* 85, September 1986, pages 277-285 ("Straus").

1. Authentication

53. I have been asked to opine on the authenticity and public access of an article authored by W. Straus and J. M. Keller, titled: "Unusual Binding Sites for Horseradish Peroxidase on the Surface of Cultured and Isolated Mammalian Cells" published in *Histochemistry*, in volume 85, number 4, September 1986 issue on pages 277-285. (EX1006, "Straus")

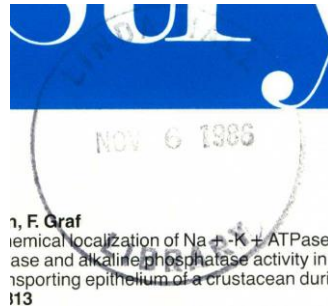
54. For consistency and clarification, Straus, when used in this declaration, refers not only to the Straus article but also the journal volume and issue in which it was published: *Histochemistry*, Volume 85, Number 4, September, 1986.

55. I have evaluated the Straus reference in three ways: (1) by assessing scans of a copy of Straus (EX1006) provided to me by counsel; (2) accessing and assessing a scan of Straus, EX1025, I obtained through Wisconsin TechSearch (WTS) from the print copy owned by the Linda Hall Library, Kansas City, Missouri, a pre-eminent research library in the areas of science, engineering and technology on September 27, 2022; and (3) by retrieving and reviewing a download, EX1026, I made on September 27, 2022 through Purdue University Libraries by my emeritus faculty status from the *Springer Link* database maintained by Springer Publishing, a proprietary database, as described above at this URL: <https://link-springer-com.ezproxy.lib.purdue.edu/content/pdf/10.1007/BF00493477.pdf>. It is available for a fee at this URL:

<https://link.springer.com/content/pdf/10.1007/BF00493477.pdf>.

56. EX1025 is a scan of Straus that includes the issue cover of *Histochemistry*, Volume 85, Number 4, 1986 with a stamp that reads “LINDA HALL LIBRARY NOV 6 1986”, as shown below (quite faint), that indicates ownership and date of receipt by the Linda Hall Library, Kansas City, Missouri. The date indicates it was received and “checked-in” to the collections of the Linda Hall

Library, on November 6, 1986; journal information pages; and the Straus article, pages 277-285.



57. All identifying characteristics, such as the stamp on EX1025 are consistent with library practice and procedure that I have observed during my career as a professional librarian. I have no cause for concern about the authenticity or accuracy of these identifying attributes. EX1025 was found within the custody of a library, the Linda Hall Library, one of the most likely locations for an authentic publication.

58. EX1026 is a copy of Straus that I retrieved on October 3, 2022, from the Purdue University Libraries by my emeritus faculty status from the *Springer Link* database maintained by Springer Publishing, a proprietary database, as described above at this URL: <https://link-springer-com.ezproxy.lib.purdue.edu/content/pdf/10.1007/BF00493477.pdf>.

It is available for a fee at this URL:

<https://link.springer.com/content/pdf/10.1007/BF00493477.pdf>.

59. After comparing Straus as it appeared in EX1025 and EX1026, I conclude, based on finding Straus in print in a library – Linda Hall Library – and online through a reputable, publisher database, *Springer Link*, through Purdue University Libraries, that Straus is an authentic document, and that EX1025 and EX1026 are authentic and accurate copies of Straus. I then compared EX1025 and EX1026 with EX1006, provided by counsel, and I found no differences between any of the three documents.

60. Therefore, I conclude and affirm Straus (EX1006) is an authentic document.

2. Public Accessibility

61. EX1027 is a true and correct copy of the *WorldCat* entry for Straus. Straus was included among the articles published in *Histochemistry*, Volume 85, Number 4, 1986, on pages 277-285. I obtained EX1027 by completing a search on *WorldCat* on October 5, 2022. The document cataloged in this record is a periodical record for *Histochemistry* as verified by title: *Histochemistry and Cell Biology* (title changed from *Histochemistry* to *Histochemistry and Cell Biology* in 1995); publisher and publication date: Springer Verlag, 1995 -. The 1995 - indicates an ‘open entry’, that is, a serial that started in 1995 and will continue into the future.

62. When undertaking the search of *WorldCat* as described above using the geographical location of Missouri, the Linda Hall Library was among the 778 libraries that hold *Histochemistry* worldwide.

63. *Histochemistry*, Straus, could have been identified and located in a library in print by searching title: *Histochemistry*; and/or by subject headings: *Cellbiology*; and/or *Histochemistry-Periodical*.

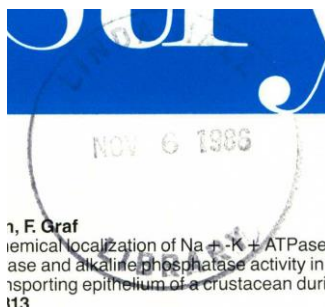
64. EX1028 is a download I made from the Linda Hall Library OPAC (online catalog) on October 4, 2022. The document cataloged in this record is a periodical record for: *Histochemistry*, publisher and publication date: Springer-Verlag, 1974-1994. Under “Item in Place” it reads as follows: “v.85 (1986) Loanable”, this string indicates that the Linda Hall Library holds the issue that includes the article by Straus, as shown below:

Item in place (0 requests) v.85(1986)
Loanable

65. Straus could have been located by searching on the Linda Hall Library OPAC (online catalog) for the title: *Histochemistry*; and/or by searching the subject heading: *Histochemistry – Periodicals*.

66. On EX1025 is the ownership and date stamp on the cover that reads “LINDA HALL NOV 6 1986 LIBRARY”, as shown below. The date of November

6, 1986 would be when receipt and the processing began on *Histochemistry*, Volume 85, Number 4, 1986 by the Linda Hall Library.



67. Consistent with standard library policy and practice, this issue would have been accessible on the shelf in the Linda Hall Library within a week to ten days after receipt by the library, that is, not later than November 16, 1986, well before November 24, 2012.

3. Conclusion

68. I conclude that Straus is an authentic document and would have been publicly accessible through the Linda Hall Library, more likely than not, at least by November 16, 1986, well before November 24, 2012.

C. EX1014. Joshua D. Thomas, et.al., “Application of Strain-Promoted Azide-Alkyne Cycloaddition and Tetrazine Ligation to Targeted Fc-Drug Conjugates,” *Bioconjugate Chemistry*, Volume 23, Number 10, October 2012, pages 2007–2013 (“Thomas”)

1. Authentication

69. I have been asked to opine on the authenticity and public access of an article authored by Joshua Thomas *et al.*, titled “Application of Strain-Promoted Azide-Alkyne Cycloaddition and Tetrazine Ligation to Targeted Fc-Drug

Conjugates,” published in *Bioconjugate Chemistry*, Volume 23, Number 10, October 2012, on pages 2007–2013. (EX1014, “Thomas”)

70. For consistency and clarification, Thomas, when used in this declaration, refers not only to the Thomas article but also the journal volume and issue in which it was published: *Bioconjugate Chemistry*, Volume 23, Number 10, October 2012.

71. I have evaluated the Thomas reference in three ways: (1) by assessing scans of a copy of Thomas (EX1014) provided to me by counsel; (2) accessing and assessing a scan of Thomas, EX1029, I obtained through Wisconsin TechSearch (WTS) from the print copy owned by the Linda Hall Library, Kansas City, Missouri, a pre-eminent research library in the areas of science, engineering and technology on September 27, 2022; and (3) by retrieving and reviewing a download, EX1030, I made on September 27, 2022 through Purdue University Libraries by my emeritus faculty status from *ACS Info Central*, a proprietary database of the American Chemical Society through this URL: <https://pubs-acsc.org.ezproxy.lib.purdue.edu/doi/pdf/10.1021/bc300052u>.

It is available for a fee at this URL:

<https://pubs.acs.org/doi/abs/10.1021/bc300052u>.

72. EX1029 is a scan of Thomas that includes the issue cover of *Bioconjugate Chemistry*, Volume 23, Number 10, October with a stamp that reads

“LINDA HALL LIBRARY OCT 25 2012”, as shown below, that indicates ownership and date of receipt by the Linda Hall Library, Kansas City, Missouri. The date indicates it was received and “checked-in” to the collections of the Linda Hall Library, on October 25, 2012; and the Thomas article, pages 2007-2013.



73. All identifying characteristics, such as the stamp on EX1029 are consistent with library practice and procedure that I have observed during my career as a professional librarian. I have no cause for concern about the authenticity or accuracy of these identifying attributes. EX1029 was found within the custody of a library, the Linda Hall Library, one of the most likely locations for an authentic publication.

74. EX1030 is a copy of Thomas that I retrieved on September 27, 2022, from the Purdue University Libraries by my emeritus faculty status through the ACS *InfoCentral* database, a proprietary database of the American Chemical Society as described above.

75. After comparing Thomas as it appeared in EX1029 and EX1030, I conclude, based on finding Thomas in print in a library – Linda Hall – and online through a reputable, publisher database, *ACS InfoCentral*, that Thomas is an authentic document, and that EX1029 and EX1030 are authentic and accurate copies of Thomas. I then compared EX1029 and EX1030 with EX1014, provided by counsel, and I found no differences between any of the three documents.

76. Therefore, I conclude and affirm Thomas (EX1014) is an authentic document.

2. Public Accessibility

77. EX1031 is a true and correct copy of the *WorldCat* entry for Thomas, *Bioconjugate Chemistry*. Thomas was included among the articles published in *Bioconjugate Chemistry*, Volume 23, Number 10, October 2012 on pages 2007-2013. I obtained EX1031 by completing a search on *WorldCat* on September 30, 2022. The document cataloged in this record is a periodical record for *Bioconjugate Chemistry* as verified by title: *Bioconjugate Chemistry*; publisher and publication date: American Chemical Society, 1990 -. The 1990- indicates an ‘open entry’, that is, a serial that started in 1990 and will continue into the future.

78. When undertaking the search of *WorldCat* as described above using the geographical location of Missouri, the Linda Hall Library was among the 1041 libraries that hold *Bioconjugate Chemistry* world-wide.

79. *Bioconjugate Chemistry* could have been identified and located in a library in print by searching title: *Bioconjugate Chemistry*; and/or by subject headings: *Biochimie*; *Biochemistry*; *Biochimie*; and/or *Bioconjugates*.

80. *Bioconjugate Chemistry* was also available on-line in 2012 as evidenced by EX1030.

81. EX1032 is a download I made from the Linda Hall Library OPAC (online catalog) on September 30, 2022. The document cataloged in this record is a periodical record for: *Bioconjugate Chemistry*; publisher and publication date: American Chemical Society, 1990- . The 1990- indicates an ‘open entry’, that is, a serial that started in 1990 and will continue into the future. Under “Item in Place” it reads as follows: “v.23, no.10 (2012, Dec)”, this string indicates that the Linda Hall Library holds the issue that includes the article by Thomas.

82. Thomas could have been located by searching on the Linda Hall Library OPAC (online catalog) for the title: *Bioconjugate Chemistry*; or by searching the subject heading: *Conjugate-periodicals*.

83. On EX1029 is the ownership and date stamp on the contents page that reads “LINDA HALL OCT 25 2012 LIBRARY”, as shown below. The date of October 25, 2012 would be when receipt and the processing began on *Bioconjugate Chemistry*, Volume 23, Number 10, October 2012 by the Linda Hall Library.



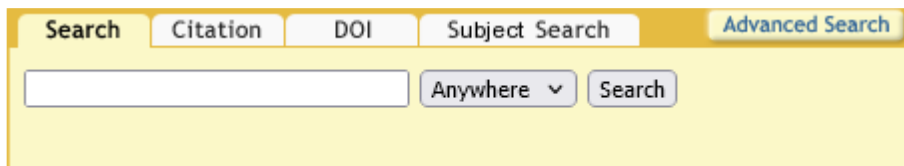
84. Consistent with standard library policy and practice, this issue would have been accessible on the shelf in the Linda Hall Library within a week to ten days after receipt by the library, that is, no later than November 4, 2012, before November 24, 2012.

85. Furthermore, and consistent with the availability of a physical copy of Thomas as described above, the publisher's website, ACS Publications <https://pubs.acs.org/doi/abs/10.1021/bc300052u> discloses that Thomas was electronically published on September 25, 2012, as shown in EX1033. In my experience such dates typically reflect the date on which the article is available to licensed users (e.g., subscribers) of the publisher's website.

86. EX1057 is a screen capture from the *Wayback Machine* from the American Chemical Society journals webpage for *Bioconjugate Chemistry* of April 6, 2011.

87. On this *Wayback Machine* webpage capture was made on April 6, 2011, I completed this screen capture on November 11, 2022 at this URL: <https://web.archive.org/web/20110406100221/http://pubs.acs.org/journal/bcches>

88. Toward the top, below the date heading, April 6, 2011, is the banner for the ACS Publications, *Bioconjugate Chemistry*. To the right of the banner, is a search box, as shown below:



89. The publisher, ACS, provided this search tool using three criteria: Citation; DOI; and Subject Search, thereby allowing a researcher to search for specific journals, authors, or for specific articles by keywords or citation. A researcher could have accessed the ACS Publications/Bioconjugate Chemistry to locate Thomas any time after its publication online on September 25, 2012.

3. Conclusion

90. I conclude that Thomas is an authentic document and would have been publicly accessible through the Linda Hall Library, more likely than not, at least by November 4, 2012, well before November 24, 2012. Additionally, Thomas would have been accessible through the American Chemical Society (ACS) website to a member of the ACS or through his/her institutional subscription (i.e., university library). This access, more likely than not, would have been concurrent with the digital publication date of September 18, 2012.

D. EX1015. Kathrin-Maria Roy, *et al*, “Sulfones and Sulfoxides,” *Ullmann’s Encyclopedia of Industrial Chemistry*, Sixth, Completely Revised Edition, Volume 34, 2003, pages 571-587 (“Roy”)

1. Authentication

91. I have been asked to opine on the authenticity and public access of an article authored by Kathrin-Maria Roy *et al.*, titled “Sulfones and Sulfoxides,” published in *Ullmann’s Encyclopedia of Industrial Chemistry*, Sixth, Completely Revised Edition, Volume 34, 2003, pages 571-587. (EX1015, “Roy”)

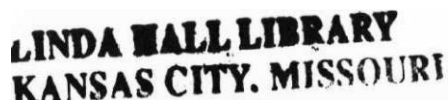
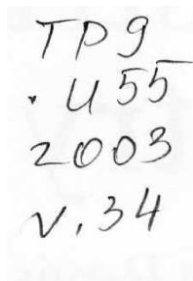
92. For consistency and clarification, Roy, when used in this declaration, refers not only to the Roy article but also *Ullmann’s Encyclopedia of Industrial Chemistry*, Sixth, Completely Revised Edition published in 2003.

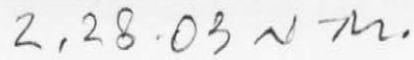
93. I have evaluated the Roy reference in three ways: (1) by assessing scans of a copy of Roy (EX1015) provided to me by counsel; (2) accessing and assessing a scan of Roy, EX1034, I obtained from the print copy owned by the Linda Hall Library, Kansas City, Missouri, a pre-eminent research library in the areas of science, engineering and technology on September 29, 2022; and (3) by retrieving and reviewing a download, EX1036, I made on September 27, 2022 through Purdue University Libraries by my emeritus faculty status from *Wiley Online Library*, a proprietary database through this URL (shown in EX1035):

https://onlinelibrary-wiley-com.ezproxy.lib.purdue.edu/doi/10.1002/14356007.a25_487.

EX1036 is the download I made through the link provided by Purdue Libraries in EX1035.

94. EX1034 is a scan of Roy that includes the cover of *Ullmann's Encyclopedia of Industrial Chemistry*, Volume 34 with a call number label that reads: TP9.U; title page; verso of the title page (copyright) with a handwritten call number that reads "TP9.U55 2003 v.34", as shown below; a partial contents page with a stamp that reads "LINDA HALL LIBRARY, KANSAS CITY, MISSOURI", as shown below, and a handwritten date and initials that read: "2-28-03 N-M", as shown below, from my experience in retrieving documents from the Linda Hall Library, this date indicates ownership and date of receipt by the Linda Hall Library, Kansas City, Missouri. The date indicates when it was received and cataloged/indexed into the collections of the Linda Hall Library, February 28, 2003; and the Roy article, pages 571-587.



Handwritten text in a light gray box: "2,28.03 ~ m."

95. All identifying characteristics, such as the stamps and handwritten call number and dates, etc. on EX1034 are consistent with library practice and procedure that I have observed during my career as a professional librarian. I have no cause for concern about the authenticity or accuracy of these identifying attributes. EX1034 was found within the custody of a library, the Linda Hall Library, one of the most likely locations for an authentic publication.

96. EX1036 is a copy of Roy that I retrieved on September 27, 2022, from the Purdue University Libraries by my emeritus faculty status through the *Wiley Online Library* database, a proprietary database, as described above.

97. After comparing Roy as it appeared in EX1034 and EX1036, I conclude, based on finding Roy in print in a library – Linda Hall – and online through a reputable, publisher database, *Wiley Online Library*, that Roy is an authentic document, and that EX1034 and EX1036 are authentic and accurate copies of Roy. I then compared EX1034 and EX1036 with EX1015, provided by counsel, and I found no differences between any of the three documents.

98. Therefore, I conclude and affirm Roy (EX1015) is an authentic document.

2. Public Accessibility

99. EX1037 is a true and correct copy of the *WorldCat* entry for Roy, *Ullmann's Encyclopedia of Industrial Chemistry*. Roy was included among the articles published in *Ullmann's Encyclopedia of Industrial Chemistry*, Volume 34, Sixth, Completely Revised Edition, 2003 on pages 571-587. I obtained EX1037 by completing a search on *WorldCat* on September 30, 2022. The document cataloged in this monographic (book) record is for *Ullmann's Encyclopedia of Industrial Chemistry* as verified by title: *Ullmann's Encyclopedia of Industrial Chemistry*, Volume 34, Sixth, Completely Revised Edition; publisher and publication date: Wiley-VCH in 2003.

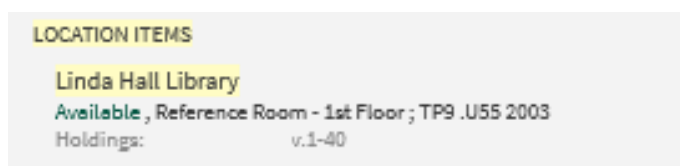
100. When undertaking the search of *WorldCat* as described above using the geographical location of Missouri, the Linda Hall Library was among the 401 libraries world-wide that hold *Ullmann's Encyclopedia of Industrial Chemistry*.

101. *Ullmann's Encyclopedia of Industrial Chemistry* could have been identified and located in a library in print by searching title: *Ullmann's Encyclopedia of Industrial Chemistry*; and/or by subject headings: *Chemical Engineering*; *Chemical Engineering Encyclopedias*; and/or *Chemistry, Industrial* (as well as subject headings in several foreign languages

102. EX1038 is a download I made from the Linda Hall Library OPAC (online catalog) on October 3, 2022. The document cataloged in this record is a

monographic record for: *Ullmann's Encyclopedia of Industrial Chemistry*, sixth edition completely revised, published by Wiley-VCH in 2003.

103. Under “Location Items’ it reads: Linda Hall Library, Available, Reference Room – 1st Floor; TP9.U55 2003 Holdings: v.1-40”, as shown below, inclusive of volume 34.



104. Roy could have been located by searching on the Linda Hall Library OPAC (online catalog) for the title: *Ullmann's Encyclopedia of Industrial Chemistry*.

105. On EX1034 is the ownership and date stamp on the contents page that reads “LINDA HALL LIBRARY, KANSAS CITY, MISSOURI”, as shown below. Also, shown on the contents page is the handwritten date and initials that read “2.28.03 N M,” as shown below, i.e., February 28, 2003. The date of February 28, 2003 would be when receipt and the processing began on *Ullmann's Encyclopedia of Industrial Chemistry*, sixth edition, expanded and revised, including volume 34, by the Linda Hall Library.

**LINDA HALL LIBRARY
KANSAS CITY, MISSOURI**

2.28.03 N M.

106. Consistent with standard library policy and practice, Roy, *Ullmann's Encyclopedia of Industrial Chemistry*, sixth edition, expanded and revised, would have been accessible on the shelf in the Linda Hall Library within a week to ten days after receipt by the library, that is, no later than March 10, 2003, well before November 24, 2012.

107. Furthermore, and consistent with the availability of a physical copy of Roy as described above, the publisher's website, Wiley On-line Library (https://onlinelibrary.wiley.com/doi/10.1002/14356007.a25_487), discloses that Roy was first published on June 15, 2000, as shown in EX1039. In my experience such dates typically reflect the date on which the article is available to licensed users (e.g., subscribers) of the publisher's website.

3. Conclusion

108. I conclude that Roy is an authentic document and would have been publicly accessible through the Linda Hall Library no later than March 10, 2003, well before November 24, 2012.

E. EX1016. Robert Y. Zhao, et al., "Synthesis and Evaluation of Hydrophilic Linkers for Antibody–Maytansinoid Conjugates," *Journal of Medicinal Chemistry*, Volume 54, Number 10, May 26, 2011: pages 3606-3623 ("Zhao")

1. Authentication

109. I have been asked to opine on the authenticity and public access of an article authored by Joshua Zhao *et al.*, titled "Synthesis and Evaluation of

Hydrophilic Linkers for Antibody–Maytansinoid Conjugates,” published in the *Journal of Medicinal Chemistry*, Volume 54, Number 10, May 26, 2011, on pages 3606-3623. (EX1016, “Zhao”)

110. For consistency and clarification, Zhao, when used in this declaration, refers not only to the Zhao article but also the journal volume and issue in which it was published: *Journal of Medicinal Chemistry*, Volume 54, Number 10, May 26, 2011.

111. I have evaluated the Zhao reference in three ways: (1) by assessing scans of a copy of Zhao (EX1016) provided to me by counsel; (2) accessing and assessing a scan of Zhao, EX1040, I obtained through Wisconsin TechSearch (WTS) from the print copy owned by the National Library of Medicine (NLM), a pre-eminent research library on November 11, 2022; and (3) by retrieving and reviewing a download, EX1041, I made on September 27, 2022 through Purdue University Libraries by my emeritus faculty status from *ACS Info Central*, a proprietary database of the American Chemical Society through this URL:

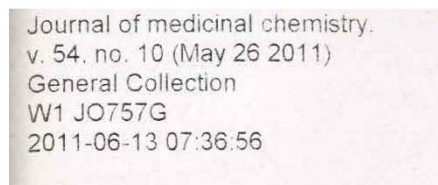
<https://pubs-acsc-org.ezproxy.lib.purdue.edu/doi/pdf/10.1021/jm2002958>.

It is available for a fee at this URL:

<https://pubs.acs.org/doi/pdf/10.1021/jm2002958>.

112. EX1040 is a scan of Zhao that includes the issue cover of *Journal of Medicinal Chemistry*, Volume 54, Number 10, May 26, 2011, with one label that

reads: “Journal of medicinal chemistry, v.54, no.10 (May 26 2011) General Collection W1 JO757G, 2011-06-13 07:36:56, as shown below, and a second label that reads: “Property of the National Library of Medicine”, as shown below:



113. The label at the top of the cover shows the date when it was received and indexed into the National Library of Medicine, 2011-06-13, equates to June 13, 2011, the remaining digits indicate time of day.

114. All identifying characteristics, such as the stamp on EX1040 are consistent with library practice and procedure that I have observed during my career as a professional librarian. I have no cause for concern about the authenticity or accuracy of these identifying attributes. EX1040 was found within the custody of a library, the National Library of Medicine, one of the most likely locations for an authentic publication.

115. EX1041 is a copy of Zhao that I retrieved on September 27, 2022, from the Purdue University Libraries by my emeritus faculty status through the ACS *InfoCentral* database, a proprietary database of the American Chemical Society as described above.

116. After comparing Zhao as it appeared in EX1040 and EX1041, I conclude, based on finding Zhao in print in a library – National Library of Medicine – and online through a reputable publisher database, *ACS InfoCentral*, that Zhao is an authentic document, and that EX1040 and EX1041 are authentic and accurate copies of Zhao. I then compared EX1040 and EX1041 with EX1016, provided by counsel, and I found no difference between any of the three documents.

117. Therefore, I conclude and affirm Zhao (EX1016) is an authentic document.

2. Public Accessibility

118. EX1042 is a true and correct copy of the *WorldCat* entry for Zhao. Zhao was included among the articles published in *Journal of Medicinal Chemistry*, Volume 54, Number 10, May 26, 2011, on pages 3606-3623. I obtained EX1042 by completing a search on *WorldCat* on November 15, 2022. The document cataloged in this record is a periodical record for *Journal of Medicinal Chemistry* as verified by title: *Journal of Medicinal Chemistry*; publisher and publication date: American Chemical Society, 1963 -. The 1963- indicates an ‘open entry’, that is, a serial that started in 1963 and will continue into the future.

119. When undertaking the search of *WorldCat* as described above using the geographical location of Maryland, the National Library of Medicine was among the 1298 libraries that hold world-wide the *Journal of Medicinal Chemistry*.

120. *Journal of Medicinal Chemistry* could have been identified and located in a library in print by searching title: *Journal of Medicinal Chemistry*; and/or by subject headings: *Chemistry, Pharmaceutical; Clinical chemistry; and/or Pharmaceutical chemistry*.

121. EX1043 is a screen capture I made from the National Library of Medicine OPAC (online catalog) on November 11, 2022. The document cataloged in this record is a periodical record for: *Journal of Medicinal Chemistry*; publisher and publication date: American Chemical Society, 1963- . The 1963- indicates an ‘open entry’, that is, a serial that started in 1963 and will continue in the future.

122. On EX 1043, under “Location Items – Summary Holdings: v.6(1963) v.59:no.23 (2016), v.60:no.1 (2017)” there is a pull down list of holdings, as shown below:

v. 54, no. 21-24 (2011)

v. 54, no. 16-20 (2011)

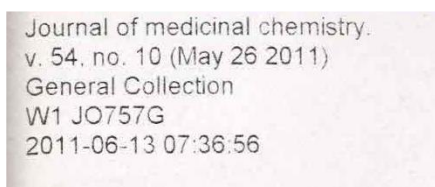
v. 54, no. 11-15 (2011)

v. 54, no. 7-10 (2011)

v. 54, no. 1-6 (2011)

123. Zhao could have been located by searching on the National Library of Medicine OPAC (online catalog) for the title: *Journal of Medicinal Chemistry*; and/or by searching the MESH subject heading: *Chemistry Pharmaceutical*.

124. On EX1040 is the ownership and date stamp on the issue cover of *Journal of Medicinal Chemistry*, Volume 54, Number 10, May 26, 2011 with a label that reads “Journal of medicinal chemistry, v.54, no.10 (May 26 2011) General Collection W1 JO757G, 2011-06-13 07:36:56”, as shown below, that indicates ownership and date of receipt by the National Library of Medicine on June 13, 2011. The date indicates Zhao (*Journal of Medicinal Chemistry*, Volume 54, Number 10, May 26, 2011) was received and “checked-in” to the collections of the National Library of Medicine on June 13, 2011.



125. Consistent with standard library policy and practice, this issue, Zhao, would have been accessible on the shelf in the National Library of Medicine within a week to ten days after receipt by the library, that is, no later than June 23, 2011, well before November 24, 2012.

126. EX1044 is a screen capture from the publisher’s website, ACS Publications at this URL: <https://pubs.acs.org/doi/abs/10.1021/jm2002958>

EX1044 captures the drop down menu for the publication record of Zhao as shown below:

Publication History

- **Received** 14 March 2011
 - **Published** online 4 May 2011
 - **Published** in issue 26 May 2011
-

127. Zhao was published online 4 May 2011 as shown in EX1044. In my experience such dates typically reflect the date on which the article is available to licensed users (e.g., subscribers) of the publisher's website.

Conclusion

128. I conclude that Zhao is an authentic document and would have been publicly accessible through the National Library of Medicine, more likely than not, at least by June 23, 2011, well before November 24, 2012. Additionally, Zhao would have been available to a researcher who had access to ACS online journals (through a research library or a personal membership) as of May 4, 2011 as shown by the search options as shown on the *Wayback Machine* record for April 6, 2011.

V. AVAILABILITY FOR CROSS-EXAMINATION

129. In signing this Declaration, I recognize that this Declaration will be filed as evidence in a contested case before the Patent Trial and Appeal Board of the U.S. Patent and Trademark Office. I also recognize that I may be subject to cross-

examination in the case and that cross-examination will take place within the United States. If cross-examination is required of me, I will appear for cross-examination within the United States during the time allotted for cross-examination.

VI. RIGHT TO SUPPLEMENT

130. I reserve the right to supplement my opinions in the future to respond to any arguments that Patent Owner or its expert(s) may raise and to take-into account new information as it becomes available to me.

VII. JURAT

131. I declare that all statements made herein of my knowledge are true, and that all statements made on information and belief are believed to be true, and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code.

Executed this January 26, 2023 in Williamsburg, Virginia


James L. Mullins, PhD