**IN THE UNITED STATES DISTRICT COURT**
**FOR THE DISTRICT OF COLUMBIA**

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| UNITED STATES OF AMERICA | : | CRIMINAL NO. _____ |
| v. | : | |
| BIOCOMPATIBLES, INC., | : | |
| Defendant. | : | |
| | : | |

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## STATEMENT OF THE OFFENSE

Pursuant to Rule 11 of the Federal Rules of Criminal Procedure, the defendant, Biocompatibles, Inc., ("Biocompatibles") agrees and stipulates as follows:

### Background

1. At all relevant times, Biocompatibles UK Ltd. was an English entity with its principal place of business in Great Britain. In or about 2008, Biocompatibles UK Ltd. acquired an entity that became Biocompatibles Inc., a Delaware corporation, with its principal place of business in Oxford, Connecticut. These entities are collectively referred to herein as "Biocompatibles." After December 31, 2010, Biocompatibles, Inc. became a wholly owned subsidiary of Biocompatibles International Ltd., an English entity, and assumed the business of Biocompatibles UK.

2. Biocompatibles developed, manufactured, marketed, sold, and distributed a medical device that at various times was named GelSpheres Embolic Agent, GelSpheres Compressible Microspheres, and LC Bead® (hereinafter "LC Bead®"). LC Bead® was used primarily to treat patients with advanced liver cancer. These patients

typically were too sick to be eligible for liver transplants and had liver tumors that were too large, or within the liver, to be surgically removed.

3. At all relevant times, the United States Food and Drug Administration ("FDA") was responsible for protecting the health and safety of the American public by enforcing the Food, Drug, and Cosmetic Act ("FDCA"). One of the purposes of the FDCA was – and is – to ensure that medical devices sold for human use are safe and effective. The FDCA requires that medical devices bear labeling that contains only true and accurate information and that provides adequate directions for use. The FDA's responsibilities under the FDCA include regulating the manufacture, labeling, and distribution of all medical devices shipped or received in interstate commerce.

4. The FDCA and its implementing regulations prohibited manufacturers from distributing in interstate commerce any medical device unless the FDA had granted marketing authorization for the device or the device was covered by an exemption not applicable here. There generally were two ways for a manufacturer to obtain FDA marketing authorization for a medical device. The first way for the manufacturer to distribute lawfully a medical device was by obtaining FDA approval of the manufacturer's application for pre-market approval of the device ("PMA approval"). The FDA would not grant PMA approval unless the information in the PMA application provided the FDA with reasonable assurance that the device was safe and effective for its intended use, as reflected in its FDA-approved labeling. The second way for the manufacturer to distribute lawfully a medical device was by obtaining FDA clearance that the medical device was substantially equivalent to a device that already was legally being marketed, i.e., a "predicate device." This process was referred to as a "510(k)

clearance." The FDA would grant 510(k) clearance if it determined, among other things, that the device had the same intended use as the predicate device and did not raise new issues of safety or effectiveness.

5. On or about December 16, 2002, Company 4, which was based in the United States, obtained 510(k) clearance from the FDA for LC Bead® to be used "for Embolization of hypervascular tumors and arteriovenous malformations." The predicate device for this 510(k) clearance was Embospheres Microspheres, a device that had received 510(k) clearance to be used "for embolization of hypervascular tumors and arteriovenous malformations." LC Bead® could be used as an embolic device in which the device was inserted by catheter into the blood vessels and positioned outside, or within the liver to block the flow of blood to the liver tumor.

6. Biocompatibles obtained the rights to LC Bead® from Company 4. Biocompatibles subsequently obtained 510(k) clearances from the FDA for LC Bead® on February 4, 2004, November 12, 2004, December 24, 2008, and April 16, 2010. Each of those subsequent 510(k) clearances was for changes such as manufacturing LC Bead® at a different location and distributing a different-sized bead. In each of those 510(k) clearances, the indicated use for LC Bead® remained the same: embolization of hypervascular tumors and arteriovenous malformations.

7. Although the original 510(k) clearance for LC Bead® was obtained in December 2002, Biocompatibles did not begin selling LC Bead® in the United States until July 2005. Biocompatibles lacked a sales force and contracted with other companies to promote and to distribute LC Bead®. From on or about July 1, 2005, through on or about May 21, 2006, Company 1, which was based in Japan but had a sales

force in the United States, was Biocompatibles' exclusive distributor of LC Bead® in the United States. Beginning on or about May 22, 2006, Company 2, which was based in the United States, became Biocompatibles' exclusive distributor of LC Bead® in the United States. On or about January 29, 2007, Company 2 was acquired by Company 3, which was based in the United States. From on or about January 29, 2007, through on or about December 31, 2011, Company 3 was Biocompatibles' exclusive distributor of LC Bead® in the United States.

**Scheme to Introduce Misbranded Medical Devices into Interstate Commerce**

8. At the time Biocompatibles began distributing LC Bead® in the United States through its distributors, health care providers used LC Bead® almost exclusively as a drug-delivery device. For this use, the device was loaded with chemotherapy drugs, inserted by catheter into the blood vessels, and positioned outside, or within, the liver, where the device reduced the flow of blood to the liver tumor and emitted chemotherapy drugs to attack the liver tumor.

*Despite the Fact that LC Bead® Would Be Promoted Almost Exclusively for Drug Delivery, Biocompatibles Assured the FDA that It Would Not Promote LC Bead® for Drug Delivery.*

9. Biocompatibles communicated with the FDA primarily through an individual based in the United States whom Biocompatibles identified to the FDA as its "official correspondent and U.S. Foreign Agent" (hereinafter Biocompatibles' consultant). All of the communications from Biocompatibles' consultant to the FDA described below were made with Biocompatibles' knowledge and approval.

10. On or about November 5, 2004, the FDA raised concerns with Biocompatibles – which was at that time seeking 510(k) clearance for a change in LC

Bead®'s manufacturing site – about whether the company would use LC Bead®'s 510(k) embolization clearance to promote LC Bead® for drug delivery. The FDA told Biocompatibles' consultant that separate FDA marketing authorization would be needed for "drug-loaded beads . . . for any indication." The FDA requested a statement that Biocompatibles' understood that separate approval would be needed.

11. On or about November 6, 2004, Biocompatibles' consultant stated in an emailed response to the FDA that "under no circumstance" would the 510(k) clearance application for LC Bead® "be use[d] to promote Drug Loading By Doctors!" Biocompatibles' agent added: "I Guarantee that there is no sl[e]ight of hand here."

12. On or about November 7, 2004, Biocompatibles' consultant stated in a letter to the FDA that Biocompatibles would market LC Bead® for only the embolization indication in the 510(k) application. The letter stated that Biocompatibles did "not plan to market or promote [LC Bead®] for the specific indication of Pre-loading any pharmaceutical, in the USA until such time that a 510K has been cleared for the appropriate indications for use." The letter was signed by Biocompatibles' consultant and stated that "[t]his letter is sent with the knowledge by and prior approval of" Biocompatibles.

13. In 2004, Biocompatibles did not have a plan to market LC Bead® in the United States as a drug-delivery device without the FDA's 510(k) clearance or PMA approval for that use. Subsequently, however, Biocompatibles, through its distributors, marketed LC Bead® in the United States as a drug-delivery device despite having neither 510(k) clearance or PMA approval for that use.

*Biocompatibles Continued to Allow LC Bead® to Be Promoted for Drug Delivery After the FDA Rejected its 510(k) Application to Promote LC Bead® for Drug Delivery.*

14. Company 2 began serving as Biocompatibles' exclusive United States' distributor of LC Bead® on or about May 22, 2006. Company 2, with input from Biocompatibles, began developing a distribution plan. At all relevant times, Biocompatibles not only participated in developing this distribution plan, but had full knowledge of it.

15. One of the slides shown in July 2006 to Company 2 sales representatives who were being trained to sell LC Bead by Company 2 commercial leaders asked "Ok So what is it??? (In a nutshell)" The answer on the slide stated: "A drug-delivery device. (Drug-eluting bead or DEB)" Representatives of Biocompatibles were present at this training session.

16. Training provided in August 2006 to new Company 2 sales representatives encouraged them to "aggressively penetrate the chemoembolization market with the LC Bead."

17. On or about October 10, 2006, Biocompatibles applied to the FDA for 510(k) clearance to promote and to distribute the LC Bead® for drug delivery. Specifically, Biocompatibles sought to market LC Bead in the United States "for embolization of hypervascular tumors and arteriovenous malformations, and use in Trans Arterial Chemoembolization (TACE)."

18. On or about March 9, 2007, the FDA informed Biocompatibles that using LC Bead® to deliver drugs constituted "a new indication" and that the device was not substantially equivalent to any predicate device because of the new indication for

use in TACE, which "alters the therapeutic effect, impacting safety and effectiveness," and for which there was no predicate device. The FDA informed Biocompatibles that it would need PMA approval before the device could be legally marketed for the proposed intended use.

19. Despite Biocompatibles' failure to obtain 510(k) clearance for LC Bead® for drug delivery, on and after March 9, 2007, Company 3, with Biocompatibles' knowledge and consent, continued to promote LC Bead as a drug delivery device.

20. On or about June 15, 2007, a Company 3 sales representative sent information to a health care provider that said "[t]he LC Bead is FDA cleared for use in hypervascularized tumors" and that claimed "LC Bead increases the level of chemo delivered locally to the tumor, the chemotherapy is better targeted and more concentrated at the site of the tumor which should result in better tumor response rates," despite the absence at that time of statistically significant evidence to support this claim.

21. On or about September 26, 2007, a Company 3 sales representative sent information to a health care provider that said "LC Beads are a precision-TACE product that are designed to elute doxyrubicin or irinotecan over a 14-day period, reducing post-embolization side effects and increasing the local concentration of chemotherapy in tumors."

22. On or about December 15, 2008, in response to a question from a health care provider who, instead of being given instructions for LC Bead® had been given instructions by a Company 3 sales representative for an identical Biocompatibles' device with a different name that was approved in Europe for drug delivery, a

Biocompatibles executive falsely explained that "[w]here there is a slight difference is that for historic reasons the 510K for LC Bead does not mention drug loading."

23. On or about November 13, 2009, a Company 3 sales representative informed a health care provider that LC Bead®'s instructions could not mention chemoembolization due to "FDA regulation[s]," but referred the United States health care provider to Biocompatibles' website for instructions for an identical Biocompatibles' device with a different name device that was approved in Europe for drug delivery.

*Biocompatibles Continued to Allow LC Bead® to Be Promoted for Drug Delivery After the FDA Rejected a PMA Application to Promote LC Bead® for Drug Delivery.*

24. On or about December 11, 2009, Biocompatibles submitted a PMA application for LC Bead® to be used "for trans-arterial chemoembolization (TACE) of unresectable hepatocellular carcinoma (HCC)."

25. On and after December 11, 2009, despite recognizing that it needed, but still lacked, PMA approval, Biocompatibles allowed Company 3 to continue to promote LC Bead® as a drug delivery device.

26. On or about December 23, 2009, a Company 3 sales representative advised a health care provider how much chemotherapy drug to load onto LC Bead® to treat a patient's tumor.

27. On or about January 11, 2010, a Company 3 sales representative wrote to a health care provider that "LC Bead releases chemo therapy as a drug-eluting device over the course of 14 days."

28. On or about February 5, 2010, the FDA informed Biocompatibles that it was refusing to file the PMA because it was deficient. The FDA informed

Biocompatibles that the FDA would not review the PMA until the deficiencies were corrected. The FDA's letter to Biocompatibles stated that in order for the FDA to file the PMA, Biocompatibles would need to include clinical data adequately demonstrating "a survival benefit" and a "statistically meaningful benefit in quality of life" measures.

29. Despite Biocompatibles' failure to obtain PMA approval for LC Bead® for drug delivery, from on or about February 2, 2010, through on or about December 31, 2010, Biocompatibles continued to allow Company 3 to promote LC Bead as a drug delivery device.

30. On or about June 4, 2010, a Company 3 sales representative told a health care provider to go to Biocompatibles' website for videos and instructions on how to load drugs onto LC Bead® and provided the health care provider with a copy of the FDA's 510(k) clearance letter for LC Bead®, dated November 12, 2004, which did not specify that the clearance applied to use of the device for embolization.

31. On or about August 24, 2010, a Company 3 sales representative sent a health care provider in the United States an email message with a link to a drug-loading instructional video on Biocompatibles' website.

32. On or about October 26, 2010, a Company 3 sales representative introduced himself to a health care provider through an email message that said he was an "oncology surgery representative specializing in chemo-embolization (LC Beads)."

33. On or about December 23, 2010, a Company 3 sales representative wrote to a health care provider that he could not send drug-loading information about LC Bead® "because of some off label issues," but instead provided the health care provider with a link to drug-loading information on Biocompatibles' website.

*Promotion in Furtherance of the Scheme and Acts in the District*

34. From on or about May 22, 2006, through on or about December 31, 2010, Company 2's and Company 3's sales representatives, consistent with the marketing plan that Biocompatibles approved, encouraged health care providers to use LC Bead® for drug delivery and demonstrated to health care providers how to use LC Bead® to deliver drugs. Company 2's and Company 3's sales representatives misled health care providers, in that there was no or insufficient data accepted by the FDA at that time to demonstrate that LC Bead® was safe and effective for use as a device to deliver chemotherapy drugs. Biocompatibles engaged in this conduct despite: (a) pledging to the FDA on or about November 6, 2004, that it would not promote LC Bead® as a drug delivery device; (b) being explicitly informed by the FDA that separate FDA marketing authorization was required to distribute LC Bead® as a drug delivery device; and (c) attempting and failing to obtain both 510(k) clearance and PMA approval.

35. From on or about May 22, 2006, through on or about December 31, 2010, Defendant BIOCOMPATIBLES received a gain in the amount of $8,751,673 by unlawfully distributing LC Bead® for the unapproved and uncleared intended use as a drug-delivery device.

36. From on or about May 22, 2006, through on or about December 31, 2010, in the District of Columbia and elsewhere, Biocompatibles caused the introduction into interstate commerce of LC Bead®, which was a device within the meaning of 21 U.S.C. § 321(h), and which was misbranded because its labeling lacked adequate directions for its intended use as a drug-delivery device, in violation of 21 U.S.C. § 352(f)(1).

37. Biocompatibles' introduction into interstate commerce of misbranded medical devices included the shipment of LC Bead® devices into the United States that ultimately were provided to a health care provider in the District of Columbia on or about November 26, 2008.

38. Biocompatibles' introduction into interstate commerce of misbranded medical devices included the shipment of LC Bead® devices into the United States that ultimately were provided to a health care provider in Houston, Texas, on or about December 16, 2010.

**Conclusion**

39. Biocompatibles' distribution of LC Bead® for drug delivery, when LC Bead® had not been approved or cleared by the FDA for drug delivery, rendered LC Bead® a misbranded device, within the meaning of 21 U.S.C. § 352(f)(1).

40. From on or about May 22, 2006, through on or about December 31, 2010, Biocompatibles aided and abetted the promotion, sale, and distribution of LC Bead® throughout the United States, including the District of Columbia, for use as a drug-delivery device. By shipping a misbranded medical device in interstate commerce, Biocompatibles violated 21 U.S.C. §§ 331(a) and 333(a)(1).

## DEFENDANT'S ACKNOWLEDGEMENT

On behalf of Biocompatibles, Inc., and as its duly authorized representative, I have read every word of this Statement of the Offense. Pursuant to Rule 11 of the Federal Rules of Criminal Procedure, and after consulting with Biocompatibles, Inc.'s counsel, I agree and stipulate to this Statement of the Offense on behalf of B.

Date: 10/4/16

Ken Pugh
President, Biocompatibles, Inc.
Duly Authorized Representative of
Biocompatibles, Inc.

## ATTORNEY'S ACKNOWLEDGEMENT

I have fully discussed this Statement of the Offense with my client.

Date: 10/4/16

Richard L. Scheff, Esq.
Attorney for Biocompatibles, Inc.