UNITED STATES DISTRICT COURT
DISTRICT OF MASSACHUSETTS

AMGEN INC., Plaintiff, v. F. HOFFMANN-LA ROCHE LTD., a Swiss Company, ROCHE DIAGNOSTICS GmbH, a German Company and HOFFMANN LAROCHE INC., a New Jersey Corporation, Defendants.	Civil Action No.: 05-12237 WGY **REDACTED VERSION**

DECLARATION OF KRISTA M. CARTER IN SUPPORT OF PLAINTIFF AMGEN INC.'S MEMORANDUM IN SUPPORT OF ITS MOTION TO COMPEL

I, Krista M. Carter, declare as follows:

1. I am an attorney admitted to practice law before all of the Courts of the State of California and before this Court (*pro hac vice*). I am an associate with the law firm of Day Casebeer Madrid & Batchelder LLP, counsel for plaintiff Amgen, Inc. in this matter.

2. I make this declaration of my own personal knowledge. If called to testify with respect to the truth of the matters stated herein, I could and would do so competently.

Roche's Production of its BLA and IND Documents

Roche's Hardcopy Production

3. Roche produced copies of its BLA (Biologics License Application) No. STN 125164/0 and IND (Investigational New Drug)[1] application to Amgen in ITC Investigation No. 337-TA-568. Roche produced a paper copy of its BLA consisting of 152,682 pages, identified as Production Numbers ITC-R-BLA00000001 – 00152682. Roche also produced a paper copy of its IND documents consisting of 12,307 pages, identified as Production Numbers ITC-R-IND-0000001 – 00122307.

4. The paper copy of Roche's BLA and IND documents was produced to Amgen without an index, in scrambled page order and in incomplete form with missing sections and pages. The paper copy also revealed the presence of thousands of hypertext links to external files, data reports, and patient records referenced in the text, but the links were simply depicted and not operable in the paper copy.

5. **No Index**. The paper copies of the BLA and IND documents produced by Roche included no index of the pages that comprise either the BLA or IND. While the BLA itself contains a section entitled "Reviewer's Guide for BLA" that includes an Overall Table of Contents, this table of contents simply divides the entire BLA into 20 broad Items and identifies in which Electronic Archive Copy Folder each Item can be found. However, it does not provide

[1] Roche's IND documents consist of Roche's original IND submission, its updates and supplements to that submission, and its annual reports.

page ranges at which each Item may be found, what quantity of documents is included within each Item, nor does Amgen's counsel have the Electronic Archive Copy Folders. (*See* Exh. 21 (ITC-R-BLA-00000014)). Furthermore, it is not always indicated on the BLA pages to which Item those pages belong. Upon request, Roche provided Amgen's counsel with almost the identical table of contents, which provides no additional information to help Amgen's counsel to organize and review the BLA. (*See* Exh. 26 (BLA Table of Contents)). Consequently, it is not possible to confirm whether all sections of the BLA and all sections of the IND were produced, or even whether the sections that were produced were in complete and in correct order.

6. **Non-Sequential Order**. The paper copy of the BLA produced by Roche was produced in scrambled page order so that if one were to read the document as it was produced, it would be incomprehensible. Large spans (200-300 pages) of Roche's BLA submission are randomly sprinkled throughout its production so that within the 152,682 pages of Roche's BLA production, there are hundreds of non-consecutive junctures between various segments or spans of the BLA. Roche apparently copied segments of its FDA filing and then produced the contents of those segments in a non-sequential order. This cannot be how Roche maintains its own BLA submission in the ordinary course of business.

7. For example, at ITC-R-BLA-00000028 – 029, two sequential pages from Roche's BLA production are quite obviously taken from completely different portions of the original BLA filing. The first page (ITC-R-BLA-00000028) indicates on its face that it is part of the BLA's "Electronic Road Map." But, the very next page (ITC-R-BLA-00000029) is page number 603 from the Chemistry, Manufacturing, and Controls section of Roche's BLA, a completely different and unrelated section. (*See* Ex 19). These non-sequential junctures occur hundreds of times throughout Roche's BLA production, needlessly making it extremely cumbersome and time consuming to reconstruct the order and sequence of Roche's BLA production. Even then, however, Amgen cannot be certain that its reconstruction is correct or complete.

8. Likewise, Roche's production of a hard copy of its IND documents was also

produced in scrambled page order, in which nonconsecutive pages in Roche's IND documents bear consecutive Production Numbers. For example, one section of the hard copy of Roche's IND bearing Production Numbers ITC-R-IND-00054159-00058044 is comprised of large, yet incomplete, chunks of various unrelated portions of Roche's IND documents. The first portion (ITC-R-IND-00054159 – 4449) appears to be the first 291 pages of Roche's IND. The next consecutive portion (ITC-R-IND-00054450 – 4715) appears to be pages 2453 – 2717 of the IND, (identified as being part of Volume 10), which is neither the complete version of Volume 10 nor related to the first portion immediately precedes it. Another section of the IND (ITC-R-IND-00056982 – 7193) consists of pages 292 – 556 (identified as being part of Volume 2). This portion is immediately followed by (ITC-R-IND-00057194 – 8044) pages 4965 – 5768 of the IND (identified as part of Volumes 20-22). (*See* Ex. 27).[2] These non-sequential junctures occur hundreds of times throughout Roche's IND production, making it virtually impossible to reverse-engineer the correct order and sequence for Roche's IND production.

Missing Submissions.

REDACTED

[2] To avoid excessively attaching an excessively large exhibit, I am attaching only the first and last page of each identified section as illustrative of the non-sequential page order.

REDACTED

Roche's Electronic Production

10. Roche also produced 10 electronic copies of its BLA on a total of 20 compact discs and 10 electronic copies of its IND documents on a total of 10 compact discs.[3] Each compact disc contains a load file, an OCR (optical character read) folder containing multiple OCR text files, and multiple folders of TIFF (Tagged Image File Format) images. The load file contains the instructions needed to view or "load" the images onto a database program that can associate the OCR text files with the TIFF images. Each OCR text file contains text from hundreds to thousands of pages of the BLA or IND documents. The TIFF folders collectively contain a separate TIFF image for each page of the BLA or IND produced by Roche. Each unique page of the BLA and IND documents has a different TIFF image. There are a total of 152,682 TIFF image files for each copy of the BLA on the BLA compact discs, corresponding to each hard-copy page of Roche's produced BLA. Likewise, there are 122,307 TIFF image files for each copy of the IND documents on the IND compact discs, corresponding to each hard-copy page of Roche's IND production. The TIFF images are themselves ***not*** text searchable.

11. **General Deficiencies.** The electronic copies produced by Roche consist of electronic images of the paper copy produced by Roche. For that reason, the electronic copies have all of the same deficiencies as the paper copy, as discussed in ¶¶ 4 – 9 above. For example, the electronic copies of Roche's BLA and IND documents were produced to Amgen without an index, in scrambled page order, with inactive hyper-text links to external files, data reports, and patient records referenced in the text, as discussed below.

12. **Inoperable Hypertext Links.** Both the paper and electronic copies of the BLA

[3] Roche produced 10 electronic copies of 6,515 pages of its IND documents on May, 31, 2006, and later produced 10 electronic copies of 122,307 pages of its IND documents, which included the 6,515 pages initially produced, on June 2, 2006. For ease of reference, I will only refer to the 10 electronic copies of the more complete set of documents produced on the later date.

and IND documents produced by Roche reveal the presence of thousands of hypertext links to external files, data reports, and patient records referenced in the text. In both the paper copy and the electronic copy of the BLA and IND documents produced by Roche, the hypertext links are inoperable. There is no operable connection between the links and the document(s) or data source(s) they ostensibly reference. To the document reviewer, the document shows a picture of a hypertext link in the text, but he or she is unable to identify or locate the referenced documents. A copy of the image presented on the produced compact discs of a typical page from Roche's BLA may be found at Production Number 00039976. (*See* Exh. 20). As can be seen, the page contains multiple hypertext links, each of which is required in order to comprehend the information submitted to FDA, but none of which are operable in either the paper or electronic copies produced by Roche.

13. Because the hyperlinks are inoperable, it is impossible for Amgen to identify all missing BLA materials and, more importantly, it is impossible for Amgen to analyze and comprehend the complete contents of Roche's BLA and IND documents. For example, the pages of Roche's BLA as produced to Amgen, bearing Production Numbers ITC-R-BLA 000399973 – 997, contain dozens of hypertext links in just 25 pages. (*See* Exh. 20). Amgen has no way to correlate the pictures of the hypertext links to the referenced information or even to confirm whether such referenced information is included at any place within Roche's production. This example is illustrative of the frequency of inactive hypertext links in Roche's BLA and IND production.

14. **Not Fully Text Searchable.** In addition to these deficiencies, the electronic copies of Roche's BLA and IND documents, as produced to Amgen, are not fully text searchable. For example, to search the text of the BLA, one must run a separate search over the OCR files to obtain a hit list of search results. Then the reviewer must open each of the OCR files that contain a match for the search term, locate the term within the OCR file to determine whether the match is in fact relevant and, if so, then determine which of the 152,682 TIFF images correspond to the located page. The review must then load and open each of the

corresponding TIFF images to view the actual production-stamped document. The magnitude of this problem is further exacerbated by the limitations Roche imposed regarding the handling of its BLA on non-networked computers, thereby preventing relevant search results from being shared among multiple BLA reviewers. I provide a step-by-step guide that describes the process for searching Roche's electronic production of its BLA and IND documents at ¶ 26 below.

Searching and Reviewing Roche's BLA and IND Documents In Its Currently Produced Form Is Unduly Burdensome

15. **Amgen's efforts.** Amgen's outside counsel has spent hundreds of hours organizing the pages of the BLA and IND because of Roche's deficient production. Even then, however, it is not possible to comprehend the full content and meaning of the documents produced because of missing sections and the inability to identify or locate thousands of referenced documents due to inoperable hypertext links and non-sequential page order.

16. **Notifying Roche.** Amgen has made Roche aware of the deficiencies discussed above and requested acceptable copies of its BLA and IND. Beginning in June of this year, just ***one day*** after Roche produced the electronic copy of its BLA and IND documents, and continuing through the present day, Amgen has informed Roche of several significant deficiencies in the production.

17. Counsel for Amgen notified Roche of several of the material deficiencies in the production of Roche's BLA and IND documents just one after Roche electronic production and two days after Roche the paper production. (*See* Exh. 18 (6/4/06 V. Smith letter to H. Suh)). In that initial notification, Amgen's counsel identified production problems that were a direct result of Roche's decision to convert the BLA and IND from its original highly organized, user-friendly electronic format into unlinked and unworkable images. (*See* Exh.18). Counsel for Amgen also requested that Roche produce the BLA to Amgen in the same electronic format as it was submitted to FDA. (*See* Exh. 18). Just two days thereafter, counsel for Amgen again notified Roche of production deficiencies in the BLA, specifically highlighting the inoperable

hypertext links and Amgen's inability to which documents correspond to particular hypertext links. (*See* Exhibit 28 (6/6/06 D. Fishman letter to H. Suh)). In fact, Amgen's counsel repeatedly notified Roche of unrectified and ongoing deficiencies in the BLA and IND production. (*See*, *e.g.*, Exh. 24 (6/30/06 D. Fishman letter to H. Suh) and Docket No. 156, Exh. 9 (11/08/06 K. Carter letter to P. Fratangelo)).

18. In an effort to cooperate with and assist Roche in prioritizing and accelerating the production of highly relevant documents, Amgen highlighted the BLA and IND documents, and supplements thereto, as being of significant import in a letter to Roche sent on November 11, 2006. (*See* Docket No. 157, Exh. 12 (11/21/06 D. Fishman letter to T. Fleming)).

19. Roche continues to refuse to produce a complete and acceptable production of its BLA and IND, as memorialized in the letter sent to Howard Suh the day of the recent meet and confer where Amgen reiterated its concerns about the deficiencies in the production and Roche confirmed its refusal. (*See* Exh. 3 (12/11/06 D. Fishman letter to H. Suh).

20. **Roche's BLA and IND in fully-searchable electronic format.** I am informed and believe that Roche has in its possession copies of its BLA and IND documents as submitted to FDA in a fully text-searchable electronic format. According to FDA's Guidance, 21 C.F.R. Part 11 instructs applicants to submit their FDA filings as PDF files: "Regulations in 21 CFR Part 11 require that the Agency be able to generate from any document provided in electronic format an accurate and complete paper copy that is both legible ("human readable") and suitable for inspection, review, and copying. Therefore, documents submitted in electronic format should:

- Enable the user to easily view a clear and legible copy of the information
- Enable the user to print each document page by page, as it would have been provided in paper, maintaining fonts, special orientations, table formats, and page numbers
- Include a well-structured table of contents and allow the user to navigate easily through the submission
- Allow the user to copy text and images electronically into common word processing documents

To achieve the above goals, you should submit all electronic documents in Portable Document Format (PDF). CDER and CBER are prepared to archive documents provided as PDF files." (*See* Exh. 22).

21. Roche has never produced a PDF version of its BLA or IND documents to Amgen.

22. When Roche first contacted Amgen regarding the production of its BLA, Roche originally sought to restrict its production to a single printed copy of the BLA for inspection only. Counsel for Amgen informed Kent Stevens and Leora Ben-Ami (counsel for Roche) that the volume and complexity of Roche's FDA filings made this proposal unacceptable and insisted on the production of an electronically searchable copy of the BLA in addition to a printed copy. Although I am informed and believe that an electronically searchable version of the BLA as submitted to FDA was readily available, in Roche's possession, and could have been to Amgen at that time, Roche did not inform Amgen of this fact, and instead represented that an electronically searchable copy of its filing would have to be created before it could be produced. (*See* Exh. 24 (6/30/06 D. Fishman to H. Suh)).

23. In a subsequent meet and confer, when Roche offered to produce the BLA in TIFF images, Mr. Day, counsel for Amgen, explained why TIFF images were not electronically searchable, and were thus not acceptable to Amgen. During that call, Mr. Day mentioned OCR as an illustration of an electronically searchable format. The suggestion that Amgen insisted on the delivery of OCR files, notwithstanding the existence of an electronically searchable, hyper-linked version previously delivered to FDA, is inaccurate. Any burden imposed on Roche in creating an OCR version was self-imposed and undertaken without Amgen's knowledge of a pre-existing and superior alternative regularly maintained by Roche in the ordinary course of business. (*See* Exh. 18 (6/4/06 V. Smith letter to H. Suh)).

24. When Amgen's counsel learned that Roche possessed its BLA submission in a substantially different and superior electronic version than the version produced to Amgen, counsel for Amgen immediately wrote to Roche to request its production. (*See* Exh. 24 (6/30/06 D. Fishman letter to H. Suh). On June 13, 2006, at the Rule 30(b)(6) deposition of Cynthia Dinella, counsel for Amgen was shown the electronic version of Roche's BLA filing as it had been submitted to FDA and ascertained that it varied in several significant respects from the version produced to Amgen. Counsel for Amgen requested on the record at that deposition that Roche produce a copy of its electronic submission to FDA and counsel for Roche refused to do so. (*See* Exh. 23).

25. On June 30, Amgen again requested a copy of the electronic version of the BLA that Roche had submitted to FDA. (*See* Exh. 24 (6/30/06 D. Fishman to H. Suh)). Roche responded by refusing to produce a copy of the electronic version it had submitted to FDA and that Roche had in its possession. (*See* Exh. 25 (7/7/06 Fratangelo letter to Fishman)).

26. To this date, Roche has never denied having in its possession the electronic version of its BLA and IND documents that it submitted to FDA. Nor does it dispute that it produced each of those documents to Amgen in a ***different*** electronic format than it submitted to FDA.

Step-By-Step Process for Searching the Electronic Form Produced by Roche.

27. The following are the steps I had to undertake in order to search Roche's production of the BLA and IND, complying with the Protective Order from the ITC Investigation:

REDACTED

REDACTED

REDACTED

REDACTED

REDACTED

REDACTED

REDACTED

REDACTED

28. **Undue Burden.** Even if Roche were to produce a complete, correctly ordered paper and electronic version of its BLA and IND filings in the OCR/TIFF format of its original production, the hypertext links would still be inoperable and counsel for Amgen would be unable to review the document in its entirety. Because the hypertext links would remain inoperable, Amgen's counsel would still be precluded from accessing the associated or referenced material or even confirming that such material or data was ever produced.

29. To date, Roche has provided two reasons for its failure to produce its BLA and IND documents to Amgen in the same format that those documents were provided to FDA.

First, Roche states that it has already produced its filings in another electronic format and should not be required to assume the burden of re-production. Second, Roche contends that it will not be able to place document control numbers (Production Numbers) on the electronic version of its BLA and IND documents that were submitted to FDA. (*See* Exh. 25 (7/7/06 P. Fratangelo letter to D. Fishman); *See also* Defendants' Cross-Motion for Protective Order and Opposition to Amgen's Motion for Entry of Protective (Docket No. 136) at 21).

30. First, Roche's contention regarding burden is misplaced. Roche does not dispute that it has in its possession the electronic form of its BLA and IND documents that Amgen is currently requesting. Making an electronic copy (or even 10 electronic copies) of its existing CDs can hardly be viewed as unduly burdensome, particularly when contrasted with the extraordinary efforts Amgen has undergone and continues to invest in an effort to organize and review Roche's production. Roche's claim of burden should be considered against the fact that Roche failed to disclose the existence of the FDA-version in its possession at the time of its original production. The Committee Notes to the newly amended F.R.C.P. 34 confirms that Roche should produce in the more usable and already-existing format filed with FDA. (*See* Exh. 29).

31. The Committee Notes to F.R.C.P. 34 states: "But the option to produce in a reasonably usable form does not mean that a responding party is free to convert electronically stored information from the form in which it is ordinarily maintained to a different form that makes it more difficult or burdensome for the requesting party to use the information efficiently in the litigation. If the responding party ordinarily maintains the information it is producing in a way that makes it searchable by electronic means, the information should not be produced in a form that removes or significantly degrades this feature." (*See* Exh. 29).

32. Second, Roche's concern that its electronic submission will lack document

control numbers is not a legitimate basis on which it can withhold production. Both my firm and I personally have been involved in several cases where responsive documents were stored in electronic form on CDs, DVDs, hard drives, backup tapes, and other such storage media where we confronted and resolved this issue.

33. Recognizing that electronic data often cannot be assigned a production or other unique document identifier in exactly the same manner as hard copy documents, the parties have always worked together to agree on a manner for identifying and tracking produced electronic data. For example, in a number of cases, the parties agreed to assign a single Production Number to each CD, DVD, etc. If either party then wanted to use a particular document stored on one of the produced CDs, DVDs, etc., that document was printed and labeled with both the source Production Number from the CD, DVD, etc., plus the file name and directory path of the electronic document. In no such case did either party avoid its production obligation simply because the software or things that were relevant and responsive to pending requests could not be assigned a unique Production Number.

Documents Cited in Amgen's Motion to Compel

34. Attached hereto as Exhibit 1 is a true and correct copy of a letter dated December 6, 2006 from D. Fishman to H. Suh.

35. Attached hereto as Exhibit 2 is a true and correct copy of a letter December 8, 2006 from Deborah E. Fishman to Howard Suh.

36. Attached hereto as Exhibit 3 is a true and correct copy of a letter dated December 11, 2006 from D. Fishman to H. Suh.

37. Attached hereto as Exhibit 4 is a true and correct copy of Roche's Responses and Objections to Amgen's First Set of Requests for the Production of Documents and Things (Nos. 1 to 224), dated December 4, 2006.

38. Attached hereto as Exhibit 5 is a true and correct copy of Roche's First Set of Requests for the Production of Documents and Things to Amgen, Inc., served on October 30, 2006.

Attached hereto as Exhibit 6 is a true and correct copy of a slide presentation

bearing Production Numbers ITC-R-00024046 – 093

REDACTED

Attached hereto as Exhibit 7 is a true and correct copy of

bearing Production Numbers ITC-R-00085385 – 393,

REDACTED

Attached hereto as Exhibit 8 is a true and correct copy of a June 26, 2006 draft of Roche's IND

REDACTED

(bearing Production Numbers ITC-R-00050548).

42. Attached hereto as Exhibit 9 is a true and correct copy of an internal Roche email-string (the most recent date on the string being January 8, 2002)

REDACTED

bearing Production Numbers ITC-R-00517745 – 747.

43. Attached hereto as Exhibit 10 is a true and correct copy of an excerpt from Roche's IND **REDACTED** bearing Production Number ITC-R-IND-00114978.

44. Attached hereto as Exhibit 11 is a true and correct copy of pages 8-14 from the June 8, 2006 deposition of Joanne Franzino in the related ITC Investigation No. 337-TA-56.

45. Attached hereto as Exhibit 12 is a true and correct copy of a document dated March 28, 2000 and **REDACTED** bearing Production Numbers ITC-R-00038885 – 887.

46. Attached hereto as Exhibit 13 is a true and correct copy of a transmittal letter dated December 4, 2001

bearing Production Number ITC-R-00004056).

47. Attached hereto as Exhibit 14 is a true and correct copy of memo dated June 13, 2003 bearing Production Numbers ITC-R-00089133-139, **REDACTED**

48. Attached hereto as Exhibit 15 is a true and correct copy of an email dated May 22, 2006 bearing Production Numbers ITC-R-00503039 – 045 **REDACTED**

49. Attached hereto as Exhibit 16 is a true and correct copy

bearing Production Number ITC-R-BLA- 00000805 **REDACTED**

50. Attached hereto as Exhibit 17 is a true and correct print-out from the Dana Farber website, located at http://www.dan-farber.org/can/dictionary/?index=r), that provides the following definition for MICERA: "Ro 50-3821…also called methoxypolyethylene glycol epoetin beta."

51. Attached hereto as Exhibit 18 is a true and correct copy of a letter dated June 4, 2006 from V. Smith to H. Suh.

52. Attached hereto as Exhibit 19 is a true and correct copy of Roche's April 18, 2006 Electronic Roadmap: BLA Submission, bearing Production Numbers ITC-R-BLA-00000028 – 029.

53. Attached hereto as Exhibit 20 is a true and correct copy of BLA pages illustrating the inoperable hypertext links in the production, bearing Production Numbers ITC-R-BLA 000399973 – 997.

54. Attached hereto as Exhibit 21 is a true and correct copy of the Roche's Attachment 2: Reviewer's Guide for BLA, as attached to its April 2006 BLA filing, bearing Production Numbers ITC-R-BLA-00000014 – 022.

55. Attached hereto as Exhibit 22 is a true and correct copy of a print-out that I made on December 12, 2006 of the FDA website located at http://www.fda.gov/cder/guidance/2867fnl.pdf, entitled "Guidance for Industry: Providing Regulatory Submissions in Electronic Format – General Considerations."

56. Attached hereto as Exhibit 23 is a true and correct copy of pages 261-263 of the June 13, 2006 Rule 30(b)(6) deposition of Cynthia Dinella.

57. Attached hereto as Exhibit 24 is a true and correct copy of a letter dated June 30, 2006 from D. Fishman to H. Suh.

58. Attached hereto as Exhibit 25 is a true and correct copy of a letter dated July 7, 2006 from P. Fratangelo to D. Fishman.

59. Attached hereto as Exhibit 26 is a true and correct copy of the BLA Table of Contents provided by Roche on May 27, 2006.

60. Attached hereto as Exhibit 27 is a true and correct copy of BLA pages illustrating sections produced in non-sequential order, bearing Production Numbers ITC-R-IND-00054449, ITC-R-IND-00054450, ITC-R-IND-00057193, and ITC-R-IND-00057194.

61. Attached hereto as Exhibit 28 is a true and correct copy of a letter dated June 6, 2006 from D. Fishman to H. Suh.

62. Attached hereto as Exhibit 29 is a true and correct copy of F.R.C.P. Rule 34 and the Committee Notes to the Rule as enacted in December of this year.

63. Attached hereto as Exhibit 30 is a true and correct copy of a letter dated December 13, 2006 from H. Suh to D. Fishman.

64. I declare under penalty of perjury under the laws of the United States of America that the foregoing is true and correct.

Dated: December 14, 2006 /s/ Krista M. Carter

Krista M. Carter