

**NOTE: CERTAIN CONFIDENTIAL INFORMATION HAS BEEN OMITTED FROM THIS DOCUMENT AND REPLACED BY “[\*]”. A COMPLETE COPY OF THIS DOCUMENT INCLUDING THE CONFIDENTIAL INFORMATION HAS BEEN FILED SEPARATELY WITH THE SECURITIES AND EXCHANGE COMMISSION.**

**COMMERCIAL MANUFACTURING AGREEMENT**

**NPS ALLELIX CORP.**

**– AND –**

**BOEHRINGER INGELHEIM AUSTRIA GmbH**

## **TABLE OF CONTENTS**

<b>1</b>	<b>DEFINITIONS.....</b>	<b>2</b>
<b>2</b>	<b>PURPOSE AND SCOPE .....</b>	<b>5</b>
<b>3</b>	<b>EQUIPMENT AND MATERIAL.....</b>	<b>6</b>
3.1	Equipment.....	6
3.1.1	Required Equipment .....	6
3.1.2	Ownership and Rights to Possession .....	6
3.1.3	Validation and Maintenance .....	7
3.2	WCB and MCB.....	7
3.2.1	Supply.....	7
3.2.2	Ownership and Insurance .....	7
3.2.3	Handling and Storage .....	8
3.3	Resins, Raw Materials and Storage Containers .....	8
3.3.1	Supply.....	8
3.3.2	Testing and Release.....	8
<b>4</b>	<b>PROCESS.....</b>	<b>8</b>
<b>5</b>	<b>TECHNOLOGY TRANSFER .....</b>	<b>8</b>
5.1	Process Transfer.....	8
5.1.1	Supply of NPS documentation.....	8
5.1.2	NPS Personnel .....	9
5.1.3	SYNCO Visit.....	9
5.1.4	BI AUSTRIA Documentation and Set-Up .....	9
5.2	SMALL SCALE BATCHES .....	9
5.3	FERMENTATION BATCHES .....	10
5.4	IMPLEMENTATION BATCHES.....	10
5.5	Method Transfer Services .....	11
<b>6</b>	<b>COMMERCIAL MANUFACTURING .....</b>	<b>11</b>
6.3	CONFORMANCE BATCHES.....	11
6.4	Long Term Commercial Manufacture of PRODUCT.....	11
6.4.1	Initiation of Commercial Manufacture of PRODUCT .....	11
6.4.2	Capacity .....	12
6.4.2.1	Reserve Capacity.....	12
6.4.2.2	Rolling Forecast .....	12
6.4.3	Facilities .....	12
6.4.4	Establishment of Price and Expected Yield.....	13
6.4.5	Documentation .....	14
6.4.6	Packaging/Labelling .....	15
6.4.7	Release.....	15
6.4.8	Shipment of PRODUCT .....	15
6.4.9	Ownership and Insurance Liabilities .....	16
6.5	Dispute Resolution for Failed Batches.....	16
6.5.1	Confirmatory Third Party Testing/Review GMP Quality.....	16
6.5.2	Replacement/Cost Reduction.....	16
6.5.3	Arbitration .....	16
<b>7</b>	<b>WAREHOUSING AND DISTRIBUTION.....</b>	<b>16</b>
7.2	Materials .....	17

	7.2.1	WCB and MCB .....	17
	7.2.2	Raw Materials and Resins .....	17
	7.2.3	PRODUCT .....	17
<b>8</b>		<b>QUALITY CONTROL AND MANAGEMENT.....</b>	<b>17</b>
	<b>8.1</b>	Separate Quality Agreement .....	17
	<b>8.2</b>	Validation Services .....	18
	8.2.1	Validation Plan .....	18
	8.2.2	System .....	18
	8.2.3	Process.....	18
	8.2.4	Test Methods .....	18
	<b>8.3</b>	SOPs .....	18
	<b>8.4</b>	Quality Control .....	19
	<b>8.5</b>	Quality Management.....	19
<b>9</b>		<b>TIMETABLE.....</b>	<b>20</b>
<b>10</b>		<b>ORGANIZATIONAL RESPONSIBILITIES .....</b>	<b>20</b>
	<b>10.1</b>	Responsible Personnel .....	20
	<b>10.2</b>	Project Management, Meetings and Planning.....	20
	<b>10.3</b>	NPS' Attendance and Input .....	21
<b>11</b>		<b>FEES AND PAYMENTS.....</b>	<b>22</b>
	<b>11.1</b>	Reservation Fee.....	22
	<b>11.2</b>	Fees for Technology Transfer and Conformance Batches .....	23
	<b>11.3</b>	Commercial Manufacturing Fees.....	23
	<b>11.4</b>	Warehousing Fees.....	23
	<b>11.5</b>	Raw Materials, Resins and Storage Containers .....	23
	<b>11.6</b>	Regulatory Filings.....	23
	<b>11.7</b>	Payments.....	23
<b>12</b>		<b>REGULATORY COMPLIANCE.....</b>	<b>23</b>
	<b>12.1</b>	General.....	23
	<b>12.2</b>	Inspections and Audits .....	24
	12.2.1	Pre-Approval and Manufacturing Audits .....	24
	12.2.2	Pre-Approval and Manufacturing Regulatory Inspections .....	24
	12.2.3	483 Citations and Warning Letters .....	25
	<b>12.3</b>	Regulatory Filings.....	25
<b>13</b>		<b>INTELLECTUAL PROPERTY .....</b>	<b>25</b>
	<b>13.1</b>	Ownership.....	25
	<b>13.2</b>	Prosecution .....	26
<b>14</b>		<b>LEGAL PROCEEDINGS.....</b>	<b>26</b>
	<b>14.1</b>	Infringement of Third Parties' Patents, Product Liability and Indemnification.....	26
<b>15</b>		<b>INSURANCE .....</b>	<b>27</b>
<b>16</b>		<b>CONFIDENTIAL INFORMATION .....</b>	<b>27</b>
<b>17</b>		<b>REPRESENTATIONS AND WARRANTIES.....</b>	<b>28</b>
<b>18</b>		<b>TERM AND TERMINATION.....</b>	<b>28</b>
	<b>18.1</b>	Term .....	28
	<b>18.2</b>	Termination.....	29

18.3	Mitigation .....	30
18.4	Effect of Termination.....	30
19	MISCELLANEOUS.....	31
19.1	Non-Competition .....	31
19.2	Knowledge Sharing with NPS .....	32
19.3	Governing Law and Arbitration.....	32
19.4	Waiver .....	32
19.5	Force Majeure.....	32
19.6	Severability .....	33
19.7	Notice .....	33
19.8	Assignment and Enurement .....	34
19.9	Language.....	34
19.10	Integration.....	34
19.11	Publicity .....	34

## **COMMERCIAL MANUFACTURING AGREEMENT**

B E T W E E N:

**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 18th day of OCTOBER, 2002 (the "EFFECTIVE DATE").

WHEREAS NPS has developed the 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 the proprietary process to manufacture rhPTH and NPS is currently sponsoring Phase III Clinical Trials for osteoporosis with ALX1-11; and

WHEREAS NPS is currently producing rhPTH under contract at Synco BioPartners B.V. at Paasheuvelweg 30, 1105 BJ Amsterdam Zuidoost, the Netherlands ("SYNCO") to be used in the Clinical Trials and early commercial launch of ALX1-11; and

WHEREAS NPS expects to file a New Drug Application (NDA) for the approval for marketing and sale of ALX1-11 in the U.S. (and similar marketing approvals in Europe and elsewhere) and requires quantities of PRODUCT (rhPTH in bulk form as defined below) for formulating into finished drug product for commercial sale targeted to begin in 2005; and

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

WHEREAS BI AUSTRIA desires to manufacture PRODUCT for NPS in accordance with NPS' requirements in order to facilitate NPS' supply of commercial PRODUCT and NPS is desirous of having BI AUSTRIA manufacture PRODUCT for formulating and finishing into ALX1-11 for commercial sale; and

WHEREAS BI AUSTRIA and NPS signed a Letter of Intent dated April 11, 2002 setting out the technology transfer and agreed upon processes for the commercial manufacture of PRODUCT so that BI AUSTRIA and NPS can initiate the technology transfer and begin incurring costs for the commercial manufacture of PRODUCT prior to the execution of this Commercial Manufacturing Agreement and said Letter of Intent has been amended extending its expiration date, with the most recent amendment dated August 30, 2002; and

WHEREAS NPS and BI AUSTRIA have executed a certain Confidential Disclosure Agreement dated May 7, 2001 intended to cover the discussions leading to and under the Letter of Intent as amended and this Commercial Manufacturing 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. 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.
- 1.2. AGREEMENT means this Commercial Manufacturing Agreement herein.
- 1.3. ASSUMED YIELD means the expected YIELD of [\*] per BATCH as of the EFFECTIVE DATE.
- 1.4. BATCH means PRODUCT produced from one fermentation and purification run using a [\*] working volume fermenter.
- 1.5. 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.
- 1.6. COMMERCIAL BATCH means a BATCH intended for clinical use or market supply.
- 1.7. 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 PRODUCT; 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 PRODUCT; NPS' and BI AUSTRIA's manufacturing, business and regulatory plans and strategies; and other data and information designated as confidential.
- 1.8. CONFORMANCE BATCHES means three (3) BATCHES to carry out the process validation and which will form part of regulatory submissions.
- 1.9. DATE AVAILABLE FOR DELIVERY means the date on which NPS requests that PRODUCT (in grams) be available for shipment.
- 1.10. EMEA means the European Medicines Evaluation Agency or any successor agency having similar jurisdiction.

- 1.11. 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 Ingredients and (d) any applicable European laws, regulations or respective guidance documents subsequently established.
- 1.12. FDA means the United States Food and Drug Administration or any successor agency having similar jurisdiction.
- 1.13. 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.
- 1.14. FERMENTATION BATCH means PRODUCT produced using NPS' proprietary WCB/MCB and NPS' proprietary fermentation process from [\*] fermentation run using a [\*] working volume fermenter.
- 1.15. FINAL RELEASE means NPS' release of a BATCH for formulating into drug product pursuant to the PRODUCT SPECIFICATIONS and GMP.
- 1.16. GMP means current Good Manufacturing Practices pursuant to FDA GMP and EUROPEAN GMP.
- 1.17. IMPLEMENTATION BATCHES mean at least the first three (3) BATCHES of PRODUCT produced by BI AUSTRIA in a [\*] working volume fermenter as provided in paragraph 5.4.
- 1.18. 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.
- 1.19. MANUFACTURER RELEASE means BI AUSTRIA's release of a BATCH for further processing.
- 1.20. MASTER BATCH RECORD means the master production instructions for manufacture of a BATCH.
- 1.21. MCB means NPS' master cell bank containing the host cell (with the plasmid incorporated therein) for fermentation of the PRODUCT. The MCB is used to generate the WCB.
- 1.22. METHOD TRANSFER SERVICES mean services provided by BI AUSTRIA in accordance with paragraph 5.5.
- 1.23. NDA means a new drug application in the U.S. FDA.

- 1.24. PARTY and PARTIES means NPS or BI AUSTRIA, or both, as applicable.
- 1.25. PRODUCT means purified bulk recombinant human parathyroid hormone (1-84) produced using NPS' proprietary WCB/MCB and NPS' proprietary process.
- 1.26. PRODUCT SPECIFICATIONS means the SPECIFICATIONS which are attached at Exhibit F.
- 1.27. QUALITY AGREEMENT means the agreement on all quality procedures and aspects related to the PRODUCT and which will be negotiated and executed by the PARTIES.
- 1.28. RAW MATERIAL means materials, reagents and solvents needed for the production of PRODUCT.
- 1.29. RAW MATERIAL SPECIFICATIONS means SPECIFICATIONS for RAW MATERIALS.
- 1.30. RESERVE CAPACITY means the maximum quantity of PRODUCT NPS can request from BI AUSTRIA in a given year based on a maximum number of BATCHES, subject to agreement otherwise by the PARTIES, as provided for in paragraph 6.4.2.1.
- 1.31. SMALL SCALE BATCHES means the production of PRODUCT in [\*] working volume fermentation batches pursuant to paragraph 5.2.
- 1.32. 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.
- 1.33. SPECIFICATIONS means tests, references to analytical procedures, appropriate acceptance criteria that are numerical limits, ranges or other criteria for which the RAW MATERIALS, PRODUCT, intermediates, or process of making the PRODUCT, must conform to in order for the PRODUCT to be acceptable for its intended use. Types of SPECIFICATIONS include but are not limited to PRODUCT SPECIFICATIONS, MASTER BATCH RECORD, RAW MATERIAL SPECIFICATIONS and in-process SPECIFICATIONS.
- 1.34. STABILITY STUDIES mean all studies necessary to assess the stability characteristics of PRODUCT which shall be used in determining appropriate storage conditions and expiration dates.
- 1.35. 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 PRODUCT will consistently meet its pre-determined and expected results.
- 1.36. VALIDATION SERVICES means any VALIDATION services required of BI AUSTRIA in the manufacture of PRODUCT.
- 1.37. WCB means NPS' working cell bank containing the host cell (with the plasmid incorporated therein) for fermentation of the PRODUCT. The WCB is generated from MCB.
- 1.38. YIELD means grams of PRODUCT produced per BATCH.



2. PURPOSE AND SCOPE

- 2.1. This AGREEMENT is intended to provide the structure under which the long-term commercial manufacturing of PRODUCT by BI AUSTRIA for NPS shall be conducted including the technology transfer to BI AUSTRIA from NPS and NPS' contracted third party SYNCO.
- 2.2. Each of the PARTIES will in good faith and in accordance with the project timelines as set out in Exhibit D initiate and complete the process of technology transfer and the negotiation, documentation, and execution of a QUALITY AGREEMENT prior to the initiation of COMMERCIAL BATCHES covering quality expectations, performance standards, testing, SOPs, and release aspects for the PRODUCT.
- 2.3. The PARTIES expect to use a team approach and NPS expects fully to support the technology transfer effort and to benefit from any gain in YIELD and reduction in associated costs of production of PRODUCT 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 PRODUCT at BI AUSTRIA shall be successful as contemplated in this paragraph 2.4. In particular, based on the [\*] working volume batch process at SYNCO with: fermentation expression rate of about [\*] fermentation broth; overall yield from a batch of approximately [\*] of PRODUCT (wherein one fermentation batch translates into one purification batch); the PARTIES have assumed that BI AUSTRIA can scale this current process up to a [\*] working volume batch scale with an overall yield of approximately [\*] of PRODUCT. A [\*] yield of purified bulk and the current contemplated costs and cost structure at BI AUSTRIA form the basis for the calculations in the Sliding Prices, Exhibit E. Final pricing will be established based on average and repetitive YIELD data early in the life of commercial production and so that the PARTIES will share the benefits or burdens arising from greater or lesser YIELDS, respectively.
- 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: Rolling Forecast Model
  - Exhibit D: Timetable and Payment Schedule for Technology Transfer
  - Exhibit E: Price Calculations and Sliding Price Model
  - Exhibit F: PRODUCT SPECIFICATIONS
  - Exhibit G: Critical Raw Materials and Storage Containers
  - Exhibit H: Documents BI AUSTRIA will provide in English
  - Exhibit I: Description of facilities for PTH production and testing
  - Exhibit J: Documents to be reviewed and approved by NPS
- 2.6. The Letter of Intent is deemed to be merged with the 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 PRODUCT during technology transfer and COMMERCIAL BATCHES in accordance with this AGREEMENT.

##### Chromatographic Columns

STEP	COLUMN SIZE [mm][*]
[*]	[*]
[*]	[*]
[*]	[*]
[*]	[*]
[*]	[*]

- 3.1.1.2. If other equipment is needed specifically for the production or Quality Control of PRODUCT, 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 PRODUCT, 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 the PRODUCT by BI AUSTRIA; termination of this AGREEMENT; 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 PRODUCT. NPS shall pay BI AUSTRIA the costs for qualification of the PRODUCT-specific equipment.

- 3.1.3.2. BI AUSTRIA is entitled to charge to NPS a one-time surcharge of [\*] percent ([\*]%) of the purchase price of PRODUCT-dedicated equipment described above in paragraphs 3.1.1.1 and 3.1.1.2 for purchasing, installing, calibrating, insuring and maintaining such PRODUCT-dedicated equipment during the term of the AGREEMENT. BI AUSTRIA shall be solely responsible for (a) reasonably maintaining the PRODUCT-dedicated equipment, (b) repairing the PRODUCT-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 PRODUCT-dedicated equipment. In the event that despite all reasonable maintenance and ordinary and intended use of such PRODUCT-dedicated equipment an irreparable damage occurs, it will be NPS' responsibility to replace such PRODUCT-dedicated equipment; provided, however, that BI AUSTRIA shall be solely responsible for costs to replace or repair any PRODUCT-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 PRODUCT-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 and WCB to be used in production of the PRODUCT by BI AUSTRIA in sufficient quantities and on a timely basis for the scheduled production of PRODUCT at BI AUSTRIA.
- 3.2.1.2. BI AUSTRIA shall conduct incoming tests for viability, identity, plasmid retention and purity to confirm that the MCB/WCB is satisfactory for the manufacture of PRODUCT. BI AUSTRIA will notify NPS if the MCB/WCB is not satisfactory according to the incoming tests and can not be used for the manufacture of PRODUCT. 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.
- 3.2.1.3. 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 Exhibits 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 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 PRODUCT under this 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 AGREEMENT shall be destroyed or returned to NPS at NPS' direction.
- 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 PRODUCT 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 [\*], 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, BI AUSTRIA shall validate and NPS shall pay for such services in accordance with paragraph 11.2.

- 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.

4. PROCESS

- 4.1. NPS shall provide BI AUSTRIA with NPS' proprietary process for manufacturing PRODUCT 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.

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 [\*] 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 PRODUCT 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 commercial manufacture of PRODUCT as set out in the AGREEMENT.
- 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 commercial phase. It is expected that NPS personnel will be available and present as needed during the process transfer, SMALL SCALE BATCHES and CONFORMANCE BATCHES.
- 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 without limitation, the project manager of each of NPS and BI AUSTRIA, with the intention to view the production and/or production facilities of PRODUCT 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, CONFORMANCE BATCHES and further COMMERCIAL BATCHES of PRODUCT, including without limitation 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 [\*] working volume batches in the BI AUSTRIA Process Engineering Suite.<sup>1</sup>

---

<sup>1</sup> 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.

- 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 and NPS shall conduct drug substance release testing on the purified SMALL SCALE BATCHES. The release testing shall be conducted in accordance with the PRODUCT SPECIFICATIONS.
- 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 the PRODUCT SPECIFICATIONS, the PARTIES will come to an agreement on steps forward.
- 5.2.5. The PRODUCT from the SMALL SCALE BATCHES shall not be used in humans.
- 5.3. FERMENTATION BATCHES
  - 5.3.1. BI AUSTRIA shall produce [\*] FERMENTATION BATCHES following acceptance by NPS of the SMALL SCALE BATCHES, unless otherwise agreed to by the PARTIES. These [\*] FERMENTATION BATCHES will undergo QC testing according to an agreed upon sampling plan (which will include yield determinations), collection of cleaning data (change over) and batch documentation. The PARTIES shall consider the yield of the FERMENTATION BATCHES and if the yields are not as expected based on the assumptions made pursuant to paragraph 2.4, the PARTIES will come to an agreement on steps forward.
- 5.4. IMPLEMENTATION BATCHES
  - 5.4.1. BI AUSTRIA will produce [\*] working volume IMPLEMENTATION BATCHES, unless otherwise agreed to by the PARTIES. BI AUSTRIA shall initiate production of the IMPLEMENTATION BATCHES in accordance with the timeline (Exhibit D) following production of the FERMENTATION BATCHES, unless otherwise agreed to by the PARTIES.
  - 5.4.2. 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 PRODUCT.
  - 5.4.3. 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.
  - 5.4.4. 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.
  - 5.4.5. BI AUSTRIA shall also conduct release testing of the IMPLEMENTATION BATCHES in accordance with the PRODUCT SPECIFICATIONS and shall provide NPS with the BATCH PRODUCTION RECORDS for each of the IMPLEMENTATION BATCHES.
  - 5.4.6. 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 the PRODUCT SPECIFICATIONS the PARTIES will come to an agreement on steps forward.
  - 5.4.7. The PRODUCT from the IMPLEMENTATION BATCHES shall not be used in humans.

5.5. METHOD TRANSFER SERVICES

- 5.5.1. 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 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.

6. COMMERCIAL MANUFACTURING

- 6.1. All PRODUCT manufactured by BI AUSTRIA and supplied to NPS, or to NPS' representatives, agents or formulation contract manufacturers, for clinical use or for market supply, shall be manufactured, released, stored and delivered in accordance with the SPECIFICATIONS (in particular, the PRODUCT SPECIFICATIONS and the MASTER BATCH RECORDS), QUALITY AGREEMENT and GMP and all applicable laws, regulations and ordinances as required in the jurisdiction. Following completion of process VALIDATION, all PRODUCT manufactured by BI AUSTRIA for clinical use or market supply shall be suitable for formulation into final drug product to be used in humans.
- 6.2. 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 PRODUCT shall be carried out in BATCHES as defined herein.
- 6.3. CONFORMANCE BATCHES
- 6.3.1. BI AUSTRIA shall manufacture CONFORMANCE BATCHES which shall be at least [\*] BATCHES, in accordance with the timeline (Exhibit D) unless otherwise agreed to by the PARTIES.
- 6.3.2. The PRODUCT produced in the CONFORMANCE BATCHES is intended for clinical use or market supply by NPS for use in humans.
- 6.3.3. Each CONFORMANCE BATCH shall undergo in-process control testing, Quality Control and testing according to the PRODUCT SPECIFICATIONS using the validated methods. NPS will conduct any release testing for which methods are not transferred to BI AUSTRIA. If the CONFORMANCE BATCHES do not meet PRODUCT SPECIFICATIONS, the PARTIES will come to an agreement on steps forward. The CONFORMANCE BATCHES will be documented in the BATCH PRODUCTION RECORDS.
- 6.4. LONG TERM COMMERCIAL MANUFACTURE OF PRODUCT
- 6.4.1. Initiation of Commercial Manufacture of PRODUCT
- 6.4.1.1. If possible, and as agreed to by NPS, BI AUSTRIA shall manufacture PRODUCT beginning no later than the first quarter of 2004 for commercial sale by NPS or NPS authorised agents, which commercial sale is currently planned to commence on or about the second quarter of 2005.

#### 6.4.2. Capacity

##### 6.4.2.1. RESERVE CAPACITY

6.4.2.1.1. The RESERVE CAPACITY as of the EFFECTIVE DATE is approximately [\*] based on [\*] COMMERCIAL BATCHES (assuming each BATCH yields [\*] annually beginning in 2005. However, NPS understands that BI AUSTRIA is only prepared to commit to [\*] COMMERCIAL BATCHES in 2004; hence, the RESERVE CAPACITY in 2004 is approximately [\*] based on [\*] COMMERCIAL BATCHES (assuming each BATCH yields [\*]).

6.4.2.1.2. On or before January 1, 2005, NPS wishes to have the option of changing the RESERVE CAPACITY which change will be effective January 1, 2007. Hence, by request from NPS to BI AUSTRIA, which request shall be made by September 1, 2004, NPS and BI AUSTRIA shall endeavour to come to a mutual agreement on a new RESERVE CAPACITY and associated Rolling Forecast in an amount not greater than [\*] COMMERCIAL BATCHES annually and not less than [\*] COMMERCIAL BATCHES annually, which will be effective January 1, 2007. At any time prior to January 1, 2005, if the possibility arises that BI AUSTRIA will not be able to provide up to [\*] COMMERCIAL BATCHES annually beginning in 2007, BI AUSTRIA shall warn NPS and at NPS' request NPS and BI AUSTRIA shall in good faith negotiate on or before January 1, 2005 to be effective on or before January 1, 2007 for any desired increase in capacity up to the maximum [\*] COMMERCIAL BATCHES annually. Notwithstanding the Rolling Forecast provisions herein, the mutually agreed to new RESERVE CAPACITY will be effective on January 1, 2007 and the Rolling Forecast will be amended accordingly effective January 1, 2007.

##### 6.4.2.2. Rolling Forecast

6.4.2.2.1. The details and timeline for the commercial manufacture of PRODUCT shall be done in accordance with the Rolling Forecast (Exhibit C) and Sliding Price Model (Exhibit E).

6.4.2.2.2. The first three-year forecast is to be submitted to BI AUSTRIA by NPS within a calendar month of the signing of this AGREEMENT for 2004-2006 with forecasting to then be provided by NPS on a quarterly basis beginning on January 1, 2003 as set out in Exhibit C.

#### 6.4.3. Facilities

6.4.3.1. BI AUSTRIA will be manufacturing PRODUCT 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 PRODUCT are set out in Exhibit I attached.

6.4.3.2. BI AUSTRIA's facilities will have, and BI AUSTRIA will continuously maintain, all required authorisations and permits necessary for the manufacture of PRODUCT for commercial sale for use in humans, as more particularly detailed in paragraph 12.1.

6.4.3.3. 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.



6.4.4. Establishment of Price and Expected YIELD

6.4.4.1. The current predicted production of PRODUCT 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 the PRODUCT 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 for the IMPLEMENTATION BATCHES, the CONFORMANCE BATCHES and COMMERCIAL BATCHES. Price adjustments and the basis for them will be mutually agreed to. Based on the assumptions currently in place, the price per BATCH is readily computable and is, for example, [\*] Euros ([\*] Euros per gram x [\*] grams) based on a [\*] BATCH annual order and a [\*] BATCH RESERVE CAPACITY.

6.4.4.2. NPS shall pay for PRODUCT on a Euro/gram basis using two computations: 1. 2004: The 2004 Payable Price per gram for all 2004 delivered COMMERCIAL BATCHES; and 2. 2005 and Beyond: The Annual Payable Price per gram. These computations are set out below in paragraphs 6.4.4.2.1 and 6.4.4.2.2.

6.4.4.2.1. 2004: The 2004 Payable Price per gram for all 2004 delivered COMMERCIAL BATCHES

The Payable Price per gram for all grams of PRODUCT delivered prior to year end 2004:

shall be computed from the first [\*] COMMERCIAL BATCHES produced before year end 2004 (assumed to be at least [\*] CONFORMANCE BATCHES as provided in paragraph 6.4.1 and not greater than [\*] COMMERCIAL BATCHES for a total of [\*] COMMERCIAL BATCHES) and

shall be computed on the basis of Payable Price per gram of PRODUCT as follows:

Payable Price per gram is computed as the total attributable cost for said first [\*] COMMERCIAL BATCHES divided by the total grams of PRODUCT delivered by BI AUSTRIA from said first [\*] COMMERCIAL BATCHES;

where the "total attributable cost" is determined in the manner reflected in paragraph 6.4.4.1 and Exhibit E.

Notwithstanding the above:

the price and payment for the CONFORMANCE BATCHES will be determined as set out in Exhibit D and will not be altered by the above computation; and

the Payable Price per gram for the first [\*] COMMERCIAL BATCHES shall be determined using the above formula using a computation based on the CONFORMANCE BATCHES instead of the first [\*] COMMERCIAL BATCHES.

6.4.4.2.2. 2005 and Beyond: The Annual Payable Price per gram

The Annual Price per gram shall be freshly computed for each calendar year of the AGREEMENT beginning for the year 2005 as follows:

The Annual Payable Price per gram = [\*]

where [\*] per gram which is the Payable Price per gram in paragraph 6.4.4.2.1 above; and

where [\*] of all COMMERCIAL BATCHES produced in the prior year divided by [\*] of PRODUCT delivered by BI AUSTRIA from said final [\*] of all COMMERCIAL BATCHES

where the "total attributable cost" is determined in the manner reflected in paragraph 6.4.4.1 and Exhibit E.

provided that the Annual Payable Price for any year shall [\*] (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.

6.4.4.3. If the forecasted quantity of PRODUCT is less than [\*], the price in Euro/gm established under paragraph 6.4.4.2 will be adjusted using the Sliding Scale factors set out in Exhibit E.

6.4.5. Documentation

6.4.5.1. BI AUSTRIA will retain complete, accurate and authentic documents and records created by BI AUSTRIA for each COMMERCIAL BATCH, 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 or agent of NPS to be designated by NPS from time to time.

6.4.5.2. During the initial manufacture of COMMERCIAL BATCHES there will be a qualification period in which NPS will qualify BI AUSTRIA as a manufacturer of PRODUCT. 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 approximately the first [\*] COMMERCIAL BATCHES. 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 than the DATE AVAILABLE FOR DELIVERY the following documents for each COMMERCIAL 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. The COA will also list (i) the PRODUCT release Quality Control tests performed by BI AUSTRIA and/or by contract testing laboratories, (ii) the PRODUCT SPECIFICATIONS and (iii) actual test results.

- (ii) COC.
  - (iii) Deviation Summary Report for each lot and photocopies of major deviation reports/investigations associated with the lot.
- 6.4.5.3. 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.
- 6.4.5.4. In addition to the documents BI AUSTRIA shall provide under paragraph 6.4.5.2, BI AUSTRIA shall provide a Trend Analysis of the process which will include in-process data and results of tests reported in the COA for the SMALL SCALE BATCHES and the IMPLEMENTATION BATCHES. All data on the CONFORMANCE BATCHES will be provided in the respective validation documentation. After market launch of ALX1-11, the Trend Analysis shall be provided in the Annual Product Review.
- 6.4.6. Packaging/Labelling
  - 6.4.6.1. BI AUSTRIA shall package and label the PRODUCT in accordance with the applicable MASTER BATCH RECORD and GMP.
- 6.4.7. Release
  - 6.4.7.1. BI AUSTRIA is responsible for the MANUFACTURER RELEASE. NPS is responsible for the FINAL RELEASE.
  - 6.4.7.2. BI AUSTRIA shall test each COMMERCIAL BATCH and provide the MANUFACTURER RELEASE as provided for in paragraph 6.4.5.2 for each COMMERCIAL BATCH by the earlier of: [\*] from the manufacture of PRODUCT; 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 pursuant to paragraph 6.4.5.1 at the time of the MANUFACTURER RELEASE of each COMMERCIAL BATCH. The review and approval of BATCH PRODUCTION RECORDS is described in paragraph 8.5.2 and will be detailed in the QUALITY AGREEMENT.
- 6.4.8. Shipment of Product
  - 6.4.8.1. All PRODUCT (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 the PRODUCT, and for paying for all customs formalities as well as duties, taxes, and other official charges payable upon importation.
- 6.4.9. Ownership and Insurance Liabilities
  - 6.4.9.1. 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 for the BATCH. NPS shall obtain the appropriate insurance on the BATCH when the BATCH is shipped from BI AUSTRIA facilities.

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

## 6.5. DISPUTE RESOLUTION FOR FAILED BATCHES

### 6.5.1. Confirmatory Third Party Testing/Review GMP Quality

- 6.5.1.1. If NPS determines PRODUCT does not meet PRODUCT SPECIFICATIONS, then NPS and/or BI AUSTRIA shall re-test the respective samples. If the PARTIES continue to disagree as to whether or not the said quantity of PRODUCT meets PRODUCT SPECIFICATIONS, or is GMP grade, and suitable for FINAL RELEASE, then a qualified independent party, acceptable to both PARTIES, will determine if the PRODUCT meets SPECIFICATIONS, is GMP grade and suitable for FINAL RELEASE. 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 the PRODUCT is not suitable for FINAL RELEASE. If the PRODUCT is determined to be suitable for FINAL RELEASE, then NPS shall bear all costs of the third party evaluation.

### 6.5.2. Replacement/Cost Reduction

- 6.5.2.1. BI AUSTRIA shall replace, with no additional charge, using commercially reasonable efforts, any quantity of PRODUCT 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 PRODUCT within a reasonable period of time, not to exceed sixty (60) days. If such PRODUCT is not replaced as provided for in this paragraph, NPS shall receive a full refund for any payment made for such PRODUCT. (Refunds shall be paid by BI AUSTRIA within thirty (30) days of the date of an invoice from NPS.)

### 6.5.3. Arbitration

- 6.5.3.1. Any dispute under paragraphs 6.5.1. and 6.5.2. 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.

## 7.2. MATERIALS

### 7.2.1. WCB and MCB

- 7.2.1.1. 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.

### 7.2.2. RAW MATERIALS and Resins

- 7.2.2.1. BI AUSTRIA shall warehouse as necessary the RAW MATERIALS and resins for use in the production of PRODUCT. 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).

### 7.2.3. PRODUCT

- 7.2.3.1. BI AUSTRIA shall warehouse PRODUCT produced in the SMALL SCALE BATCHES and the IMPLEMENTATION BATCHES as requested by NPS. NPS shall decide on either disposing, or shipping such PRODUCT within [\*] months of the release testing by BI AUSTRIA and NPS.
- 7.2.3.2. BI AUSTRIA shall warehouse PRODUCT produced in accordance with this AGREEMENT. BI AUSTRIA shall warehouse PRODUCT [\*] up to the DATE AVAILABLE FOR DELIVERY plus a further [\*] months provided BI AUSTRIA's obligations under paragraphs 6.4.5.2 and 6.4.7 for MANUFACTURER RELEASE have been met. It is currently intended by the PARTIES that the PRODUCT 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 as adapted by NPS for formulation of PRODUCT into its final drug product for commercial sale.
- 7.2.3.3. PRODUCT not subject to FINAL RELEASE by NPS shall be properly quarantined from PRODUCT which has undergone FINAL RELEASE.
- 7.2.3.4. NPS shall specify the DATE(S) AVAILABLE FOR DELIVERY on the Purchase Order for PRODUCT. NPS shall submit a Purchase Order for PRODUCT [\*] months in advance of the quarter for which it has been forecasted. BI AUSTRIA shall deliver on a timely basis the released PRODUCT in accordance with the Purchase Order and the AGREEMENT herein.
- 7.2.3.5. 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 6.4.5.2 and 6.4.7.

## 8. QUALITY CONTROL AND MANAGEMENT

### 8.1. SEPARATE QUALITY AGREEMENT

- 8.1.1. Each of the PARTIES will in good faith expeditiously initiate the negotiation, documentation, and execution of a QUALITY AGREEMENT prior to the initiation of production of COMMERCIAL BATCHES.
- 8.2. VALIDATION SERVICES
  - 8.2.1. Validation Plan
    - 8.2.1.1. 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. 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.
  - 8.2.2. System
    - 8.2.2.1. BI AUSTRIA shall validate, if not currently validated, relevant for the manufacture of PRODUCT. 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.
  - 8.2.3. Process
    - 8.2.3.1. BI AUSTRIA shall validate processes critical to the manufacturing of PRODUCT 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.
  - 8.2.4. Test Methods
    - 8.2.4.1. BI AUSTRIA shall validate those test methods which control critical characteristics or processes in the manufacture of PRODUCT, including without limitation YIELD, purity and bioburden.
- 8.3. SOPs
  - 8.3.1. BI AUSTRIA shall have established, or establish, SOPs for the manufacture of PRODUCT 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.

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

8.3.3. BI AUSTRIA shall establish, maintain and implement SOPs for all warehousing, including warehousing of the MCB/WCB, RAW MATERIALS and resins, and PRODUCT.

8.3.4. Unless otherwise provided for in English as set out in paragraph 6.4.5.3, SOPs shall be in German. BI AUSTRIA shall make SOPs available for review by NPS on-site.

#### 8.4. QUALITY CONTROL

8.4.1. 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 PRODUCT. The Quality Control unit shall have adequate facilities for conducting the necessary tests.

8.4.2. 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.

#### 8.5. QUALITY MANAGEMENT

8.5.1. 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.

8.5.2. 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.

- 8.5.3. BI AUSTRIA 's Quality Management unit shall also ensure that BI AUSTRIA 's facilities and manufacturing operations for PRODUCT 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 PRODUCT.
- 8.5.4. 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 PRODUCT.
- 8.5.5. 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.

## 9. TIMETABLE

- 9.1. The PARTIES have agreed to a timeline as set out in Exhibit D for the Technology Transfer, CONFORMANCE BATCHES, initiation of commercial manufacturing and establishment of Quality Control and Quality Management.
- 9.2. 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.
- 9.3. Each PARTY acknowledges and agrees that it shall perform in a timely manner all of its obligations in this AGREEMENT.

## 10. ORGANIZATIONAL RESPONSIBILITIES

### 10.1. RESPONSIBLE PERSONNEL

- 10.1.1. Each PARTY shall appoint a Project Manager to the Technology Transfer and the commercial manufacture of PRODUCT.
- 10.1.2. All BI AUSTRIA and NPS personnel involved in the manufacture of PRODUCT 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; commercial production; and warehousing.

### 10.2. PROJECT MANAGEMENT, MEETINGS AND PLANNING



- 10.2.1. The day-to-day operational responsibilities of the PARTIES with respect to the Technology Transfer and the manufacture of PRODUCT under this AGREEMENT shall be overseen by the Project Team. The Project Team shall be responsible for deciding operational and scientific issues.
- 10.2.2. 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 members of the Project Team will be appointed prior to or shortly after the EFFECTIVE DATE.
- 10.2.3. There will be regularly scheduled meetings of the Project Team throughout the Technology Transfer phase and continuing at least until [\*] after the first [\*] COMMERCIAL BATCHES, 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.
- 10.2.4. The PARTIES will come to an agreement on the need for regularly scheduled meetings beginning in [\*] 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 PRODUCT or the scheduling of the production for PRODUCT and in particular if a DELIVERY DATE FOR PRODUCT potentially will not be met by BI AUSTRIA.
- 10.2.5. 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.
- 10.2.6. 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.
- 10.2.7. 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.
- 10.3. NPS' ATTENDANCE AND INPUT
  - 10.3.1. NPS personnel shall be in attendance during the Technology Transfer as set out in paragraph 5.1.2.
  - 10.3.2. NPS personnel may be on-site during FDA inspections concerning the PRODUCT or other regulatory inspections concerning the PRODUCT, at NPS' discretion. Any questions which an inspector may have concerning the manufacturing of the PRODUCT shall be answered by BI AUSTRIA unless the inspector directs the question to NPS to answer. Any questions concerning the further processing of the PRODUCT, or marketing or use of the finished drug ALX 1-11, shall be answered by NPS.

- 10.3.3. NPS personnel may be in attendance during commercial manufacture of PRODUCT 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.

## 11. FEES AND PAYMENTS

### 11.1. RESERVATION FEE

- 11.1.1. A reservation fee for the runs currently scheduled for 2004, 2005 and 2006 shall be paid by NPS to BI AUSTRIA. The reservation fee is to be creditable against commercial production costs (beginning with NPS' acceptance of first production shipments) and against any Termination Penalty which may become payable. The reservation fee shall be [\*] Euros and shall be paid as follows:

One Initial Installment on Signing  
of this AGREEMENT

– [\*] Euros

[\*] Installments of  
[\*] Euros each

– beginning on the EFFECTIVE DATE  
and thereafter on the first day of each  
calendar quarter ending Oct 1, 2004

### 11.2. FEES FOR TECHNOLOGY TRANSFER AND CONFORMANCE BATCHES

- 11.2.1. The costs and fee schedule for the technology transfer and the CONFORMANCE BATCHES are set out in Exhibit D. Costs for RAW MATERIALS, components and resins for the Technology Transfer and for the CONFORMANCE BATCHES are not included in the fees but shall be invoiced separately in accordance with paragraph 11.5.
- 11.2.2. NPS shall pay a cost of [\*] Euro for delivery and release of PRODUCT produced in the SMALL SCALE BATCHES at the [\*] working volume scale and in the [\*] IMPLEMENTATION BATCHES. [\*] percent ([\*]%) of this cost has already been paid as of the signing of the Letter of Intent. The remainder shall be paid on timely receipt of an invoice and upon acceptance by NPS of the final BATCH of the three IMPLEMENTATION BATCHES, such acceptance not to be unreasonably delayed or declined.
- 11.2.3. NPS shall pay a purchase price of [\*] Euro for the [\*] CONFORMANCE BATCHES. [\*] percent ([\*]%) of this cost shall be paid on initiation of the first CONFORMANCE BATCH and [\*] percent ([\*]%) shall be paid on timely receipt of an invoice by NPS and such invoice shall be issued by BI AUSTRIA promptly upon NPS' FINAL RELEASE of the final BATCH of the [\*] CONFORMANCE BATCHES, such FINAL RELEASE shall not be unreasonably delayed or declined.
- 11.2.4. NPS shall pay a cost of [\*] Euros for the FERMENTATION BATCHES. [\*] percent ([\*]%) of this cost shall be paid on initiation and [\*] percent ([\*]%) shall be paid on timely receipt of an invoice to be issued by BI AUSTRIA promptly upon conclusion of said FERMENTATION BATCHES.
- 11.2.5. NPS shall pay for METHOD TRANSFER SERVICES which are currently estimated to be about [\*] Euro, upon receipt of a timely invoice. These Services will be agreed to promptly

following the signing of the AGREEMENT and will be addressed in separate written proposals as set out in paragraph 5.5.1.

- 11.2.6. 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 and shall be paid in accordance with Exhibit D and paragraph 11.7.

### 11.3. COMMERCIAL MANUFACTURING FEES

- 11.3.1. The cost for GMP commercial manufacture, other than the CONFORMANCE BATCHES shall be determined in accordance with paragraph 6.4.4 and Exhibit E.

- 11.3.2. For the manufacture and delivery of each COMMERCIAL BATCH, NPS shall pay BI AUSTRIA as specified in paragraph 6.4.4 and in Exhibit E. For each COMMERCIAL BATCH manufactured by BI AUSTRIA, BI AUSTRIA shall invoice NPS on or after BI AUSTRIA has completed its obligations pursuant to paragraphs 6.4.5 and 6.4.7 in order to have PRODUCT available for shipment as of the DATE AVAILABLE FOR DELIVERY.

### 11.4. WAREHOUSING FEES

- 11.4.1. The PARTIES shall agree on the cost to be charged to NPS by BI AUSTRIA for warehousing.

### 11.5. RAW MATERIALS AND RESINS, AND STORAGE CONTAINERS

- 11.5.1. BI AUSTRIA shall invoice NPS for the RAW MATERIALS, components and resins used during the technology transfer and CONFORMANCE BATCHES 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 [\*] Euro per resin and [\*] Euro per raw material.

- 11.5.2. BI AUSTRIA shall invoice NPS for the cost of the Storage Containers and for VALIDATION thereof.

### 11.6. REGULATORY FILINGS

- 11.6.1. NPS shall pay for BI AUSTRIA's work pursuant to paragraph 12.3 for the regulatory filing, particularly the Chemistry, Manufacturing and Controls (CMC) section thereof, at a mutually agreeable and reasonable rate.

### 11.7. PAYMENTS

- 11.7.1. All payments by NPS to BI AUSTRIA shall be made within [\*] days of the submission of the appropriate invoice by BI AUSTRIA detailing the matter to which the invoice applies and the price in Euros.

## 12. REGULATORY COMPLIANCE

### 12.1. GENERAL

- 12.1.1. BI AUSTRIA will exercise all reasonable skill, care and diligence customary in the industry in the performance of its duties under this AGREEMENT and in accordance with the requirements of EUROPEAN GMP and FDA GMP. BI AUSTRIA shall obtain and maintain all permits required under Austrian legislation in order to manufacture PRODUCT. BI AUSTRIA will inform NPS of all permits filed under Austrian legislation or otherwise and their status with respect to approval.
- 12.1.2. 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 PRODUCT and its manufacture in BI AUSTRIA's facility. BI AUSTRIA shall also co-operate with similar filings in other countries at NPS' expense.
- 12.1.3. 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 the PRODUCT. BI AUSTRIA shall notify NPS of any communication with the FDA (or other such agency) concerning the PRODUCT or impacting the PRODUCT and shall co-operate with NPS in the scheduling of any planned inspection concerning the PRODUCT. NPS shall have the right to be on-site during such inspections.
- 12.2. INSPECTIONS AND AUDITS
  - 12.2.1. Pre-Approval and Manufacturing Audits
    - 12.2.1.1. NPS or its designated representatives may audit the Facilities for the purpose of reviewing manufacturing of PRODUCT, Quality Management, Quality Control and VALIDATION and for determining compliance with GMP and the SPECIFICATIONS during the term of this AGREEMENT.
    - 12.2.1.2. 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 12.2.1.1. All NPS representatives who are not NPS personnel 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 PRODUCT.
  - 12.2.2. Pre-Approval and Manufacturing Regulatory Inspections
    - 12.2.2.1. 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.

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

12.2.3. 483 Citations and Warning Letters

12.2.3.1. 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 the PRODUCT (or similar European EMEA notifications) or if BI AUSTRIA receives notification of any planned or unplanned FDA inspection directed or applicable to the PRODUCT during the term of this AGREEMENT.

12.2.3.2. BI AUSTRIA shall take immediate steps to address and correct any/all concerns raised by the FDA (EMA, 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, EMA or other regulatory authority, with NPS' input and provided NPS pays for such modifications which are process or PRODUCT 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.

12.3. REGULATORY FILINGS

12.3.1. 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 the PRODUCT 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.

13. INTELLECTUAL PROPERTY

13.1. OWNERSHIP

13.1.1. All INTELLECTUAL PROPERTY generated pursuant to this AGREEMENT 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 PRODUCT or ALX-0600 (a 1-33 amino acid glucagon-like peptide-2 analog) or the production, use, or sale thereof, then BI AUSTRIA hereby grants to NPS an exclusive license from BI AUSTRIA to the INTELLECTUAL PROPERTY for production, use or sale of PRODUCT or ALX-0600 (a 1-33 amino acid glucagon-like peptide-2 analog), which license is royalty free, worldwide sublicenseable, and paid up.

13.1.2. 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 PRODUCT or ALX-0600 or the exclusive production, use or sale of any of them 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 PRODUCT 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).

## 13.2. PROSECUTION

13.2.1. NPS shall be solely responsible for the filing, prosecution and maintenance of all INTELLECTUAL PROPERTY which is owned by NPS pursuant to paragraph 13.1.1(b). 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 13.1.1(c) if such INTELLECTUAL PROPERTY is solely related to PRODUCT or ALX-0600 or the exclusive production, use or sale of any of them, including costs associated therewith.

13.2.2. BI AUSTRIA shall be responsible for the filing, prosecution and maintenance of all INTELLECTUAL PROPERTY which is owned by BI AUSTRIA pursuant to paragraph 13.1.1(a). 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 PRODUCT 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 PRODUCT or ALX-0600 or the production, use or sale of any of them and hence subject to the exclusive license to NPS as described above in paragraph 13.1.1, 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.

## 14. LEGAL PROCEEDINGS

### 14.1. INFRINGEMENT OF THIRD PARTIES' PATENTS, PRODUCT LIABILITY AND INDEMNIFICATION

14.1.1. Subject to paragraph 14.1.2, 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 PRODUCT 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 PRODUCT 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.

14.1.2. 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 in connection with this AGREEMENT.

- 14.1.3. 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.
- 14.1.4. 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 [\*] pursuant to this AGREEMENT.

## 15. INSURANCE

- 15.1. Each PARTY shall maintain adequate liability insurance in such amounts and with such scope of coverage as is adequate to cover each PARTY's respective potential liabilities to the other PARTY under this AGREEMENT. Either PARTY may any time after the EFFECTIVE DATE request the other PARTY to provide a certificate of insurance showing the respective PARTY's liability insurance.

## 16. CONFIDENTIAL INFORMATION

- 16.1. A PARTY receiving CONFIDENTIAL INFORMATION from the other PARTY or developing such information hereunder 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 PRODUCT for NPS by BI AUSTRIA according to this AGREEMENT, 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 this 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 the PARTIES entered into a Confidential Disclosure Agreement governing the disclosure and use of information concerning the matters addressed in this AGREEMENT. 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 the PRODUCT 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 AGREEMENT for producing PRODUCT.

- 17.2. BI AUSTRIA represents that after completion of the process validation the manufacture of PRODUCT (including the process, plant, equipment and personnel) and the storage/release/delivery of PRODUCT, RAW MATERIALS and resins and WCB and MCB will all be done in accordance with the relevant SPECIFICATIONS and GMP.

- 17.3. BI AUSTRIA represents that it shall maintain all necessary permits and authorisations as required under applicable local or state laws and under FDA GMP and European GMP in order to manufacture PRODUCT.

- 17.4. BI AUSTRIA represents that its facilities which will be used to commercially manufacture PRODUCT 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 the PRODUCT or if BI AUSTRIA receives notification of any planned or unplanned inspection directed to the PRODUCT 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 PRODUCT from being manufactured, packaged or stored in accordance with this 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 expire on December 31, 2010. However, the PARTIES may agree to extend this AGREEMENT on or before December 31, 2008 for a further period of up to ten (10) years based substantially on the same terms as set out in this AGREEMENT.



18.2. TERMINATION

- 18.2.1. NPS reserves the right to terminate this AGREEMENT after the IMPLEMENTATION BATCHES if:
- 18.2.1.1. BI AUSTRIA could not implement the process for technical reasons then NPS, in its discretion, may terminate on thirty (30) days notice and without payment of a [\*] or any remaining [\*] by NPS whereupon NPS will have no further financial obligation to BI AUSTRIA arising under or related to the subject matter of this AGREEMENT; or
- 18.2.1.2. The YIELDS are not as expected for reasons related to the production process, NPS, in its discretion, may terminate on thirty (30) days notice and upon payment of the full reservation fee (“Termination Penalty”) whereupon NPS will have no further financial obligation to BI AUSTRIA arising under or related to the subject matter of this AGREEMENT.
- 18.2.2. Either PARTY may terminate this AGREEMENT at any time on or after December 31, 2005, upon twenty-four (24) months’ prior written notice given to the other PARTY, provided that BI AUSTRIA shall continue to manufacture and deliver PRODUCT as forecasted/ordered and NPS shall continue to purchase and accept such PRODUCT for the full twenty-four (24) months.
- 18.2.3. NPS reserves the right to terminate this AGREEMENT at any time upon thirty (30) days notice if:
- 18.2.3.1. NPS decides it must delay or terminate the production or market entry of PRODUCT, provided NPS shall be liable to BI AUSTRIA for the following (collectively called, the “Termination Penalty”):
- 100% of the costs for (i) all the Services already performed, (ii) RAW MATERIAL and Components (plus the appropriate markup) already purchased for use in manufacturing PRODUCT, and/or (iii) PRODUCT already manufactured according to a valid Purchase Order, at the date of receipt of such notice of termination less any paid Reservation fee or other prepaid amounts; and
- [\*]% of the total costs that would be coming due to BI AUSTRIA over the next [\*] months, being [\*]%, of either the equivalent value of Services already purchased, or portion thereof, or the applicable equivalent of the purchase price of PRODUCT already requested by NPS in the red zone, and the blue zone of the then current Rolling Forecast (Exhibit C) at the date of receipt of such notice of termination less any prepaid amounts; or
- 18.2.3.2. NPS terminates under paragraph 18.2.3.1 in the event ALX1-11 fails in Phase III clinical trials, then the Termination Penalty shall not include and NPS shall not be liable for the blue zone of the then current Rolling Forecast (Exhibit C) or for any remaining unpaid Reservation fee; or
- 18.2.3.3. For any other reason provided NPS shall be liable to BI AUSTRIA for the following (collectively called, the “Termination Penalty”):

100% of the costs for (i) all the Services already performed, (ii) RAW MATERIAL and Components (plus the appropriate markup) already purchased for use in manufacturing the PRODUCT, and/or (iii) PRODUCT already manufactured according to a valid Purchase Order, at the date of receipt of such notice of termination less any prepaid amounts; and

[\*]% of the total costs that would be coming due to BI AUSTRIA over the next [\*] months, being [\*]%, of either the equivalent value of Services already purchased, or portion thereof, or the applicable equivalent of the purchase price of PRODUCT already requested by NPS in the red zone, and the blue zone of the then current Rolling Forecast (Exhibit C) at the date of receipt of such notice of termination less any prepaid amounts.

plus the [\*] not previously credited.

- 18.2.4. BI AUSTRIA reserves the right to terminate this AGREEMENT in the event that ALX1-11 fails in Phase III clinical trials. For the purpose of clarity, in such event NPS shall come up within [\*] months with a detailed assessment and action plan revealing the impact of such clinical trial failure for this AGREEMENT. As far as the manufacture of PRODUCT at BI AUSTRIA is concerned, such action plan shall be subject to mutual agreement. In the event NPS will not provide BI AUSTRIA with such detailed assessment and action plan, BI AUSTRIA has the right to terminate the AGREEMENT, and NPS shall be liable to BI AUSTRIA for the Termination Penalty in accordance with paragraph 18.2.3.2.
- 18.2.5. Any reservation fee paid to date by NPS shall be set off against the applicable Termination Penalty under either 18.2.1.2, 18.2.3.1, 18.2.3.2 or 18.2.3.3.
- 18.2.6. Any Termination Penalty will be reduced by any amounts saved through success of BI AUSTRIA in mitigation efforts under paragraph 18.3.
- 18.3. MITIGATION
  - 18.3.1. BI AUSTRIA will use reasonable commercial efforts to mitigate any Termination Penalty set out in Paragraph 18, including without limitation attempting to use internally or resell its services and the manufacturing capacity that was dedicated to or reserved for the manufacture of PRODUCT after termination by NPS.
- 18.4. EFFECT OF TERMINATION
  - 18.4.1. Paragraph 13, 14, and 18 shall survive termination or expiration of this AGREEMENT (as the case may be) and shall remain in full force and effect.
  - 18.4.2. The provisions of paragraph 16 shall survive termination or expiration of this AGREEMENT (as the case may be) and shall remain in full force and effect for ten (10) years after termination or expiration of this AGREEMENT.
  - 18.4.3. The provisions of paragraph 3.1.2.1 shall survive termination or expiration of this AGREEMENT (as the case may be) and shall remain in full force and effect for two (2) years after termination or expiration of this AGREEMENT.
  - 18.4.4. 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.

- 18.4.5. 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.
- 18.4.6. BI AUSTRIA shall deliver all PRODUCT-specific equipment in accordance with paragraph 3.1.2.1, all materials, including but not limited to samples, PRODUCT, and intermediate products, and all PRODUCT-specific documentation generated during the term and within the scope of this AGREEMENT to NPS. In the event the AGREEMENT is terminated by NPS according to paragraph 18.2.1.1, or by BI AUSTRIA according to paragraph 18.2.2, all reasonable costs for such delivery shall be to the charge of BI AUSTRIA. In all other cases such costs shall be to the charge of NPS.
- 18.4.7. In the event this AGREEMENT is terminated by NPS according to paragraph 18.2.3.3, 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 13.1.1.

## 19. MISCELLANEOUS

### 19.1. NON-COMPETITION

- 19.1.1. BI AUSTRIA will not enter into an agreement to manufacture rhPTH or any Related Compound for a third party for as long as BI AUSTRIA is manufacturing PRODUCT for NPS according to this AGREEMENT. "Related Compound" for this paragraph, paragraph 19.1.1, means a compound that: (i) competes with PRODUCT for [\*].
- 19.1.2. Notwithstanding paragraph 19.1.3, BI AUSTRIA will not manufacture rhPTH or a [\*] of rhPTH for commercial sale for itself or its AFFILIATES for as long as BI AUSTRIA is manufacturing PRODUCT for NPS according to this AGREEMENT.
- 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 a Related Compound 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 a Related Compound. "Related Compound" for this paragraph, paragraph 19.1.3, means a compound that will be used in the treatment of osteoporosis and that: (i) competes with rhPTH for [\*]. If NPS receives such a notification from BI AUSTRIA, NPS has the option to terminate this AGREEMENT upon twenty-four (24) months' prior written notice given to BI AUSTRIA, provided that NPS shall continue to purchase and accept, acceptable production as defined for the full twenty-four (24) months.

### 19.2. KNOWLEDGE SHARING WITH NPS

- 19.2.1. To the extent not otherwise provided for in the AGREEMENT, 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 PRODUCT, including, without limitation, Component Production Records, MASTER BATCH RECORDS, RAW MATERIAL SPECIFICATIONS, Analytical Methods, VALIDATION Documentation and any other available PRODUCT specific production data/research data.

### 19.3. GOVERNING LAW AND ARBITRATION

- 19.3.1. This 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 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 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. Judgement 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 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 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:

Attention:  
NPS Allelix Corp.  
6850 Goreway Drive  
Mississauga, Ontario  
Canada L4V 1V7  
Attn: Rick Wilcocks, Manager, Protein Purification

with a copy to:

NPS Pharmaceuticals Inc.  
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 AGREEMENT to its AFFILIATES. This AGREEMENT may be assigned by either PARTY to any third party with the prior written consent of the other PARTY, such consent not to be unreasonably withheld or delayed.

19.8.2. This 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 This AGREEMENT 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 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 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.**

**BOEHRINGER INGELHEIM  
AUSTRIA GmbH**

By: \_\_\_\_\_  
Name: Hunter Jackson  
Title: President

By: \_\_\_\_\_  
Name: Dr. Kurt Konopitzky  
Title: Head of Division Biopharmaceuticals/  
Operations

Date: \_\_\_\_\_

Date: \_\_\_\_\_

By: \_\_\_\_\_  
Name: Prof. Rolf G. Werner  
Title: Head, Corporate Division Biopharmaceuticals

Date: \_\_\_\_\_

**EXHIBIT A**

**MANUFACTURING DOCUMENTS**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

**[\*]**

**EXHIBIT B**

**MANUFACTURING DOCUMENTS**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

**[\*]**



**EXHIBIT C**

**ROLLING FORECAST MODEL**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

[\*]

**EXHIBIT D**

**DETAILED TIMELINE AND FEE SCHEDULE FOR SCALE UP BATCHES  
AND CONFORMANCE BATCHES**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

[\*]

**EXHIBIT E**

**SLIDING PRICE MODEL**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

[\*]

**EXHIBIT F**

**PRODUCT SPECIFICATIONS**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

**[\*]**

**EXHIBIT G**

**CRITICAL RAW MATERIALS AND STORAGE CONTAINERS**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

[\*]

**EXHIBIT H**

**DOCUMENTS BI AUSTRIA WILL PROVIDE IN ENGLISH**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

[\*]

**EXHIBIT I**

**DESCRIPTION OF FACILITIES FOR PTH PRODUCTION AND TESTING**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

[\*]

**EXHIBIT J**

**DOCUMENTS TO BE REVIEWED AND APPROVED BY NPS**

**An Exhibit to the Commercial Manufacturing Agreement  
Between  
NPS Allelix Corp. and Boehringer Ingelheim Austria  
Dated 18 October, 2002**

[\*]