APPROVED STANDARD OPERATING PROCEDURE

Title: CHANGE CONTROL PROCEDURE FOR PARTS MANUFACTURED FOR PHARMACEUTICAL CUSTOMERS

DOC Number: SOPPH/001.

Supersedes: 21 Jul 2015

Issue Date: 10 Aug 2015

Prepared by	Head of Quality Assurance	
G. P. Crawley	Signature: -	Date :- 10 Aug 2015
Approved by	Production Leader	
S. G. Harris	Signature: -	Date :- 10 Aug 15
Approved by	Engineering Director / General Manager	
C. J. Green	Signature: - C. J. Green	Date :- 10 Aug 2015

1 Purpose

The purpose of the document is to define the procedures to be followed by Advanex Europe Ltd (AEU), in order to communicate any proposed product or procedural changes.

2 Scope

This document will apply to the manufacture of any designated pharmaceutical product by Advanex Europe Ltd.

This document provides a generic procedure to be followed where no customer(s) specific requirements have been provided. If customer(s) specific requirements are provided they automatically supersede this document.

3 Associated paperwork

Change request form : AEU00108

4 Responsibilities

4.1 **Head of QA**:
Will ensure:

4.1.1 That proposed changes are communicated to potentially affected interested parties, as defined in this document.

4.1.2 That any required customer(s) acceptance has been received prior to implementation of changes (as defined in this document) to a validated process

4.2 Engineering Director / General Manager

4.2.1 The Engineering Director will review change request forms before submission.

4.3 Production Leader

4.3.1 The Production Leader will review change request forms before submission.

5 Definitions

5.1 Change

For the purpose of this SOP a "change" is regarded as a modification to a process. Maintenance and "like for like" replacements are not Considered changes in the context of this SOP.

Changes are categorised in the following ways:

5.1.1 Category (i): Changes that require notification but do not require re-validation of either the components or process.

5.1.2 Category (ii): Changes that require re-validation of the component or process

5.1.3 Category (iii): Changes that require re-validation of the component and process.

5.2 Process

For the purpose of this SOP the process includes the machine type, tooling design, material type, any washing, heat treatment or other secondary process, & procedures and packaging specifications as outlined in, or referred to in the relevant DMF or control plan.

6 Changes that require notification

It is the responsibility of the Head of Quality Assurance to ensure that customers are informed and their approval sought of any proposed changes as listed below (6.1 – 6.6)

Any significant changes to the manufacturing area for product supplied to medical or pharmaceutical customers will be communicated to the accredited ISO13485 certification body.

6.1 Change to raw materials

Any proposed changes to the raw material used to produce any product supplied. This will include any changes of raw material supplier, material grade / type, and material size.

6.2 Changes to secondary process / operation

Any proposed changes to any secondary process as defined in the relevant DMF or control plan. This will include any changes of plant, settings, timings, chemicals / solvents used.

6.3 Changes to the manufacturing process

Proposed changes to the manufacturing process. This will include any changes to the machines and associated tooling heat treatment furnaces and their settings and any new technologies that are introduced.

6.4 Changes to the site of supply

If product is to be supplied from any site other than the current approved site.

6.5 Product changes

Any proposed changes to the dimensional or operational characteristics of the supplied product.

6.6 Regulatory changes

Any known changes to the regulatory status of supplied product.

7 Procedure (change category (i))

7.1 General

Category (i) changes only include minor changes that do not affect the basic tool layout or process and will have no bearing on the components.

7.2 Process

Any proposed change will be formally requested by the completion of section 'A' of a sequentially numbered Advanex Change Request Form (0000274)
This is forwarded to the Head of Quality Assurance who will circulate the request to the Manufacturing and Engineering departments for comment and / or a signature of acceptance. The signature of the Head of Quality Assurance approves the change proposal for the issue to customer(s).
A copy of the form will be issued to the customer(s) for completion of section D 'Notification of the stated change has been received' The signature of the customer(s) representative in section D only acknowledges receipt of the information and does not approve the change.

7.3 Evaluation of change

AEU will be responsible for ensuring that the change has been effective.

7.4 Change approval

AEU will be responsible for approving any category (i) change.
Completion of section E by the Head of Quality Assurance, formally closes the change procedure.

8 Procedure (change category ii & iii)

8.1 General

Until written approval has been received from the customer(s), all products supplied will be from existing processes (excluding any category (i) changes) and materials and will conform to customer(s) agreed or supplied specifications.

8.2 Process change request

Any proposed change will be formally requested by the completion of section 'A' of a sequentially numbered Change Request Form.
This is forwarded to the Head of Quality Assurance who will circulate the request to the Manufacturing and Engineering departments for comment and / or a signature of acceptance.
The signature of the Head of Quality Assurance approves the change proposal for issue to the customer(s). Before any changes to the process are

undertaken, AEU will formally request agreement from the customer(s) by issuing the change request form.

8.3 Submission requirements

If the customer(s) is in agreement that the change can be made for trial purposes, section 'B' of the Change Request Form is completed and returned to AEU.

The customer(s) will itemise any requirement for documentation or samples that will be required to evaluate the change.

NOTE: Unless otherwise agreed in writing the requirement of samples only permits production to be made under the following controlled conditions for trial purposes:

8.3.1 Only an agreed quantity of change affected product will be produced. The batch size(s) and period of testing will be agreed by AEU and the customer(s) and will be dependent upon the change being made and the potential impact on the finished product.

8.3.2 Any product produced for trial purposes will be clearly identified as a trial batch.

8.3.3 Trial batches will be segregated from normal production.

8.4 Evaluation of change

AEU QA, Production & Engineering will monitor and statistically analyse the resulting inspection data to establish the capability of the changed process.

8.5 Change approval

The customer(s) will evaluate the sample product (where applicable) and supporting data and, if satisfied that the change is not detrimental to the product or their own processes will formally approve the change by completing section D of the change request form and returning it to AEU.

8.6 Implementation

Completion of section E by the Head of Quality Assurance, formally closes the change procedure.

Once final approval has been received the change can be incorporated into the production process. A changeover period will be agreed by both AEU & the customer(s), after which all product will incorporate the agreed change. During this period product identification may be used to identify product with the changes incorporated.