March 15, 2004

AMENDING AGREEMENT

NPS ALLELIX CORP.

– AND –

BOEHRINGER INGELHEIM AUSTRIA GmbH

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AMENDING AGREEMENT

BETWEEN:

NPS ALLELIX CORP.
an Ontario corporation, having an address at 6850 Goreway Drive,
Mississauga, Ontario, Canada L4V 1V7
("**NPS**")

- and -

BOEHRINGER INGELHEIM AUSTRIA GmbH
a corporation of the Federal Republic of Austria, having an address at
Dr. Boehringer-Gasse 5 – 11, A-1121 Vienna, Austria
("**BI AUSTRIA**")

This AGREEMENT is effective this 15th day of March, 2004 (the "EFFECTIVE DATE").

WHEREAS **NPS** has developed a proprietary product ALX-0600, a recombinant 1-33 amino acid analog of glucagon-like peptide-2 (also known as "teduglutide"), and the proprietary process to manufacture it, and **NPS** is currently in Clinical Trials with ALX-0600; and

WHEREAS **BI AUSTRIA** manufactures recombinant pharmaceutical proteins under GMP conditions for commercial sale for use in humans in the U.S., Europe and elsewhere; and

WHEREAS **BI AUSTRIA** desires to manufacture ALX-0600 for **NPS** in accordance with **NPS'** requirements in order to facilitate **NPS'** supply of ALX-0600 for clinical use and provided the product successfully passes clinical development for market use and **NPS** is desirous of having **BI AUSTRIA** manufacture bulk GMP ALX-0600; and

WHEREAS **NPS** and **BI AUSTRIA** have entered into a COMMERCIAL MANUFACTURING AGREEMENT dated October 18, 2002 for the manufacture of **NPS'** proprietary product ALX1-11 (also known as PREOS™), for which the active ingredient is recombinant human parathyroid hormone eighty-four (84) amino acids ("rhPTH"); and

WHEREAS **NPS** and **BI AUSTRIA** have now completed some of the technology transfer for rhPTH and have determined that [redacted] batches of rhPTH can be produced in a [redacted] (and not [redacted] batches as previously assumed) at an increased cost of [redacted] Euros per Batch for a total reserved capacity equivalent to [redacted] batches of rhPTH for [redacted] of production (and not a total reserved capacity of [redacted] batches of rhPTH as previously assumed); and

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WHEREAS **NPS** and **BI AUSTRIA** have agreed that **NPS'** financial obligation for the manufacture of rhPTH under the COMMERCIAL MANUFACTURING AGREEMENT will be met by **NPS'** manufacture of rhPTH alone, ALX-0600 alone, or both rhPTH and ALX-0600 together in accordance with the submitted forecasts; and

WHEREAS **NPS** and **BI AUSTRIA** have entered into a Letter of Intent effective as of September 1, 2003 for the manufacture of ALX-0600 and now desire to enter into an agreement amending the COMMERCIAL MANUFACTURING AGREEMENT to provide for the manufacture of ALX-0600 and to provide for the revised costing and reserve capacity for rhPTH("AMENDING AGREEMENT"); and

WHEREAS **NPS** and **BI AUSTRIA** have executed a certain Confidential Disclosure Agreement dated May 7, 2001, as amended March 6, 2003, which is intended to cover the discussions leading to and under the Letter of Intent and this Amending Agreement;

NOW THEREFORE in consideration of the foregoing premises, the mutual covenants and obligations hereinafter contained, and other good and valuable consideration, receipt and sufficiency of which is hereby acknowledged, THE PARTIES AGREE AS FOLLOWS:

1. DEFINITIONS

1.1 Some of the definitions set out in the COMMERCIAL MANUFACTURING AGREEMENT will likewise apply herein as applicable and are repeated below for convenience:

1.1.1 AFFILIATE means any entity that directly or indirectly owns, is owned by, or is under common ownership with, **NPS** or **BI AUSTRIA**, where "own" or "ownership" means possession or control of at least 50% of the outstanding voting securities of a corporation or a comparable equity interest in any other type of entity.

1.1.2 BATCH PRODUCTION RECORD ("BPR") means the complete written record of the history of the BATCH and its production thereof as required under GMP and in accordance with the MASTER BATCH RECORD.

1.1.3 CONFORMANCE BATCHES means three (3) BATCHES to carry out the process validation and which will form part of regulatory submissions.

1.1.4 EMEA means the European Medicines Evaluation Agency or any successor agency having similar jurisdiction.

1.1.5 EUROPEAN GMP means current Good Manufacturing Practices pursuant to (a) EEC Directive 91/356/EEC of 13 June 1991, (b) the EC Guide to Good Manufacturing Practice for Medicinal Products, (c) relevant current International Conference on Harmonisation (ICH) guidance documents, in particular ICH Guidance Q7A Good Manufacturing Practice Guide for Active Pharmaceutical

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Ingredients and (d) any applicable European laws, regulations or respective guidance documents subsequently established.

1.1.6 FDA means the United States Food and Drug Administration or any successor agency having similar jurisdiction.

1.1.7 FDA GMP means current Good Manufacturing Practices pursuant to (a) the U.S. Federal Food, Drug and Cosmetics Act as amended (21 USC 301 et seq.), (b) relevant U.S. regulations found in Title 21 of the U.S. Code of Federal Regulations (including Parts 11, 210, and 211), (c) relevant current International Conference on Harmonisation (ICH) guidance documents, in particular ICH Guidance Q7A Good Manufacturing Practice Guide for Active Pharmaceutical Ingredients and (d) any applicable U.S. laws, regulations or respective guidance documents subsequently established.

1.1.8 FINAL RELEASE means **NPS**' release of a BATCH for formulating into drug product pursuant to the PRODUCT SPECIFICATIONS and GMP.

1.1.9 GMP means current Good Manufacturing Practices pursuant to FDA GMP and EUROPEAN GMP.

1.1.10 INTELLECTUAL PROPERTY means patents, trade secrets, trade marks, service marks, registered designs, lab notebooks, applications for any of the foregoing, trade and business names, unregistered trade marks and service marks, copyrights, rights in designs, inventions, know-how, rights under licenses, consents, orders, statutes or otherwise in relation to any such rights, and rights of the same or similar effect or nature, in any part of the world.

1.1.11 MANUFACTURER RELEASE means **BI AUSTRIA**'s release of a BATCH for further processing.

1.1.12 MASTER BATCH RECORD means the master production instructions for manufacture of a BATCH.

1.1.13 NDA means a new drug application in the U.S. FDA.

1.1.14 PARTY and PARTIES means **NPS** or **BI AUSTRIA**, or both, as applicable.

1.1.15 SOPs mean written standard operating procedures established, or to be established, by **BI AUSTRIA** and employed in the production, Quality Control, quality assurance, warehousing and labelling and packaging, among other things.

1.2 The following definitions are hereby amended from the COMMERCIAL MANUFACTURING AGREEMENT to refer to ALX-0600, or are new definitions, and provided herein for use in the AMENDING AGREEMENT:

1.2.1 ALX-0600 means purified bulk recombinant [gly2] glucagon-like peptide-2(1-33) produced using NPS' proprietary WCB/MCB and NPS' proprietary process.

1.2.2 ALX-0600 RELATED PROTEIN means a compound that: [redacted]

1.2.3 ALX-0600 SPECIFICATIONS means the SPECIFICATIONS which are attached at Exhibit F.

1.2.4 BATCH means ALX-0600 produced from [redacted] fermentation and purification run using a [redacted] working volume fermenter.

1.2.5 CONFIDENTIAL INFORMATION means any information disclosed to, or developed by either PARTY, or an AFFILIATE or agent of either PARTY, which is confidential in accordance with paragraph 16, which information includes, but is not limited to: WCB; MCB; the processes and methods employed in the manufacture of ALX-0600; BATCH PRODUCTION RECORDS, SPECIFICATIONS; information related to the facilities at **BI AUSTRIA**; information related to recombinant production processes or to any products produced at the **BI AUSTRIA** facilities; any prices and costs of **BI AUSTRIA**; regulatory filings for the ALX-0600; **NPS'** and **BI AUSTRIA's** manufacturing, business and regulatory plans and strategies; and other data and information designated as confidential.

1.2.6 DATE AVAILABLE FOR DELIVERY means the date on which **NPS** requests that ALX-0600 (in grams) be available for shipment.

1.2.7 IMPLEMENTATION BATCHES mean at least the [redacted] BATCHES of ALX-0600 produced by **BI AUSTRIA** in a [redacted] working volume fermenter as provided herein.

1.2.8 MCB means **NPS'** master cell bank containing the host cell (with the plasmid incorporated therein) for fermentation of the ALX-0600. The MCB is used to generate the WCB.

1.2.9 METHOD TRANSFER SERVICES mean services provided by **BI AUSTRIA** in accordance with paragraph 5.4.

1.2.10 QUALITY AGREEMENT means the agreement on all quality procedures and aspects related to ALX-0600 and which will be negotiated and executed by the PARTIES.

1.2.11 RAW MATERIAL means materials, reagents and solvents needed for the production of ALX-0600.

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1.2.12 RAW MATERIAL SPECIFICATIONS means SPECIFICATIONS for RAW MATERIALS.

1.2.13 rhPTH means the PRODUCT as defined under the COMMERCIAL MANUFACTURING AGREEMENT.

1.2.14 RESERVE CAPACITY means the maximum quantity of ALX-0600 and/or rhPTH (in total) NPS can request from BI AUSTRIA in a given year based on a maximum number of batches, subject to agreement otherwise by the PARTIES.

1.2.15 SMALL SCALE BATCHES means the production of ALX-0600 in [redacted] working volume fermentation batches pursuant to paragraph 5.2 in the AMENDING AGREEMENT.

1.2.16 SPECIFICATIONS means tests, references to analytical procedures, appropriate acceptance criteria that are numerical limits, ranges or other criteria for which the RAW MATERIALS, ALX-0600, intermediates, or process of making the ALX-0600, must conform to in order for the ALX-0600 to be acceptable for its intended use. Types of SPECIFICATIONS include but are not limited to ALX-0600 SPECIFICATIONS, MASTER BATCH RECORD, RAW MATERIAL SPECIFICATIONS and in-process SPECIFICATIONS.

1.2.17 STABILITY STUDIES mean all studies necessary to assess the stability characteristics of ALX-0600 which shall be used in determining appropriate storage conditions and expiration dates.

1.2.18 TERRITORY means the U.S., Europe (member states of the European Union) and Canada and any other country agreed to by the Parties.

1.2.19 VALIDATION means documented evidence which provides a high degree of assurance that a specific process, activity, piece of equipment, SOP or other component required or used in the manufacture of ALX-0600 will consistently meet its pre-determined and expected results.

1.2.20 VALIDATION SERVICES means any VALIDATION services required of BI AUSTRIA in the manufacture of ALX-0600.

1.2.21 WCB means NPS' working cell bank containing the host cell (with the plasmid incorporated therein) for fermentation of the ALX-0600. The WCB is generated from MCB.

1.2.22 YIELD means grams of ALX-0600 produced per BATCH.

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2. PURPOSE AND SCOPE

2.1 This AMENDING AGREEMENT is intended to provide the revised structure under which the manufacture of ALX-0600 AND rhPTH shall be conducted by **BI AUSTRIA** for **NPS**. This AMENDING AGREEMENT is also intended to provide the structure for the technology transfer to **BI AUSTRIA** from **NPS** and **NPS'** contracted third party SYNCO of ALX-0600. Furthermore, unless particularly amended in this AMENDING AGREEMENT the provisions in the COMMERICAL MANUFACTURING AGREEMENT continue to apply as set out therein for the manufacture of rhPTH.

2.2 In addition, this AMENDING AGREEMENT is intended to revise the costing, reserve capacity and corresponding financial obligations set out in the COMMERCIAL MANUFACTURING AGREEMENT.

2.3 The PARTIES expect to use a team approach and **NPS** expects fully to support the technology transfer effort and to benefit from a reduction in associated costs of production of ALX-0600 experienced over time during the technology transfer phase and the commercial production that differs from current expectations. Likewise, **BI AUSTRIA** expects to receive strong predictable and viable revenues over time for a set and reasonable percentage of its production capacity at its Vienna, Austria production facility.

2.4 Based on the current production at SYNCO, the PARTIES have assumed the process to manufacture ALX-0600 at **BI AUSTRIA** shall be successful as contemplated in this paragraph. In particular, based on the [redacted] working volume batch process at SYNCO with: fermentation expression rate of about [redacted] fermentation broth; overall yield from a batch of approximately [redacted] grams of ALX-0600 (wherein one fermentation batch translates into one purification batch); the PARTIES have assumed that **BI AUSTRIA** can scale this current process up to a [redacted] working volume batch scale with an overall yield of approximately [redacted] of ALX-0600. It is expected that [redacted] batches of ALX-0600 will be manufactured per [redacted] and as such the current expected price per BATCH is [redacted] Euros per BATCH. Based on the current assumptions, there is no substantial increase expected in this BATCH price. In the event these assumptions change, the PARTIES shall mutually agree on steps forward.

2.5 Exhibits that are attached hereto are incorporated in, and are deemed to be an integral part, of this AGREEMENT. Exhibits may be amended and additional exhibits may be added from time to time after execution of this AGREEMENT. At the time of execution of this AGREEMENT the Exhibits are:

Exhibit A:	Process Flow Diagram
Exhibit B:	List of Manufacturing Documents Used at SYNCO
Exhibit C:	Testing Parameters
Exhibit D:	Timetable and Payment Schedule for Technology Transfer
Exhibit E:	Assumptions

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Exhibit F:	ALX-0600 SPECIFICATIONS and IPC SPECIFICATIONS
Exhibit G:	Critical Raw Materials and Storage Containers
Exhibit H:	Documents BI AUSTRIA will provide in English
Exhibit I:	Description of facilities for ALX-0600 production and testing
Exhibit J:	Documents to be reviewed and approved by NPS
Exhibit K:	NPS Patents to WCB/MCB
Exhibit L:	BI AUSTRIA's QMS Timeframes regarding deviations
Exhibit M:	Financial Obligations for the manufacture of ALX-0600, rhPTH
Exhibit N:	Forecasts – 2004, 2005, 2006, 2007
Exhibit O:	Initial Validation Plan
Exhibit P:	Documentation for WCB/MCB

2.6 The Letter of Intent for ALX-0600, effective 01 September 2003, is deemed to be merged with this AMENDING AGREEMENT.

3. EQUIPMENT AND MATERIAL

3.1. EQUIPMENT

3.1.1 Required Equipment

3.1.1.1. **NPS** shall pay for the following equipment, which equipment will be the property of **BI AUSTRIA. NPS** and **BI AUSTRIA** will co-operate, as appropriate, in exploring and identifying the best possible supplier of the equipment. This equipment will only be used for production of ALX-0600 in accordance with this AGREEMENT.

[redacted]

3.1.1.2. If other equipment is needed specifically for the production or Quality Control of ALX-0600, **NPS** shall pay for such equipment and **BI AUSTRIA** shall own such equipment, which equipment **BI AUSTRIA** will not use in the production or Quality Control of other products.

3.1.1.3. If any additional equipment is used in the production of ALX-0600, including Quality Control, under this AGREEMENT or the QUALITY AGREEMENT, other than as specified in paragraph 3.1.1.1 and 3.1.1.2, **BI AUSTRIA** shall be responsible for purchasing, obtaining, validating, calibrating and implementing such equipment and **BI AUSTRIA** shall own such equipment.

3.1.2 Ownership and Rights to Possession

3.1.2.1 **BI AUSTRIA** shall own the equipment purchased by **NPS** pursuant to paragraphs 3.1.1.1 and 3.1.1.2. However, **NPS** has the right for 1.00 Euro on 30 days advance notice and without other obligation or performance, to purchase, take possession of, and remove from **BI AUSTRIA** any or all of the equipment that **NPS** originally purchases in circumstances such as: termination of manufacturing of ALX-0600 or winding up of **BI AUSTRIA**'s biopharmaceutical production.

3.1.3 Validation and Maintenance

3.1.3.1 **BI AUSTRIA** shall be responsible for setting-up, calibrating, cleaning, qualifying, and maintaining all equipment required in the production of ALX-0600. **NPS** shall pay **BI AUSTRIA** the costs for qualification of the ALX-0600-dedicated equipment.

3.1.3.2 **BI AUSTRIA** is entitled to charge to **NPS** a one-time surcharge of [redacted] percent [redacted] of [redacted] of ALX-0600-dedicated equipment described above in paragraphs 3.1.1.1 and 3.1.1.2 for purchasing, installing, calibrating, insuring and maintaining such ALX-0600-dedicated equipment during the term of the AGREEMENT. **BI AUSTRIA** shall be solely responsible for (a) reasonably maintaining the ALX-0600-dedicated equipment, (b) repairing the ALX-0600-dedicated equipment as a result of ordinary and intended use of such equipment for the purposes of this AGREEMENT, and (c) insuring against loss of such ALX-0600-dedicated equipment. In the event that despite all reasonable maintenance and ordinary and intended use of such ALX-0600-dedicated equipment an irreparable damage occurs, it will be **NPS**' responsibility to replace such ALX-0600-dedicated equipment; provided, however, that **BI AUSTRIA** shall be solely responsible for costs to replace or repair any ALX-0600-dedicated equipment that is damaged due to (x) any abnormal or unintended uses of such equipment, (y) any accident, fire, flood or other incident for which **BI AUSTRIA**'s insurance is intended to cover, or (z) the failure to reasonably maintain the ALX-0600-dedicated equipment.

3.2. WCB AND MCB

3.2.1 Supply

3.2.1.1 Unless otherwise agreed to by the PARTIES, **NPS** shall provide the MCB (if needed) and WCB to be used in production of ALX-0600 by **BI AUSTRIA** in sufficient quantities and on a timely basis for the scheduled production of ALX-0600 at **BI AUSTRIA**. **NPS** shall provide **BI AUSTRIA** with the GMP WCB and documentation on the GMP WCB and GMP MCB within thirty (30) days of the Effective Date of the Letter of Intent. Set out in Exhibit P is the documentation **NPS** will provide.

3.2.1.2 **BI AUSTRIA** shall review the documentation and conduct incoming tests for viability, identity, plasmid retention and purity to confirm that the MCB/WCB is satisfactory for the manufacture of ALX-0600. **BI AUSTRIA** shall complete this analysis and inform **NPS** of the results of any testing and the suitability of the GMP WCB and GMP/MCB, as applicable, within sixty (60) days of its receipt of all of the documentation and GMP WCB or GMP MCB, as applicable.

Except for such documentation review and the aforementioned incoming tests conducted by **BI AUSTRIA**, **BI AUSTRIA** does not represent or assume any responsibility whatsoever that the MCB/WCB is satisfactory for the GMP manufacture of ALX-0600 in a GMP multi-product plant.

3.2.1.3 **BI AUSTRIA** will maintain records of usage of the MCB/WCB and will inform **NPS** of needs for additional quantities or changes in characteristics thereof in a timely manner for use in any subsequent production.

3.2.1.4 **BI AUSTRIA** shall describe and conduct appropriate STABILITY STUDIES on the WCB, as required and as agreed to by the PARTIES in accordance with a separate stability protocol and cost proposal which will form an Exhibit to this AGREEMENT.

3.2.2 Ownership and Insurance

3.2.2.1 **NPS** holds all the INTELLECTUAL PROPERTY rights to the WCB and the MCB (including the patent rights set out in Exhibit K) except for the limited license granted to **BI AUSTRIA** hereunder for the purposes hereof. For greater clarity, **BI AUSTRIA** acquires hereunder no ownership, license or security interest rights in the WCB or MCB beyond the limited use license granted for production of ALX-0600 under this AMENDING AGREEMENT. All INTELLECTUAL PROPERTY rights relative to the WCB and the MCB or their use are and remain the exclusive rights of NPS.

3.2.2.2 **BI AUSTRIA** shall not transfer the WCB or MCB to any third party without the prior written permission of **NPS** and any unused quantities at the termination of the manufacture of ALX-0600 shall be destroyed or returned to **NPS** at **NPS'** direction.

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3.2.2.3 **NPS** shall maintain the appropriate insurance on the WCB and MCB whether or not it is stored at **BI AUSTRIA**.

3.2.3 Handling and Storage

3.2.3.1 **BI AUSTRIA** shall be responsible for handling and storage of the WCB provided by **NPS** and the MCB if the PARTIES agree to store the MCB at **BI AUSTRIA**.

3.3. RESINS, RAW MATERIALS AND STORAGE CONTAINERS

3.3.1 Supply

3.3.1.1. **BI AUSTRIA** shall purchase all RAW MATERIALS, resins and storage containers required for the manufacture and storage of ALX-0600 unless otherwise agreed to by the PARTIES.

3.3.1.2. It is acknowledged that **BI AUSTRIA** has established and qualified suppliers for resins and RAW MATERIALS and the PARTIES shall mutually agree on the SPECIFICATIONS and supplier for each RAW MATERIAL. For RAW MATERIALS, such as yeast extract and tryptone, and for storage containers which **NPS** considers critical **BI AUSTRIA** is willing to accept **NPS'** proposed supplier and SPECIFICATIONS. The RAW MATERIALS and storage containers **NPS** considers critical are set out in Exhibit G attached.

3.3.2 Testing and Release

3.3.2.1 **BI AUSTRIA** will ensure suppliers of RAW MATERIALS and resins have Vendor Qualification in accordance with GMP or conduct standard pharmacopoeia methods or other appropriate methods for release of RAW MATERIALS. Such methods shall be documented and utilised by **BI AUSTRIA**, as required. For RAW MATERIALS and storage containers which **NPS** considers critical, **NPS** and **BI AUSTRIA** will agree to appropriate methods for release testing. If **NPS'** requests, or if validation is required and agreed to by the PARTIES, **BI AUSTRIA** shall validate and **NPS** shall pay for such services.

3.3.2.2 The PARTIES shall agree on the methods for handling, cleaning and storing the storage containers and **BI AUSTRIA** shall document and validate such methods.

Stainless steel containers (Warminster, PA, USA, ref PSF 18 316L) will be supplied by **NPS** to **BI AUSTRIA**.

4. PROCESS

4.1. **NPS** shall provide **BI AUSTRIA** with **NPS'** proprietary process for manufacturing ALX-0600 which **BI AUSTRIA** will implement and validate in accordance with the SPECIFICATIONS, in particular the MASTER BATCH RECORD and GMP. The overall process is described in Exhibit A and the initial plan for validation is described in Exhibit O. The manufacturing process as transferred from SYNCO to **BI AUSTRIA** as per the Effective Date is proprietary to **NPS**.

5. TECHNOLOGY TRANSFER

5.1. PROCESS TRANSFER

5.1.1 Supply of NPS Documentation

5.1.1.1. **NPS** shall supply copies of documentation and records currently being used for the [redacted] scale process at SYNCO, including Component Production Records, SYNCO Batch Production Records, SYNCO Raw Material Specifications, SYNCO Analytical Methods, SYNCO Validation documentation, SYNCO Standard Operating Procedures and any other available production data/research data/quality data as needed to support the process transfer. Attached hereto as Exhibit B is a list of the main documents used in the manufacture of ALX-0600 at SYNCO.

5.1.1.2. **NPS** shall work with **BI AUSTRIA** to ensure that all necessary documentation, data, methods, and information has been provided to **BI AUSTRIA** in order that **BI AUSTRIA** will be in a position to complete the Technology Transfer in accordance with the timetable set out in Exhibit D and initiate and maintain manufacture of ALX-0600 as set out herein.

5.1.2 **NPS** Personnel

5.1.2.1 **NPS** shall use good faith reasonable commercial efforts to make **NPS** personnel available to **BI AUSTRIA** as needed during the Technology Transfer phase and manufacture phase. It is expected that **NPS** personnel will be available and present as needed during the process transfer, SMALL SCALE BATCHES and IMPLEMENTATION BATCHES. Implementation activities are under the sole control of **BI AUSTRIA** and therefore unsolicited intervention by **NPS** personnel shall not take place. It is mutually agreed that **NPS** shall have the right to have technical personnel, namely, as a general rule two (2) employees may be present during manufacture of a BATCH. It is understood that the PARTIES may agree to exceptions to this general rule as needed.

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5.1.3 SYNCO Visit

5.1.3.1 **NPS** will endeavour to arrange a visit to SYNCO and both **NPS** and **BI AUSTRIA** personnel will attend, including, but not limited to, the project manager of each of **NPS** and **BI AUSTRIA**, with the intention to view the production of ALX-0600 and/or production facilities at SYNCO. At **NPS'** reasonable request, **BI AUSTRIA** will execute an appropriate and reasonable confidential disclosure agreement with SYNCO.

5.1.4 **BI AUSTRIA** Documentation and Set-Up

5.1.4.1 **BI AUSTRIA** shall study the relevant documentation necessary to set-up and run the SMALL SCALE BATCHES, IMPLEMENTATION BATCHES and BATCHES for clinical supply, including, but not limited to, the documentation provided by **NPS** pursuant to paragraph 5.1.1.

5.1.4.2 **BI AUSTRIA** shall draft all necessary documentation, including SPECIFICATIONS, MASTER BATCH RECORD and SOPs, based on the documentation supplied by **NPS** and GMP. The documentation listed in Exhibit J shall be reviewed, approved, and supplied to **NPS**. Any additional documentation generated by **BI AUSTRIA** under this AGREEMENT shall be reviewed, approved, and supplied to **NPS**, as the PARTIES may agree.

5.2 SMALL SCALE BATCHES

5.2.1 **BI AUSTRIA** will produce at least [redacted] working volume batches in the **BI AUSTRIA** Process Engineering Suite.[1]

5.2.2 **BI AUSTRIA** shall purify the SMALL SCALE BATCHES in accordance with procedures agreed upon by the PARTIES.

5.2.3 **BI AUSTRIA** shall conduct in-process testing and their own bulk release testing (Bioburden and Endotoxin) on the purified SMALL SCALE BATCHES as agreed to by the PARTIES.

5.2.4 The PARTIES shall consider the yield and purity of the SMALL SCALE BATCHES and if the SMALL SCALE BATCHES do not meet the specified purity standards or the expected yields based on ALX-0600 SPECIFICATIONS, the PARTIES will come to an agreement on steps forward.

5.2.5 ALX-0600 from the SMALL SCALE BATCHES shall not be used in humans.

5.3 IMPLEMENTATION BATCHES

5.3.1 **BI AUSTRIA** will produce [redacted] working volume IMPLEMENTATION BATCHES, unless otherwise agreed to by the PARTIES.

[1] The Process Engineering Suite is an area with no official room classification according to Federal Standard 209. However, there are HEPA filters and an installed HVAC system to provide continuous air quality and controlled airflow. There is controlled access for material and personnel and gowning procedures for personnel.

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BI AUSTRIA shall initiate production of the IMPLEMENTATION BATCHES in accordance with the timeline (Exhibit D) following production of the SMALL SCALE BATCHES, unless otherwise agreed to by the PARTIES.

5.3.2 The IMPLEMENTATION BATCHES shall be produced in the GMP production units at **BI AUSTRIA** to ensure the technical equipment is qualified with respect to the specific requirements for the commercial manufacture of ALX-0600.

5.3.3 **BI AUSTRIA** shall purify each IMPLEMENTATION BATCH in accordance with the process description which shall be established in a draft MASTER BATCH RECORD to be agreed on by the PARTIES.

5.3.4 **BI AUSTRIA** shall conduct in-process control testing, on each manufacture run of the IMPLEMENTATION BATCHES for methods which have been transferred to **BI AUSTRIA** in accordance with the MASTER BATCH RECORD/ SPECIFICATIONS, unless otherwise agreed to by the PARTIES.

5.3.5 **BI AUSTRIA** shall also conduct their own bulk substance release testing (Bioburden and Endotoxin) of the IMPLEMENTATION BATCHES as agreed to by the PARTIES and shall provide **NPS** with the BATCH PRODUCTION RECORDS for each of the IMPLEMENTATION BATCHES.

5.3.6 The PARTIES shall consider the yield and purity of the IMPLEMENTATION BATCHES and if the IMPLEMENTATION BATCHES do not meet the expected purity standards or expected yields based on ALX-0600 SPECIFICATIONS the PARTIES will come to an agreement on steps forward. **BI AUSTRIA** does not warrant that the IMPLEMENTATION BATCHES shall meet the ALX-0600 SPECIFICATIONS.

5.3.7 ALX-0600 from the IMPLEMENTATION BATCHES shall not be used in humans. However, at least two (2) of the IMPLEMENTATION BATCHES are intended to be used by **NPS** for toxicity studies in animals. The suitability of materials for toxicity studies will be evaluated by **NPS** and used at **NPS'** risk.

BI AUSTRIA shall not bear any responsibility with regard to the use of the IMPLEMENTATION BATCHES for toxicity studies nor any conclusions drawn for subsequent application in humans.

5.4 METHOD TRANSFER SERVICES

5.4.1 In the event that additional METHOD TRANSFER SERVICES are required by **BI AUSTRIA, BI AUSTRIA** shall provide to **NPS** appropriate METHOD TRANSFER SERVICES as agreed to by the PARTIES in separate written protocols including documentation and implementation of analytical methods for in-process and bulk testing. Costs for such services will be addressed in the separate written proposals. The additional METHOD TRANSFER SERVICES and associated costs will be attached hereto as an Exhibit to be added to the AGREEMENT and will form an integral part of this AGREEMENT.

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For testing of general analytical parameters (e.g. bioburden, viability, identity, etc.) **BI AUSTRIA** shall use its general and established methods. Should **NPS** request that any of these general methods shall be established as product-specific methods (whereby this establishment includes the compilation of analytical procedures and/or laboratory testing), **NPS** shall bear the respective costs.

5.4.2 **BI AUSTRIA** shall provide to **NPS** the following Method Transfer Services for in-process testing:

[redacted]

5.4.3 It is understood between the PARTIES, that additional IPC methods may be required to be transferred to **BI AUSTRIA** at **NPS'** costs. If the PARTIES agree that **NPS** shall conduct in-process or process robustness testing, **BI AUSTRIA** shall give **NPS** notice as soon as possible and no later than the date the samples are shipped for testing and **NPS** shall test and supply QA reviewed results for any IPC testing within two (2) weeks of receipt of the samples and for process robustness testing within four (4) weeks. If the circumstances require, **NPS** shall inform **BI AUSTRIA** and the PARTIES shall agree on possible extensions of such periods.

5.4.4 It is **NPS'** request that **BI AUSTRIA** shall perform in-process testing and up to January 2006 **NPS** shall perform bulk release testing. After January 2006, **BI AUSTRIA** shall perform the analytical testing for all release parameters, unless otherwise agreed to by the PARTIES. These Method Transfer Services shall be addressed in separate written protocols. Costs for such services will be addressed in the separate written proposals.

5.4.5 Up to January 2006, **NPS** shall endeavour to provide full analytical support to investigations required by **BI AUSTRIA** in the case of deviations. In such cases **NPS** shall provide such analytical support in such timeframes as required by **BI**

[2] **BI AUSTRIA** shall do a peptide map based on the method **NPS** provides to **BI AUSTRIA**. **NPS** shall provide samples and data associated with the method. However, the parties understand that **NPS** will not support a method transfer and validation for the peptide map testing.

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AUSTRIA Quality Management System (QMS) provided **NPS** is immediately notified of such deviation and investigation and immediately advised of required analytical support. The timeframes dictated by QMS are attached in Exhibit L.

5.4.6 In the event **NPS** does not meet the requirements of the **BI AUSTRIA** QMS as set out in paragraph 5.4.5, all necessary release testing analytical methods shall be transferred to **BI AUSTRIA** at **NPS'** costs. **NPS** acknowledges that such transfer may influence the timelines.

6. MANUFACTURE OF ALX-0600

6.1 Clinical Manufacturing

6.1.1 All ALX-0600 manufactured by **BI AUSTRIA** and supplied to **NPS**, or to **NPS'** representatives, agents or formulation contract manufacturers, for clinical use shall be manufactured, stored and prepared for shipment in accordance with the SPECIFICATIONS (in particular, the MASTER BATCH RECORD), QUALITY AGREEMENT and GMP and all applicable laws, regulations and ordinances as required in the TERRITORY. **BI AUSTRIA** is also responsible for the MANUFACTURER RELEASE of ALX-0600. Up to January 2006, **BI AUSTRIA** shall provide MANUFACTURER RELEASE which will consist of **BI AUSTRIA's** QA review and release of the BATCH PRODUCTION RECORD. After January 2006, **BI AUSTRIA** shall provide all release testing as provided for in Exhibit F, unless otherwise agreed to by the PARTIES.

6.1.2 All ALX-0600 manufactured by **BI AUSTRIA** for clinical use shall be suitable for formulation into final drug product to be used in humans. **NPS** is responsible for the FINAL RELEASE of ALX-0600.

6.1.3 Details of the MANUFACTURER RELEASE, Quality Assurance (also called Quality Management), Quality Control, Validation, Inspections, Audits and other Regulatory requirements shall be detailed in the QUALITY AGREEMENT. The manufacture of ALX-0600 shall be carried out in BATCHES as defined herein.

6.2 Commercial Supply and CONFORMANCE BATCHES

6.2.1 If clinical trials are successful and commercial supply is required, the PARTIES shall agree on the commercial supply of ALX-0600 by **BI AUSTRIA** which will include agreement on the supply of CONFORMANCE BATCHES. The PARTIES acknowledge that as of the EFFECTIVE DATE the requirements for commercial supply are unknown, including the timing of commercial supply, the required quantities and the potential changes in the commercial process for ALX-0600. NPS shall keep BI AUSTRIA informed of the ALX-0600 clinical programs initiated and completed.

6.2.2 Conformance Runs. As to be agreed on by the PARTIES, **BI AUSTRIA** shall produce three (3) batches of GMP ALX-0600 at the [redacted] working volume

scale intending to deliver such GMP ALX-0600 to NPS, in time and quality, reasonably acceptable to NPS. These Conformance Batches shall be done under GMP conditions in accordance with batch documentation established with NPS Specifications as set out in Exhibit B and F. The bulk GMP ALX-0600 shall undergo IPC-testing and QC Manufacturer's Release testing in accordance with the validated methods. All runs will be documented as required by GMP. The GMP ALX-0600 produced in the Conformance Batches is intended for commercial sale by NPS.

6.3 Initiation of Manufacture of ALX-0600

6.3.1. In accordance with the Binding Forecast for 2004 set out in Exhibit N, **BI AUSTRIA** shall manufacture and supply ALX-0600 for clinical use beginning no later than the last quarter of 2004, unless otherwise agreed to by the PARTIES.

6.4 Capacity

6.4.1 RESERVE CAPACITY

6.4.1.1 Revised rhPTH Reserve Capacity

6.4.1.1.1 This paragraph 6.4.1.1.1 amends paragraph 6.4.2.1.1 of the COMMERCIAL MANUFACTURING AGREEMENT. It has been ascertained and agreed by the PARTIES: (i) that only [redacted] batches of rhPTH per week will be manufactured by **BI AUSTRIA** and not [redacted] batches as assumed in the COMMERCIAL MANUFACTURING AGREEMENT, (ii) the new cost of rhPTH is [redacted] €/BATCH, and (iii) the reserve capacity of [redacted] batches of rhPTH set out in paragraph 6.4.2.1 of the COMMERCIAL MANUFACTURING AGREEMENT is revised to [redacted] batches of rhPTH beginning in 2005. The Batch price for rhPTH of [redacted] Batch excludes raw materials, resins and component costs.

6.4.1.2 ALX-0600 Reserve Capacity

6.4.1.2.1 NPS shall not reserve separate capacity for ALX-0600.

For the years 2004, 2005 and 2006, NPS' reserved capacity and financial obligation for the manufacture and technology transfer of rhPTH/ALX-0600 is set out in Exhibit M.

For the years 2007 onwards, NPS shall use the total reserved capacity and concurrent financial obligation as set out in paragraph 6.4.1.1.1 of this Amending Agreement and paragraph 6.4.2.1.2 of the COMMERCIAL MANUFACTURING AGREEMENT for ordering both rhPTH and ALX-0600 and any substitution thereof. Accordingly, at NPS' discretion, and according to the Rolling Forecast NPS has submitted for rhPTH and any timely substitution thereof with ALX-

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0600, NPS may order for any given calendar quarter with no penalty: (i) all rhPTH, (ii) all ALX-0600 or (iii) both rhPTH and ALX-0600 to meet its total commitment on a per batch basis pursuant to paragraph 6.4.1.1.1 of this Amending Agreement and paragraph 6.4.2.1.2 of the COMMERCIAL MANUFACTURING AGREEMENT in any given year. However, in all of these cases, the total commitment on a per batch basis for any given year will not exceed the reserved capacity pursuant to the COMMERCIAL MANUFACTURING AGREEMENT of between [redacted] batches (previously understood to be [redacted] batches of rhPTH based on [redacted] batches per week) and [redacted] batches (previously understood to be one hundred (100) batches of rhPTH based on [redacted] batches per week) of rhPTH and/or ALX-0600, unless otherwise agreed to by the PARTIES.

6.4.1.2.2 There are no sliding prices for ALX-0600. If capacity and the current financial obligations established in 6.4.1.2 is not fulfilled in any given year by rhPTH together with ALX-0600, then any shortfall will be used to price rhPTH with the sliding scale as set out in the COMMERCIAL MANUFACTURING AGREEMENT.

6.5 Rolling Forecast

6.5.1 NPS shall order its required ALX-0600 supply without penalty from NPS forecast for rhPTH pursuant to the COMMERCIAL MANUFACTURING AGREEMENT. For every batch forecasted amount of rhPTH or forecasted BATCH of ALX-0600, NPS may on twelve (12) months notice, replace such forecasted batch amount of rhPTH with a BATCH of ALX-0600 or replace such forecasted Batch of ALX-0600 with a batch of rhPTH, respectively.

6.5.2 The Rolling Forecast in the COMMERCIAL MANUFACTURING AGREEMENT will apply to the manufacture of rhPTH and ALX-0600. A forecast is attached as Exhibit N. If NPS replaces a batch of rhPTH with a BATCH of ALX-0600, or vice versa, on twelve (12) months notice, NPS shall also provide with such notice the DATE AVAILABLE FOR DELIVERY.

6.6 Facilities

6.6.1 **BI AUSTRIA** will be manufacturing ALX-0600 on a BATCH basis at its facilities at Dr. Boehringer-Gasse 5 – 11, A-1121 Vienna, Austria, which are operated and maintained under GMP conditions. A description of the facilities showing the areas and equipment designated for manufacture of ALX-0600 are set out in Exhibit I attached.

6.6.2 **BI AUSTRIA**'s facilities will have, and **BI AUSTRIA** will continuously maintain, all required authorisations and permits necessary for the manufacture of ALX-0600 for clinical and commercial sale for use in humans.

6.6.3 For said facilities, **BI AUSTRIA** has established, or will establish as necessary, GMP compliant rules concerning clothing, hygiene, restrictions in movement, safety, and observations of SOPS.

6.7 Establishment of Price and Expected YIELD

6.7.1 Revised Calculation for Price/Gram for rhPTH

6.7.1.1 In view of the new forecasts for production of rhPTH and ALX-0600 in Exhibit N, the establishment of a price/gram as set out in paragraph 6.4.4.2 of the COMMERCIAL MANUFACTURING AGREEMENT is revised as follows:

6.7.1.1.1 NPS shall pay for rhPTH on a Euro/gram basis using two computations: 1. 2004 and 2005: The 2004 and 2005 Payable Price per gram for all 2004 and 2005 delivered COMMERCIAL BATCHES; and 2. 2006 and Beyond: The Annual Payable Price per gram. These computations are set out below in paragraphs 6.7.1.1.2, 6.7.1.1.3 and 6.7.1.1.4.

6.7.1.1.2 2004 and 2005: The 2004 and 2005 Payable Price per gram for all 2004 and 2005 delivered COMMERCIAL BATCHES

The Payable Price per gram for all grams of rhPTH delivered prior to year end 2005 shall be computed in accordance with paragraph 6.4.4.2.1 of the COMMERCIAL MANUFACTURING AGREEMENT wherein the first [redacted] COMMERCIAL BATCHES are produced in years 2004 and 2005 (instead of 2004).

6.7.1.1.3 2006 and Beyond: The Annual Payable Price per gram

The Annual Payable Price per gram shall be freshly computed for each calendar year of the AGREEMENT beginning for the year 2006 (and not beginning in the year 2005) as described in paragraph 6.4.4.2.2 of the COMMERCIAL MANUFACTURING AGREEMENT. However, "B", the total attributable cost, will be calculated using the final [redacted] of all BATCHES, or at least the last [redacted] BATCHES, produced in the prior year.

6.7.1.1.4 Furthermore, paragraph 6.4.4.3 of the COMMERCIAL MANUFACTURING AGREEMENT is revised such that if the forecasted quantity of rhPTH and ALX-0600 is less than the financial obligation corresponding to the RESERVE CAPACITY, the price in Euro per gram established for rhPTH will be adjusted using the Sliding Scale factors set out in Exhibit E of the COMMERCIAL MANUFACTURING AGREEMENT.

6.7.2 Calculation of Price/Gram for ALX-0600 and Expected Yield

6.7.2.1 The current predicted production of ALX-0600 at **BI AUSTRIA** together with the costing is based on certain mutual assumptions (see Exhibit E). The PARTIES understand that once the production process for ALX-0600 is fully transferred to **BI AUSTRIA**, **BI AUSTRIA** and **NPS** will be able to confirm whether or not the assumptions made for cost, capacity and resources needed were accurate and

whether any price adjustment is required. Price adjustments and the basis for them will be mutually agreed to. Based on the assumptions currently in place, the price for ALX-0600 is readily computable and is [redacted] per BATCH. At this time, there is no indication that there should be any significant price adjustment. The cost of ALX-0600 of [redacted] per BATCH excludes raw materials, resins and component costs.

6.7.2.2 NPS shall pay for ALX-0600 on a Euro/gram basis using two computations: 1. 2004 and 2005: The 2004 and 2005 Payable Price per gram for all 2004 and 2005 delivered BATCHES; and 2. 2006 and Beyond: The Annual Payable Price per gram. These computations are set out below in paragraphs 6.7.2.3 and 6.7.2.4.

6.7.2.3 2004 and 2005: The 2004 and 2005 Payable Price per gram for all 2004 and 2005 delivered BATCHES

The Payable Price per gram for all grams of clinical BATCHES delivered prior to year end 2005: shall be computed from the first [redacted] BATCHES produced for clinical trials before year end 2005 and shall be computed on the basis of Payable Price per gram of ALX-0600 as follows:

Payable Price per gram is computed as the total attributable cost for said first [redacted] BATCHES for clinical supply divided by the total grams of ALX-0600 delivered by **BI AUSTRIA** from said first [redacted] BATCHES;

where the "total attributable cost" is determined in the manner reflected in paragraph 6.7.2.1 and Exhibit E.

6.7.2.4 2006 and Beyond: The Annual Payable Price per gram

The Annual Payable Price per gram shall be freshly computed for each calendar year of the AGREEMENT beginning for the year 2006 as follows:

The Annual Payable Price per gram = [redacted]

where "A" is the [redacted] per gram which is the [redacted] in paragraph 6.7.2.3 above; and

where "B" is the [redacted] produced in the prior year divided by the total grams of ALX-0600 delivered by **BI AUSTRIA** from said final [redacted] of all BATCHES or said last [redacted] BATCHES, whichever is applicable, where the "total attributable cost" is determined in the manner reflected in paragraph 6.7.2.1 and Exhibit E provided that the Annual Payable Price for any year shall not be greater than for prior year (before inflation price adjustments and cost adjustments for Third Party Materials and Services).

BI AUSTRIA shall invoice and **NPS** shall pay for deliveries the "Annual Payable" price per gram plus the inflation price adjustment and cost adjustments as provided for in Exhibit E.

6.8 Documentation

6.8.1 **BI AUSTRIA** will retain complete, accurate and authentic documents and records created by **BI AUSTRIA** for each BATCH for clinical or commercial supply, including documents on manufacturing data, test records, BATCH PRODUCTION RECORDS, deviation reports, SOPs, VALIDATION documentation, SPECIFICATIONS and RAW MATERIAL samples and any other documents, samples and information as required by GMP or at **NPS'** request. **BI AUSTRIA** shall permit **NPS** access to all originals under reasonable notice and will accommodate **NPS** by providing a suitable working space with access to photocopy, telephone (voice and data) and facsimile for an employee, representative or consultant of **NPS** to be designated by **NPS** from time to time. All NPS representatives or consultants who are not NPS personnel and are on-site at BI AUSTRIA pursuant to this paragraph 6.8.1 for ALX-0600, or pursuant to paragraph 6.4.5.1 of the COMMERCIAL MANUFACTURING AGREEMENT for rhPTH, need to be approved by BI AUSTRIA, approval not to be unreasonably withheld. As a general rule, **NPS** shall ensure that any and all such personnel required for on-site review of a certain set of documents shall be present concurrently. The parties understand that there may be certain circumstances in which this general rule cannot be complied with.

6.8.2 During the initial manufacture of BATCHES for clinical supply there will be a qualification period in which **NPS** will qualify **BI AUSTRIA** as a manufacturer of ALX-0600. During the qualification period **BI AUSTRIA** will send copies of the following original documents to **NPS**: BATCH PRODUCTION RECORDS, deviation summary reports, deviation reports/investigations, Certificate of Analysis (COA) and Certificate or statement of GMP Compliance (COC). Deviation summary reports will provide a description of the deviations, investigations, actions taken and follow-up measures. It is currently estimated that **BI AUSTRIA** will have to send to **NPS** the documentation on the first ten (10) BATCHES for clinical supply. If the documentation is reasonably satisfactory to **NPS** and meets GMP requirements, then **NPS** will qualify **BI AUSTRIA**. Once **BI AUSTRIA** is qualified, **BI AUSTRIA** will provide to **NPS** by no later then the DATE AVAILABLE FOR DELIVERY the following documents for each BATCH produced and released by **BI AUSTRIA** pursuant to a MANUFACTURER RELEASE:

(i) COA. This document will include the name of the product, the lot number and the date of manufacture.

(ii) COC.

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(iii) Deviation Summary Report for each lot and photocopies of major deviation reports/investigations associated with the lot.

6.8.3 Documents and records created by and for **BI AUSTRIA** shall be in German or English. The specific documents to be drafted in English or for which **BI AUSTRIA** will translate into English are listed in Exhibit H attached.

6.8.4 In addition to the documents **BI AUSTRIA** shall provide under paragraph 6.8.2, **BI AUSTRIA** shall provide a Trend Analysis of the process which will include in-process data and results of tests for all GMP Batches.

6.9 Packaging/Labelling

6.9.1 **BI AUSTRIA** shall package and label ALX-0600 in accordance with the applicable MASTER BATCH RECORD and GMP.

6.10 Release

6.10.1 **BI AUSTRIA** is responsible for the MANUFACTURER RELEASE. **NPS** is responsible for the FINAL RELEASE.

6.10.2 **BI AUSTRIA** shall test each BATCH and provide the MANUFACTURER RELEASE as provided for in paragraph 6.8.2 for each BATCH by the earlier of: three (3) months from the manufacture of ALX-0600; or the DATE AVAILABLE FOR DELIVERY. **BI AUSTRIA** and **NPS** shall establish an acceptable GMP procedure for BATCH PRODUCTION RECORD review. Original BATCH PRODUCTION RECORDS will be completed and available for review on site at **BI AUSTRIA** by **NPS** upon request of **NPS** at the time of the MANUFACTURER RELEASE of each BATCH. The review and approval of BATCH PRODUCTION RECORDS is described in paragraph 9.5.2 and will be detailed in the QUALITY AGREEMENT.

6.11 Shipment of ALX-0600

6.11.1 All ALX-0600 (and any samples thereof) shall be shipped to **NPS** or a location designated by **NPS** according to the Incoterm 2000 EXW ("ex works") **BI AUSTRIA**'s facility. **NPS** shall be responsible for obtaining any import license or other official authorisation and carrying out any other customs formalities necessary for importation of ALX-0600, and for paying for all customs formalities as well as duties, taxes, and other official charges payable upon importation.

6.12 Ownership and Insurance Liabilities

6.12.1 **BI AUSTRIA** shall retain title (but not the intellectual property therein) in the work-in progress and to any BATCH which has not yet been paid for in full by **NPS**. Title to a BATCH shall pass to NPS on payment in full to **BI AUSTRIA**

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for the BATCH. **NPS** shall obtain the appropriate insurance on the BATCH when the BATCH is shipped from **BI AUSTRIA** facilities.

6.12.2 **BI AUSTRIA** shall hold appropriate insurance for the work-in-progress and BATCHES which are on site at **BI AUSTRIA** facilities.

6.13 Dispute Resolution For Failed Batches

6.13.1 Confirmatory Third Party Testing/Review GMP Quality

6.13.1.1 If **NPS** determines ALX-0600 was not manufactured in accordance with the MASTER BATCH RECORD or is not GMP, then **NPS** shall notify **BI AUSTRIA**. If the PARTIES disagree as to whether or not the said quantity of ALX-0600 is in accordance with the MASTER BATCH RECORD, or is GMP grade, or is suitable for FINAL RELEASE in accordance with the testing parameters set forth in Exhibit C, then a qualified independent party, acceptable to both PARTIES, will determine if ALX-0600 was manufactured in accordance with the MASTER BATCH RECORD, or is GMP grade, or is suitable for FINAL RELEASE in accordance with the testing parameters set forth in Exhibit C. After January 2006, if **NPS** determines that ALX-0600 does not meet ALX-0600 SPECIFICATIONS or is not suitable for FINAL RELEASE in accordance with the testing parameters set forth in Exhibit F and **BI AUSTRIA** disagrees, a qualified independent party, acceptable to both PARTIES, will determine its suitability for FINAL RELEASE in accordance with the testing parameters set forth in Exhibit F. The resulting determination will be final and binding on **BI AUSTRIA** and **NPS**. **BI AUSTRIA** will bear the cost of the third party evaluation if the testing demonstrates that ALX-0600 is not suitable for FINAL RELEASE in accordance with the testing parameters set forth in Exhibit C or F, as applicable. If ALX-0600 is determined to be suitable for FINAL RELEASE in accordance with the testing parameters set forth in Exhibit C or F, as applicable, then **NPS** shall bear all costs of the third party evaluation.

6.13.2 Replacement/Cost Reduction

6.13.2.1 **BI AUSTRIA** shall replace, with no additional charge, using commercially reasonable efforts, any quantity of ALX-0600 which is not suitable for FINAL RELEASE provided **NPS** notifies **BI AUSTRIA** in writing upon discovery of the defect or non-conformity within a period of ninety (90) days after receipt of all documentation and information from **BI AUSTRIA** regarding the BATCH. **BI AUSTRIA** shall evaluate the claim and test the said quantity of ALX-0600 within a reasonable period of time, not to exceed sixty (60) days. If such ALX-0600 is not replaced as provided for in this paragraph, **NPS** shall receive a full refund for any payment made for such ALX-0600. (Refunds shall be paid by **BI AUSTRIA** within thirty (30) days of the date of an invoice from **NPS**.)

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6.13.3 Arbitration

6.13.3.1 Any dispute under paragraphs 6.13.1.1 and 6.13..2.1 shall be handled in accordance with the Arbitration provisions provided herein.

7. WAREHOUSING AND DISTRIBUTION

7.1 All warehousing and distribution shall be done in accordance with GMP and the applicable SPECIFICATIONS, as detailed in the QUALITY AGREEMENT.

8. MATERIALS

8.1 WCB and MCB

8.1.1 **BI AUSTRIA** shall be responsible for storage of the WCB and/or MCB at its facilities, which storage conditions shall be agreed to by the PARTIES.

8.2 RAW MATERIALS and Resins

8.2.1 **BI AUSTRIA** shall warehouse as necessary the RAW MATERIALS and resins for use in the production of ALX-0600. Until **BI AUSTRIA** releases such stored RAW MATERIALS or resins, **BI AUSTRIA** shall document the quarantine status of such RAW MATERIALS and resins in **BI AUSTRIA**'s ERP system and as required under GMP (randomised storage).

8.3 ALX-0600

8.3.1 **BI AUSTRIA** shall warehouse ALX-0600 produced in the SMALL SCALE BATCHES and the IMPLEMENTATION BATCHES as requested by **NPS**. **NPS** shall decide on either disposing or shipping such ALX-0600 within three (3) months of all testing by **BI AUSTRIA** and **NPS**. **NPS** intends to use [redacted] of the IMPLEMENTATION BATCHES for toxicity studies in animals.

8.3.2 **BI AUSTRIA** shall warehouse ALX-0600 produced in accordance with this AGREEMENT. **BI AUSTRIA** shall warehouse ALX-0600 free of charge up to the DATE AVAILABLE FOR DELIVERY plus a further [redacted] months provided **BI AUSTRIA**'s obligations under paragraphs 6.1 and 6.8.2 for MANUFACTURER RELEASE have been met. It is currently intended by the PARTIES that ALX-0600 shall be warehoused from time to time by **BI AUSTRIA** for a period of time up to and after FINAL RELEASE by **NPS**, which will be agreed to by the PARTIES and as can be accommodated by **BI AUSTRIA** and which period of time will depend to a great extent on the production schedule

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as adapted by **NPS** for formulation of ALX-0600 into its final drug product for commercial sale.

8.3.3 ALX-0600 not subject to FINAL RELEASE by **NPS** shall be properly quarantined from ALX-0600 which has undergone FINAL RELEASE.

8.3.4 **NPS** shall specify the DATE(S) AVAILABLE FOR DELIVERY on the Purchase Order for ALX-0600. **NPS** shall submit a Purchase Order for ALX-0600 three (3) months in advance of the quarter for which it has been forecasted. **BI AUSTRIA** shall deliver on a timely basis the released ALX-0600 in accordance with the Purchase Order and the AMENDING AGREEMENT herein. **BI AUSTRIA** shall deliver ALX-0600 as requested by **NPS** after the MANUFACTURER RELEASE. FINAL RELEASE is not required before such delivery.

8.3.5 On or before the DATE AVAILABLE FOR DELIVERY, **BI AUSTRIA** shall approve the BATCH PRODUCTION RECORDS, investigate all deviations, provide the MANUFACTURER RELEASE and supply **NPS** with documentation pursuant to paragraphs 6.1 and 6.8.2.

9 QUALITY CONTROL AND MANAGEMENT

9.1 SEPARATE QUALITY AGREEMENT

9.1.1 Each of the PARTIES will in good faith expeditiously initiate the negotiation, documentation, and execution of a QUALITY AGREEMENT by the end of 2004.

9.2 VALIDATION SERVICES

9.2.1 Validation Plan

9.2.1.1 The PARTIES shall agree on a VALIDATION plan which shall establish the priorities and timetable for validating all critical systems, processes, tests and equipment, among other things. The initial VALIDATION plan as agreed to by the PARTIES is set out in Exhibit O. Consideration shall be given to whether currently validated systems, processes and tests need to be re-validated by **BI AUSTRIA**. Based on the VALIDATION plan, individual VALIDATION protocols shall be created.

9.2.2 System

9.2.2.1 **BI AUSTRIA** shall validate systems, if not currently validated, relevant for the manufacture of ALX-0600. VALIDATION of critical systems not already validated will be done in accordance with specified individual validation protocols, to be approved of by **BI AUSTRIA** Quality Management.

9.2.3 Process

9.2.3.1 **BI AUSTRIA** shall validate processes critical to the manufacturing of ALX-0600 including operation of sterilizers, bioreactor controls, chromatography process and cleaning and filtration equipment. VALIDATION of the processes will be done in accordance with specified individual validation protocols to be approved of by **BI AUSTRIA** Quality Management.

9.2.4 Test Methods

9.2.4.1 **BI AUSTRIA** shall validate those test methods which control critical characteristics or processes in the manufacture of ALX-0600, including without limitation YIELD, purity and bioburden.

9.3 SOPs

9.3.1 **BI AUSTRIA** shall have established, or establish, SOPs for the manufacture of ALX-0600 to cover:

personnel responsibilities;

facility operation, cleaning and maintenance;

procedures to be followed during inspections by FDA, EMEA or other regulatory agency;

staff safety and hygiene measures;

equipment operation, calibration, cleaning and maintenance;

production and process controls; reporting and justifying deviations; change control; equipment ID; sampling and testing in-process materials; cleaning and change-over procedures;

packaging and labelling control;

warehousing and distribution;

laboratory controls, including, without limitation, SOPs for analytical methods, stability testing, reserve samples and reagents; and

records and documentation, including, without limitation, BATCH PRODUCTION RECORDS, investigation of deviations, control and distribution records.

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9.3.2 In particular, SOPs shall be established for the production and testing of ALX-0600 including in-process controls and in-process samples.

9.3.3 **BI AUSTRIA** shall establish, maintain and implement SOPs for all warehousing, including warehousing of the cell banks, raw materials and resins, and ALX-0600.

9.3.4 Unless otherwise provided for in English as set out in paragraph 6.8.3, SOPs shall be in German. **BI AUSTRIA** shall make SOPs available for review by **NPS** on-site.

9.4 QUALITY CONTROL

9.4.1 **BI AUSTRIA** shall maintain a separate Quality Control unit which shall operate separately from the production staff for ensuring Quality Control in the manufacture of ALX-0600. The Quality Control unit shall have adequate facilities for conducting the necessary tests.

9.4.2 The Quality Control unit at **BI AUSTRIA** will conduct the testing of: RAW MATERIALS; resins and components; packaging components; in-process products; and MANUFACTURER RELEASE.

9.5 QUALITY MANAGEMENT

9.5.1 **BI AUSTRIA** shall maintain a Quality Management unit, which will be separate from the Quality Control unit and production staff. The responsibilities of the Quality Management unit will be detailed in the QUALITY AGREEMENT.

9.5.2 **BI AUSTRIA**'s Quality Management unit shall review and approve all BATCH PRODUCTION RECORDS and shall investigate all deviations on such BATCH PRODUCTION RECORDS on a timely basis, but in any event within three (3) months of production unless otherwise agreed to by the PARTIES. **BI AUSTRIA** shall follow-up with corrective and preventative actions, as required.

9.5.3 **BI AUSTRIA**'s Quality Management unit shall also ensure that **BI AUSTRIA**'s facilities and manufacturing operations for ALX-0600 are in compliance with the SPECIFICATIONS, FDA GMP, EUROPEAN GMP and **BI AUSTRIA**'s SOPs and with any other applicable law or regulation in effect during the time of manufacture of ALX-0600.

9.5.4 The Quality Management unit at **BI AUSTRIA** shall maintain appropriate SOPs, review and approve VALIDATION protocols, review proposed process changes and determine whether re-validation is required, approve all procedures or applicable SPECIFICATIONS, particularly those effecting identity, quality and purity of ALX-0600.

9.5.5 The **BI AUSTRIA** Quality Management unit shall ensure that changes in packaging, equipment, processes, warehousing and distribution that could affect product effectiveness or product characteristics are re-validated.

10 TIMETABLE

10.1 The PARTIES have agreed to a timeline as set out in Exhibit D for the Technology Transfer, initiation of manufacturing of clinical BATCHES and establishment of analytical methods.

10.2 The PARTIES will use commercially reasonable efforts to meet the expected timelines. However, if during the Technology Transfer, **BI AUSTRIA** becomes aware of circumstances which suggest that the estimated timelines in Exhibit D will not be met, **BI AUSTRIA** shall notify **NPS** and the PARTIES will agree on next steps.

10.3 Each PARTY acknowledges and agrees that it shall perform in a timely manner all of its obligations in this AGREEMENT.

11 ORGANIZATIONAL RESPONSIBILITIES

11.1 RESPONSIBLE PERSONNEL

11.1.1 Each PARTY shall appoint a Project Manager to the Technology Transfer and the commercial manufacture of ALX-0600.

11.1.2 All **BI AUSTRIA** and **NPS** personnel involved in the manufacture of ALX-0600 shall have the appropriate credentials, experience and training to conduct the work required of them under this AGREEMENT. Accordingly, the credentials, experience and training of the personnel shall be given due consideration for each function required, including: Quality Management; Quality Control; each stage of Technology Transfer; manufacturing; and warehousing.

11.2 PROJECT MANAGEMENT, MEETINGS AND PLANNING

11.2.1 The day-to-day operational responsibilities of the PARTIES with respect to the Technology Transfer and the manufacture of ALX-0600 under this AGREEMENT shall be overseen by the Project Team. The Project Team shall be responsible for deciding operational and scientific issues.

11.2.2 The Project Team shall be a team consisting of an equal number of people representing each PARTY, unless otherwise agreed to by the PARTIES. Each PARTY will appoint its representatives. Each member of the Project Team shall be a person of appropriate skill and experience. Either PARTY may change its own designated Project Team members. **NPS'** and **BI AUSTRIA's** respective

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members of the Project Team will be appointed prior to or shortly after the EFFECTIVE DATE.

11.2.3 There will be regularly scheduled meetings of the Project Team throughout the Technology Transfer phase and continuing at least until the end of 2004, which meetings will occur on a regular basis as required and as agreed to by the PARTIES. These meetings will include a report on scheduled production, progress made, problems encountered, next stages and longer term planning.

11.2.4 The PARTIES will come to an agreement on the need for regularly scheduled meetings beginning in 2005 but it is expected that there will be regularly scheduled meetings at least semi-annually. Ad hoc meetings may also be called to deal with any problems which may affect the production of ALX-0600 or the scheduling of the production for ALX-0600 and in particular if a DATE AVAILABLE FOR DELIVERY for ALX-0600 potentially will not be met by **BI AUSTRIA**.

11.2.5 Decisions of the Project Team shall be reflected in the approved Minutes prepared alternately by each PARTY. Meeting Minutes shall be approved by the Project Managers and should record all issues discussed and decisions made. As a general rule, the PARTIES will compile and provide to the other PARTY for review minutes of: (i) telecons within three (3) days and; (ii) face-to-face meetings within six (6) days. As a general rule, the reviewing PARTY will provide comments on such minutes as follows: (i) for telecons within three (3) days of receipt; and (ii) for face-to-face meetings, within six (6) days of receipt. If these time periods cannot be met, the PARTIES will agree on reasonable extensions of these periods.

11.2.6 In the event that the Project Team is unable to reach agreement on any issue and is unable to make decisions arising out of operational and scientific issues then the matter will be referred to the Steering Committee for resolution.

11.2.7 The Steering Committee shall consist of the Project Manager of each PARTY and an equal number of representatives of each PARTY. Each PARTY shall appoint permanent representatives from among its employees. It is the expectation of the PARTIES that appointees will change infrequently. The Steering Committee shall be responsible for unanimously agreeing in good faith on all issues on which the Project Team has been unable to reach agreement on. **NPS'** and **BI AUSTRIA's** respective members of the Steering Committee will be appointed on or shortly after the EFFECTIVE DATE of this AMENDING AGREEMENT.

11.3 **NPS' ATTENDANCE AND INPUT**

11.3.1 **NPS** personnel shall be in attendance during the Technology Transfer as set out in paragraph 5.1.2.

11.3.2 **NPS** personnel may be on-site during FDA inspections concerning ALX-0600 or other regulatory inspections concerning ALX-0600 and may attend the inspection opening and close-out meetings. Any questions which an inspector may have

concerning the manufacturing of ALX-0600 shall be answered by **BI AUSTRIA** unless the inspector directs the question to **NPS** to answer. Any questions concerning the further processing of ALX-0600, or marketing or use of the finished drug, shall be answered by **NPS**.

11.3.4 **NPS** personnel may be in attendance during commercial manufacture of ALX-0600 during a scheduled audit, or at a request by **BI AUSTRIA** or on reasonable notice by **NPS**, or unless otherwise agreed to by the PARTIES. **BI AUSTRIA** shall accommodate **NPS** personnel during such visits by providing an office area with access to photocopiers, telephone (voice and data) and facsimile.

12 FEES AND PAYMENTS

12.1 RESERVATION FEE

12.1.1 There is no separate reservation fee for ALX-0600; instead, the reservation fee for ALX-0600 shall be included in the reservation fee paid by **NPS** to **BI AUSTRIA** under the COMMERCIAL MANUFACTURING AGREEMENT. The reservation fee is to be creditable against the production costs of ALX-0600, as well as the costs for rhPTH as provided for in the COMMERCIAL MANUFACTURING AGREEMENT, and against any Termination Penalty which may become payable.

12.2 FEES FOR TECHNOLOGY TRANSFER

12.2.1 The costs and fee schedule for the technology transfer are set out in Exhibit D. Costs for RAW MATERIALS, components and resins for the Technology Transfer are not included in the fees but shall be invoiced separately.

12.2.2 **NPS** shall pay a cost of [redacted] Euros for delivery and release of ALX-0600 produced in the SMALL SCALE BATCHES at the [redacted] working volume scale and for delivery and release of the three (3) IMPLEMENTATION BATCHES. **NPS** shall pay for these services on performance and on receiving an invoice for such services.

12.2.3 **NPS** shall pay for METHOD TRANSFER SERVICES which are currently estimated for four methods to be about [redacted] Euro, upon receipt of a timely invoice. These Services will be agreed to promptly following the signing of the AMENDING AGREEMENT and will be addressed in separate written proposals.

12.2.4 **NPS** may request and upon performance, **NPS** will pay **BI AUSTRIA** for VALIDATION SERVICES and STABILITY STUDIES conducted by **BI AUSTRIA**. The cost will be determined based on industry standard pricing for such services, but is currently estimated to be approximately [redacted] Euros for VALIDATION SERVICES and [redacted] Euros for the Buffer STABILITY STUDIES.

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12.3 MANUFACTURING FEES

12.3.1 The cost for GMP clinical and commercial manufacture is currently estimated to be [redacted] Euros per BATCH. This cost per BATCH does not include RAW MATERIALS, components and resins. The calculation and establishment of a price/gram of ALX-0600 is set out in paragraph 6.7.2 herein.

12.3.2 For each BATCH manufactured by **BI AUSTRIA**, **BI AUSTRIA** shall invoice **NPS** on or after **BI AUSTRIA** has completed its obligations pursuant to paragraphs 6.8 and 6.10 in order to have ALX-0600 available for shipment as of the DATE AVAILABLE FOR DELIVERY.

12.4 WAREHOUSING FEES

12.4.1 The PARTIES shall agree on the cost to be charged to **NPS** by **BI AUSTRIA** for warehousing as provided for in paragraph 8.3.2.

12.5 RAW MATERIALS AND RESINS, AND STORAGE CONTAINERS

12.5.1 **BI AUSTRIA** shall invoice **NPS** for the RAW MATERIALS, components and resins used during the technology transfer at cost plus a flat fee for **BI AUSTRIA**'s services for purchasing, QC testing and storage, among other things. The flat fee will be 1.175 Euro per resin and 775 Euro per raw material.

12.5.2 **BI AUSTRIA** shall invoice **NPS** for the cost of the Storage Containers and for VALIDATION thereof.

12.6 REGULATORY FILINGS

12.6.1 **NPS** shall pay for **BI AUSTRIA**'s work pursuant to paragraph 13 for the regulatory filing, particularly the Chemistry, Manufacturing and Controls (CMC) section thereof, at a mutually agreeable and reasonable rate.

12.7 PAYMENTS

12.7.1 All payments by **NPS** to **BI AUSTRIA** shall be made within forty-five (45) days of the submission of the appropriate invoice by **BI AUSTRIA** detailing the matter to which the invoice applies and the price in Euros.

13 REGULATORY COMPLIANCE

13.1 GENERAL

13.1.1 **BI AUSTRIA** will exercise all reasonable skill, care and diligence customary in the industry in the performance of its duties under this AMENDING AGREEMENT and in accordance with the requirements of EUROPEAN GMP

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and FDA GMP. **BI AUSTRIA** shall obtain and maintain all permits required under Austrian legislation in order to manufacture ALX-0600. **BI AUSTRIA** will inform **NPS** of all permits filed under Austrian legislation or otherwise and their status with respect to approval.

13.1.2 **BI AUSTRIA** will file and maintain for its facility in Austria a Drug Master File (DMF), or such equivalent, as required by the U.S. FDA and a Site Master File (SMF), or such equivalent, as required by the EMEA. In addition, **BI AUSTRIA** will file and maintain a similar file in Canada for which the details and costs associated with such filing are to be agreed to by the PARTIES. For regulatory purposes, including the filing of an NDA or an amendment thereto, or equivalent thereof, **NPS** shall have rights to refer to the DMF, SMF or to other similar documents and **BI AUSTRIA** will give **NPS** access to information in the DMF, SMF and other similar documents which are necessary to complete regulatory documentation in U.S., Canada and Europe and are related to ALX-0600 and its manufacture in **BI AUSTRIA**'s facility. **BI AUSTRIA** shall also co-operate with similar filings in other countries at **NPS**' expense.

13.1.3 **BI AUSTRIA** shall co-operate with the FDA, EMEA or other such regulatory body, as requested by **NPS** and in response to matters concerning or impacting ALX-0600. **BI AUSTRIA** shall notify **NPS** of any communication with the FDA (or other such agency) concerning ALX-0600 or impacting ALX-0600 and shall co-operate with **NPS** in the scheduling of any planned inspection concerning ALX-0600.

13.2 INSPECTIONS AND AUDITS

13.2.1 Pre-Approval and Manufacturing Audits

13.2.1.1 **NPS** or its designated representatives may audit the Facilities for the purpose of reviewing manufacturing of ALX-0600, Quality Management, Quality Control and VALIDATION and for determining compliance with GMP and the SPECIFICATIONS during the term of this AMENDING AGREEMENT.

13.2.1.2 Subject to reasonable prior notice, **BI AUSTRIA** shall permit, and cooperate with, such audits as **NPS** may reasonably request at the **BI AUSTRIA** facilities by **NPS** personnel or representatives during business hours in order for **NPS** to carry out its review pursuant to 13.2.1.1. All **NPS** representatives or consultants who are not **NPS** personnel and are auditing the manufacture of ALX-0600 or rhPTH need to be approved by **BI AUSTRIA**, approval not to be unreasonably withheld. More than one (1) audit per year will not be permitted unless it is an audit for cause, which shall include, without limitation, a manufacturing or facility issue affecting or potentially affecting in any manner the production or quality of ALX-0600.

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13.2.2 Pre-Approval and Manufacturing Regulatory Inspections

13.2.2.1 As applicable, and as agreed to by the PARTIES, the PARTIES shall cooperate fully in preparing for and passing a Pre-Approval Inspection as required by the U.S. FDA or another regulatory agency.

13.2.2.2 **BI AUSTRIA** shall have in place, or put in place, a corporate policy, SOPs and the QUALITY AGREEMENT governing regulatory inspections.

13.2.3 483 Citations and Warning Letters

13.2.3.1 **BI AUSTRIA** shall notify **NPS** if it receives any FDA 483s, FDA Warning Letters, FDA non-compliance letters or other comparable FDA notifications concerning or impacting ALX-0600 (or similar European EMEA notifications) or if **BI AUSTRIA** receives notification of any planned or unplanned FDA inspection directed or applicable to ALX-0600 during the term of this AMENDING AGREEMENT.

13.2.3.2 **BI AUSTRIA** shall take immediate steps to address and correct any/all concerns raised by the FDA (EMEA, or other regulatory agency). Any concerns which are raised as a result of an FDA inspection including 483's or Warning Letters, will be promptly responded to. Issues which are facility related and/or which are quality system violations or deficiencies shall be paid for by **BI AUSTRIA**. **BI AUSTRIA** will promptly modify the manufacturing process as required or recommended by the FDA, EMEA or other regulatory authority, with **NPS'** input and provided **NPS** pays for such modifications which are process or ALX-0600 related. **NPS** shall be informed of any and all such communications and will be given the opportunity to have input in these communications as appropriate and in any event on any communication related to a time change or cost to **NPS**.

13.3 REGULATORY FILINGS

13.3.1 The PARTIES will mutually agree as to each PARTY's responsibilities in ensuring the requisite information required for the regulatory filings is available and submitted. The PARTIES shall work together to ensure all necessary and sufficient information and data for the CMC section of any regulatory filing is completed as required (including, but without limitation, chemistry, manufacturing and Quality Control/Quality Management information) which shall include **BI AUSTRIA's** participation in the writing of, and approval of, the sections of the CMC directed to ALX-0600 as produced by **BI AUSTRIA** prior to submission to the regulatory agencies. The timelines for **BI AUSTRIA's** review and approval of such documents will be agreed between the PARTIES.

All and any regulatory correspondence in which **BI AUSTRIA** is first named as manufacturer of PRODUCT or in which data provided by **BI AUSTRIA** are included, and all and any regulatory submissions relating to the manufacture of

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PRODUCT and updates thereof shall be subject to review by **BI AUSTRIA** prior to submission to a regulatory agency. **BI AUSTRIA** has rights of approval with respect to any such correspondence, submission or update relevant to **BI AUSTRIA**'s manufacture and testing of ALX-0600 at BI AUSTRIA's facilities. Such approvals are subject to strict timeframes. **NPS** shall endeavour to give **BI AUSTRIA** as much notice as possible. However, in some instances **BI AUSTRIA** may only have twenty-four (24) hours' notice to approve.

14 INTELLECTUAL PROPERTY

14.1 OWNERSHIP and LICENSING

14.1.1 All INTELLECTUAL PROPERTY generated pursuant to this AMENDING AGREEMENT with respect to the technology transfer and manufacture of ALX-0600 shall be owned by: (a) **BI AUSTRIA** if invented by **BI AUSTRIA** employees and/or agents; (b) **NPS** if invented by **NPS** employees and/or agents; and (c) shall be owned jointly by **BI AUSTRIA** and **NPS** if invented by employees and/or agents of both **BI AUSTRIA** and **NPS**. However, if **BI AUSTRIA** has some ownership in the INTELLECTUAL PROPERTY under (a) or (c), and this INTELLECTUAL PROPERTY is related to rhPTH or ALX-0600 or the production, use, or sale thereof, then **BI AUSTRIA** hereby grants to **NPS** an exclusive license from **BI AUSTRIA** to the INTELLECTUAL PROPERTY pursuant to this section for production, use or sale of rhPTH or ALX-0600, which license is royalty free, worldwide sublicensable, and paid up. For the avoidance of doubt, BI AUSTRIA shall be entitled to use all INTELLECUAL PROPERTY generated pursuant to subsection (a) and (c) of this paragraph 14.1.1 for all other products other than rhPTH and ALX-0600.

14.1.2 **BI AUSTRIA** shall promptly notify **NPS** in writing when it becomes aware of any INTELLECTUAL PROPERTY and **NPS** shall make the final determination on whether or not such INTELLECTUAL PROPERTY which is solely related to rhPTH or ALX-0600 or the exclusive production, use or sale of rhPTH or ALX-0600 shall be made the subject of any patent application(s) and issued patent(s) whereas **BI AUSTRIA** shall make the final determination on whether or not such INTELLECTUAL PROPERTY which is related to manufacturing processes and/or devices and which may either be applied (i) for the production, use or sale of rhPTH or ALX-0600 and other substances or (ii) for the exclusive production of other substances shall be made the subject of any patent application(s) and issued patent(s).

14.1.3 Any INTELLECTUAL PROPERTY owned by **BI AUSTRIA** pursuant to paragraph 14.1.1 shall not be licensed to a third party for the production, use or sale of an ALX-0600 RELATED PROTEIN.

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14.2 PROSECUTION

14.2.1 **NPS** shall be solely responsible for the filing, prosecution and maintenance of all INTELLECTUAL PROPERTY which is owned by **NPS** pursuant to paragraph 14.1.1. NPS shall also be solely responsible for filing, prosecution and maintenance of all INTELLECTUAL PROPERTY which is jointly owned by the PARTIES pursuant to paragraph 14.1.1 if such INTELLECTUAL PROPERTY is solely related to rhPTH or ALX-0600 and/or an ALX-0600 RELATED PROTEIN or the exclusive production, use or sale of ALX-0600 and/or an ALX-0600 RELATED PROTEIN, including costs associated therewith.

14.2.2 **BI AUSTRIA** shall be responsible for the filing, prosecution and maintenance of all INTELLECTUAL PROPERTY which is owned by **BI AUSTRIA** pursuant to paragraph 14.1.1. **BI AUSTRIA** shall be responsible for the filing, prosecution and maintenance of all INTELLECTUAL PROPERTY which is related to manufacturing processes and/or devices and which may either be applied (i) for the production, use or sale of rhPTH or ALX-0600 and other substances or (ii) for the exclusive production of other substances. However, even if the INTELLECTUAL PROPERTY is generally related to manufacturing processes and/or devices, if it is also related to rhPTH or ALX-0600 or an ALX-0600 RELATED PROTEIN or the production, use or sale of any of them, then **BI AUSTRIA** shall consult with **NPS** on such filings, prosecution and maintenance. If **BI AUSTRIA** elects not to file, prosecute or maintain such INTELLECTUAL PROPERTY, **NPS**, at its sole discretion, may file, prosecute or maintain such INTELLECTUAL PROPERTY.

15 LEGAL PROCEEDINGS

15.1 INFRINGEMENT OF THIRD PARTIES' PATENTS, PRODUCT LIABILITY AND INDEMNIFICATION

15.1.1 Subject to paragraph 15.1.2, NPS will indemnify and hold **BI AUSTRIA** and its AFFILIATES harmless from and against any and all losses, claims, damages or liabilities (including but not limited to reasonable attorney's fees), arising from (a) any use, including clinical trials, or sale by NPS or any **NPS** agent of any ALX-0600 supplied by **BI AUSTRIA** hereunder; (b) any allegation by any third party of infringement of its intellectual property rights by reason of the manufacture, use or sale of ALX-0600 by **BI AUSTRIA**, **NPS** or **NPS'** agents; (c) breach by **NPS** of its representations, warranties or covenants under this AGREEMENT; or (d) any negligent or reckless activities or omissions of **NPS**.

15.1.2 **BI AUSTRIA** shall be liable to **NPS**, and shall indemnify **NPS**, for any losses, claims or damages brought against **NPS** that are due to the negligent or reckless activities or omissions of **BI AUSTRIA**, its officers, employees or agents, or as a result of, in respect of, or arising out of any breach of any representation, warranty, covenant or guarantee of **BI AUSTRIA**.

15.1.3 If any claim is made for which a PARTY may seek indemnification from the other, the PARTY seeking indemnity shall promptly notify the other PARTY of the nature and basis of such claims and amounts thereof, to the extent known. In the event any action, suit or proceeding is brought against a PARTY with respect to which the other PARTY will have full liability hereunder, the other PARTY may, at its option and at its own expense, elect to assume the defence of any such action, suit or proceeding itself, and if it does not so elect, the PARTY having the action, suit or proceeding brought against it, will assume the defence thereof. If a PARTY may have only partial liability for any such action, suit or proceeding, the PARTIES will come to an agreement on how best to defend any such action, suit or proceeding. Neither PARTY shall make any settlement of claims without the written consent of the other PARTY, which consent shall not be unreasonably withheld.

15.1.4 In no event, whether directly or by indemnification, shall either PARTY be liable for any special, incidental, indirect or consequential losses or damages (including any loss of profits) arising out of or relating to each PARTY's performance or failure to perform its obligations hereunder. Each PARTY's total liability hereunder to the other shall not exceed the amounts paid or obligated to be paid to **BI AUSTRIA** by **NPS** pursuant to the COMMERCIAL MANUFACTURING AGREEMENT.

16 CONFIDENTIAL INFORMATION

16.1 A PARTY receiving CONFIDENTIAL INFORMATION from the other PARTY or developing such information pursuant to the COMMERCIAL MANUFACTURING AGREEMENT or the AMENDING AGREEMENT shall not disclose such information to any third party. Each PARTY shall keep CONFIDENTIAL INFORMATION in strict confidence, use it solely for the purposes authorised herein and shall not disclose such information, for a period extending ten (10) years from the termination of all manufacturing of rhPTH and ALX-0600 for **NPS** by **BI AUSTRIA**, except as follows:

To the extent such information is or becomes general public knowledge through no fault of the recipient PARTY; or

To the extent such information can be shown by contemporaneous documentation of the recipient PARTY to have been in its possession prior to receipt thereof hereunder; or

To the extent such information is received by the recipient PARTY from a third party without any breach of an obligation by the disclosing PARTY; or

To the extent such information can be shown by contemporaneous documentation of the recipient PARTY to have been independently developed by the recipient PARTY; or

To the extent required by law, by local authorities for regulatory purposes or is necessary to perform its obligations under the COMMERCIAL MANUFACTURING AGREEMENT and this AMENDING AGREEMENT, in which case, the recipient PARTY may disclose the information if the recipient PARTY gives the other PARTY prior notice of such disclosure and an opportunity to comment upon the content of the disclosure.

16.2 On or about May 7, 2001, as amended on March 6, 2003, the PARTIES entered into a Confidential Disclosure Agreement governing the disclosure and use of information concerning the matters addressed herein. Except as amended hereby, that CDA remains in full force and effect.

17 REPRESENTATIONS AND WARRANTIES

17.1 **BI AUSTRIA** represents that it will obtain **NPS'** written approval, not to be unreasonably withheld, in advance of any changes concerning or having impact on ALX-0600 and as further defined in the QUALITY AGREEMENT. None of these changes will be inconsistent with maintaining compliance with the SPECIFICATIONS and GMP or to the applicable law or regulations to the extent required under this AMENDING AGREEMENT for producing ALX-0600.

17.2 **BI AUSTRIA** represents that the GMP manufacture of ALX-0600 (including the process, plant, equipment and personnel) and the storage and preparation for shipment of ALX-0600 will all be done in accordance with the SPECIFICATIONS agreed upon by the PARTIES and GMP. Up to January 2006, and in accordance with **NPS'** express request, **BI AUSTRIA** shall only perform limited testing of ALX-0600, as set forth in Exhibit C, and hence **BI AUSTRIA's** representations as to conformity of ALX-0600 with the ALX-0600 SPECIFICATION (Exhibit F) are limited to those test parameters given in Exhibit C. Beginning in January 2006, **BI AUSTRIA** represents that the release of ALX-0600 will be done in accordance with the SPECIFICATIONS and GMP.

17.3 **BI AUSTRIA** represents that it shall maintain all necessary permits and authorisations as required under Austrian laws and under FDA GMP and European GMP in order to manufacture ALX-0600.

17.4 **BI AUSTRIA** represents that its facilities which will be used to commercially manufacture ALX-0600 have undergone an FDA inspection and **BI AUSTRIA** represents that it has not received any FDA Warning Letters or other such comparable FDA notifications. **BI AUSTRIA** represents that it shall notify **NPS** if it receives any FDA 483s, FDA Warning Letters, FDA non-compliance letters or other comparable FDA notifications (or similar European EMEA notifications) concerning or having impact on ALX-0600 or if **BI AUSTRIA** receives

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notification of any planned or unplanned inspection directed to ALX-0600 during the term of this AGREEMENT.

17.5 **BI AUSTRIA** represents that it will not carry on any activities in its facilities which **BI AUSTRIA** knows or should know could reasonably prevent ALX-0600 from being manufactured, packaged or stored in accordance with this AMENDING AGREEMENT.

17.6 **NPS** represents that any INTELLECTUAL PROPERTY owned or controlled by **NPS** and provided by **NPS** to **BI AUSTRIA** under this AGREEMENT has no defects of title, nor has any claim of infringement been threatened or asserted, nor is such a claim pending.

18 TERM AND TERMINATION

18.1 TERM

18.1.1 The term of this AGREEMENT shall coincide with the term of the COMMERCIAL MANUFACTURING AGREEMENT. Pursuant to paragraph 18.1 of the COMMERCIAL MANUFACTURING AGREEMENT, unless terminated earlier, the COMMERCIAL MANUFACTURING AGREEMENT will expire on December 31, 2010.

18.2 TERMINATION

18.2.1 There are no separate termination provisions for the manufacture of ALX-0600. In the situation wherein **NPS** terminates rhPTH manufacturing under paragraph 18.2.1.1, 18.2.1.2, 18.2.3.1 or 18.2.3.2, or **BI AUSTRIA** terminates under 18.2.4, of the COMMERCIAL MANUFACTURING AGREEMENT, the manufacturing of ALX-0600 shall remain unaffected, with the reserve capacity and other provisions to be negotiated in good faith by the PARTIES. The Termination provisions 18.2.2 and 18.2.3.3 of the COMMERCIAL MANUFACTURING AGREEMENT shall govern in the case where both the manufacture of ALX-0600 together with the manufacture of rhPTH is terminated.

18.3 EFFECT OF TERMINATION

18.3.1 Paragraphs 14, 15 and 18 shall survive termination or expiration of this AMENDING AGREEMENT (as the case may be) and shall remain in full force and effect.

18.3.2 The provisions of paragraph 16 shall survive termination or expiration of this AMENDING AGREEMENT (as the case may be) and shall remain in full force and effect for ten (10) years after termination or expiration of this AMENDING AGREEMENT.

18.3.3 The provisions of paragraph 3.1.2 shall survive termination or expiration of this AMENDING AGREEMENT (as the case may be) and shall remain in full force and effect for two (2) years after termination or expiration of this AMENDING AGREEMENT.

18.3.4 Termination of this AGREEMENT shall not release any PARTY from any liability for payment accrued or accruing to the other PARTY prior to the termination date.

18.3.5 In the event of termination, each PARTY shall promptly return to the other PARTY all of the other PARTY's CONFIDENTIAL INFORMATION. Each PARTY shall maintain copies of documentation or samples as required by that PARTY under GMP and may also keep one copy or sample for recordal purposes.

18.3.6 **BI AUSTRIA** shall deliver all PRODUCT-specific equipment in accordance with paragraph 3.1.2.1, all materials, including but not limited to samples, ALX-0600, and intermediate products, and all PRODUCT-specific documentation generated during the term and within the scope of this AGREEMENT to **NPS**.

18.3.7 In the event, **BI AUSTRIA** is not manufacturing ALX-0600 or rhPTH, as applicable, **NPS** hereby agrees to financially compensate **BI AUSTRIA** in accordance with industry standards for the further use of license rights granted by **BI AUSTRIA** in accordance with paragraph 14.1.

19 MISCELLANEOUS

19.1 NON-COMPETITION

19.1.1 **BI AUSTRIA** will not enter into an agreement to manufacture ALX-0600 or any ALX-0600 RELATED PROTEIN for a third party for as long as **BI AUSTRIA** is manufacturing ALX-0600 for **NPS** according to this AMENDING AGREEMENT.

19.1.2 Notwithstanding paragraph 19.1.3, **BI AUSTRIA** will not manufacture ALX-0600 for commercial sale for itself or its AFFILIATES for as long as **BI AUSTRIA** is manufacturing ALX-0600 for **NPS**.

19.1.3 **BI AUSTRIA** shall notify **NPS** as soon as it becomes aware of any intention by **BI AUSTRIA** or **BI AUSTRIA**'s AFFILIATES to have **BI AUSTRIA** develop or manufacture an ALX-0600 RELATED PROTEIN for commercial sale. Without limiting the generality of the foregoing sentence, **BI AUSTRIA** will be deemed to be aware of such intention at the point in time that **BI AUSTRIA** has herein been paid to do any material services applicable to and directed to such manufacture of an ALX-0600 RELATED PROTEIN. If **NPS** receives such notification from **BI AUSTRIA**, **NPS** has the option to terminate this AMENDING AGREEMENT as it applies to the manufacture of ALX-0600.

19.2 KNOWLEDGE SHARING WITH NPS

19.2.1 To the extent not otherwise provided for, **BI AUSTRIA** shall supply, or make available, to **NPS** on a timely basis all documentation and records created by **BI AUSTRIA**, for the commercial manufacture of ALX-0600, including, without limitation, Component Production Records, MASTER BATCH RECORDS, RAW MATERIAL SPECIFICATIONS, Analytical Methods, VALIDATION Documentation and any other available ALX-0600 specific production data/research data.

19.3 GOVERNING LAW AND ARBITRATION

19.3.1 This AMENDING AGREEMENT shall be governed, construed and interpreted by the laws of Austria without recourse to the conflict of laws provisions.

19.3.2 The PARTIES hereto agree to consult with each other and to use their best efforts to resolve any dispute and to refer a matter to arbitration only as a last resort. If the PARTIES are unable to resolve any dispute arising under this AMENDING AGREEMENT, a PARTY who desires to submit a dispute to arbitration shall deliver notice to that effect to the other PARTY. The PARTIES agree that all disputes between them arising out of or relating to this AMENDING AGREEMENT shall be settled by arbitration in accordance with the rules of arbitration of the International Chamber of Commerce by three arbitrators appointed in accordance with such rules. The arbitration proceedings shall take place in Paris, France and shall be conducted in the English language. The arbitration shall result in a binding decision. Judgment on the award may be issued by and enforced by any court of competent jurisdiction

19.4 WAIVER

19.4.1 The failure by any PARTY at any time to enforce any of the terms or provisions or conditions herein or exercise any right hereunder shall not constitute a waiver of the same or affect the validity of this AMENDING AGREEMENT or any part hereof, or that PARTY's rights thereafter to enforce or exercise the same. No waiver by a PARTY shall be valid or binding, except if in writing and signed by a duly authorised representative of the waiving PARTY.

19.5 FORCE MAJEURE

19.5.1 A PARTY shall not be held liable to the other for any delay in performance or non-performance of that PARTY directly or indirectly caused by reason of force majeure including, but not limited to, industrial disputes, strike, lockouts, riots, mobs, fires, floods, or other natural disasters, civil strife, embargo, lack or failure of transport facilities, currency restrictions, or events caused by reason of laws, regulations or orders by any government, governmental agency or instrumentality or by any other supervening circumstances beyond the control of either PARTY.

Provided, however, that the PARTY affected shall: give prompt written notice to the other PARTY of the date of commencement of the force majeure, the nature thereof, and expected duration; and shall use its best efforts to avoid or remove the force majeure to the extent it is able to do so; and shall make up, continue on and complete performance when such cause is removed to the extent it is able to do so. Either PARTY has the right to terminate with immediate effect, upon written notice to the other PARTY, should the force majeure continue after three months (3) following the first notification.

19.6 SEVERABILITY

19.6.1 In case one or more of the provisions contained herein shall, for any reason, be held invalid, illegal or unenforceable in any respect, such holding shall not affect any other provisions herein, but this AMENDING AGREEMENT shall be construed by limiting such provision to such extent as would nearly as possible reflect the intent, purpose and economic effect of such provision, or, if such is not possible, by deleting such, provided that the remaining provisions reflect the intent of the PARTIES.

19.7 NOTICE

19.7.1 All written communications, reports and notices between the PARTIES shall be in English and shall be delivered or sent by prepaid mail, registered mail, Federal Express or other recognised overnight courier, or facsimile transmission to the attention of the PARTY at the addresses noted below, or any other addresses of which either PARTY shall notify the other PARTY in writing.

Notices to **BI AUSTRIA** shall be to:
Boehringer Ingelheim Austria GmbH
Dr. Boehringer-Gasse 5 – 11
A-1121 Vienna
AUSTRIA
Attn: Dr. Kurt Konopitzky

Notices to **NPS** shall be to:

NPS Allelix Corp.
6850 Goreway Drive
Mississauga, Ontario
Canada L4V 1V7
Attn: Stephen Parrish, Vice-President, Manufacturing

with a copy to:

NPS Pharmaceuticals Inc.

March 15, 2004

420 Chipeta Way, Salt Lake City, Utah 84108
Tel: (801) 583-4939
Fax: (801) 583-4961
Attn: Legal Department

19.8 ASSIGNMENT AND ENUREMENT

19.8.1 Either PARTY shall have the right to assign this AMENDING AGREEMENT to its AFFILIATES. Any assignment of the Letter of Intent and/or the COMMERCIAL MANUFACTURING AGREEMENT and/or the AMENDING AGREEMENT (altogether "the Agreements") and the rights and obligations under the Agreements to any third party other than an AFFILIATE existing on the EFFECTIVE DATE herein whether by merger, divestiture, succession, acquisition, operation of law or otherwise shall not be permitted without the prior written consent of the other PARTY which shall not be unreasonably withheld or delayed.

19.8.2 If an assignment is not consented to pursuant to 19.8.1, the Agreements shall terminate in the manner provided below:

(a) Non-consent by **BI AUSTRIA** to such assignment leads to termination of the COMMERCIAL MANUFACTURING AGREEMENT and the Amending Agreement; such termination is not governed by section 18.2.2 of the COMMERCIAL MANUFACTURING AGREEMENT;

(b) Termination shall be effective upon the expiry of two (2) years after **BI AUSTRIA** has notified **NPS** of non-consent in order to enable inventory build-up parallel to **NPS'** technology transfer to a new manufacturer;

(c) All orders already placed under the red and blue zone of the Rolling Forecast remain unaffected; in particular section 18.4.4 of the COMMERCIAL MANUFACTURING AGREEMENT apply;

(d) Section 18.4 of the COMMERCIAL MANUFACTURING AGREEMENT applies upon the expiry of the two (2) year period set forth under (b). **BI AUSTRIA** shall have no further obligations with regard to technology transfer to a new manufacturer; and

(e) For the avoidance of doubt, any audits until termination becomes effective shall be conducted by **NPS** personnel only or by an independent consultant agreed to by both PARTIES. This also applies to on-site visits and personnel present during the manufacture of ALX-0600 or rhPTH. Such personnel shall be personnel who are not or have not been employees of the third party as set forth in section 19.8.1 at the time of assignment.

19.8.3 This AMENDING AGREEMENT shall be binding on all successors and permitted assignees.

19.9 LANGUAGE

19.9.1 All communications, written and oral between **NPS** and **BI AUSTRIA** shall be in English.

19.10 INTEGRATION

19.10.1 The COMMERCIAL MANUFACTURING AGREEMENT is merged herein with this AMENDING AGREEMENT and represents the entire understanding of the PARTIES and supercedes all other agreements, expressed or implied, between the PARTIES concerning the subject matter herein.

19.11 PUBLICITY

19.11.1 Each PARTY shall maintain the confidentiality of all provisions of this AGREEMENT, and, without the prior consent of the other PARTY, neither PARTY shall make any press release or other public announcement of or otherwise disclose this AMENDING AGREEMENT or any of its provisions to any third party (other than to its officers and employees and attorneys, accountants, investment bankers and other professional advisers whose duties require familiarity with this AMENDING AGREEMENT), except for such disclosures as may be required by applicable law or governmental regulation.

IN WITNESS WHEREOF, the PARTIES hereto have caused this Agreement to be executed by their duly authorised representatives.

NPS ALLELIX CORP.

By: _____
Name: Stephen R. Parrish

Title: Vice President, Manufacturing

Date: March 15TH 2004

BOEHRINGER INGELHEIM AUSTRIA GmbH

By: _____
Name: Dr. Kurt Konopitzky

Title: Head, Division Biopharmaceuticals/Operations

Date: 15 March 2004

By: _____
Name: Prof. Ralf G. Werner
Title: Head, Corporate Division Biopharmaceuticals

Date: 15 March 2004