



FINAL REPORT

## **Sino-implant (II) Initiative: 2012 Quality Assurance Evaluation**

December 15, 2012

Submitted by:

FHI 360

---

Markus Steiner, Ph.D.  
Sino-implant (II) Project Director  
P.O. Box 13950  
Research Triangle Park, NC 27709  
Tel: +1.919.544.7040  
FAX: +1.919.544.7261

## Final Report

# Sino-implant (II): 2012 Quality Assurance Evaluation

**FHI 360**

**David W. Jenkins, Ph.D.**

**Associate Scientist II**

Product Quality and Compliance Department

2810 Meridian Parkway, Suite 133

Durham, NC 27713

E-mail: [djenkins@fhi360.org](mailto:djenkins@fhi360.org)

Phone: 919-544-7040 ext. 11617

Fax: 919-544-5849

**Derek H. Owen, Ph.D.**

**Scientist I**

Clinical Sciences

2224 E. NC Hwy. 54, Durham NC 27713

E-mail: [dowen@fhi360.org](mailto:dowen@fhi360.org)

Telephone: 919-544-7040 ext. 11168

Fax: 919-544-7261

**Markus Steiner, Ph.D.**

**Sino-implant (II) Project Director**

Clinical Sciences

2224 E. NC Hwy. 54, Durham NC 27713

E-mail: [msteiner@fhi360.org](mailto:msteiner@fhi360.org)

Telephone: 919-544-7040 ext. 11346

Fax: 919-544-7261

## Table of Contents

Final Report .....	i
Executive Summary .....	iv
Introduction.....	1
Section I: Quality Assurance Monitoring of Sino-implant (II).....	2
Brief Description of Sino-implant (II) Commercial Lot Release Testing .....	2
Results of Sino-implant (II) Commercial Lot Release Verification .....	3
Conclusion of 2012 Quality Assurance Monitoring of Commercial Lots of Sino-implant (II) .....	3
Section II: Annual Quality Assurance Evaluation of Sino-implant (II) .....	4
Levonorgestrel: Active Pharmaceutical Ingredient (API) Quality Assurance Evaluation .....	4
Levonorgestrel CP Evaluation .....	4
Levonorgestrel BP Evaluation .....	5
Conclusion of Levonorgestrel: Active Ingredient Quality Assurance Evaluation.....	6
Sino-implant (II): Final Product Quality Assurance Evaluation.....	7
Sino-implant (II) Sample Lot Release Verification .....	7
Ethylene Oxide Residuals Evaluation.....	8
Inorganic Impurities Evaluation .....	9
Residual Solvents Evaluation .....	13
Bacterial Endotoxin Evaluation .....	14
Cytotoxicity Evaluation .....	15
Sino-implant (II): Packaging Material Evaluation.....	15
Packaging Physicochemical Evaluation .....	16
Package Integrity Evaluation .....	16
Section III: Summary of Results of the 2012 Comprehensive Quality Assurance Evaluation ....	18

## Tables

Table 1. Summary of the quality assurance evaluation of Sino-implant (II).....	v
Table 2. Sino-implant (II) commercial lot release verification test results.....	3
Table 3. Levonorgestrel: lot release verification test results analyzed using the Chinese Pharmacopeia monograph.....	5
Table 4. Levonorgestrel: lot release verification test results analyzed using the BP monograph.	5
Table 5. Sino-implant (II) sample lot release verification results.....	7
Table 6. Ethylene oxide residuals test results of Sino-implant (II).....	8
Table 7. ICP-MS test results of Sino-implant (II): USP inorganic impurities (Heavy Metals)...	11
Table 8. ICP-MS test results of Sino-implant (II): additional inorganic impurities. ....	12
Table 9. Residual solvents test results of Sino-implant (II).....	14
Table 10. Limulus Amebocyte Lysate Test (Kinetic Turbidimetric Technique) test results of Sino-implant (II). ....	14
Table 11. MEM elution test results of Sino-implant (II). ....	15
Table 12. Physicochemical test results of Sino-implant (II) packaging film.....	16
Table 13. Bubble emission test results of Sino-implant (II). ....	17
Table 14. Comprehensive tabulated summary of the quality assurance results of Sino-implant (II) tests conducted.....	18

## Executive Summary

A quality assurance evaluation and monitoring program was implemented by FHI 360 to verify that Sino-implant (II) meets lot release specifications for the product. This report expands on the results obtained after the quality assurance evaluation and monitoring program conducted from 2008 to 2011.

Commercial lot release testing verification was conducted for all eight lots of Sino-implant (II) that were shipped to countries as part of the Sino-implant (II) introduction in developing countries. In all instances results were in compliance with Sino-implant (II) lot release specifications (Table 1).

A more extensive battery of tests was conducted to evaluate if Sino-implant (II) meets international quality standards. The battery of tests selected was based on standards from the United States Pharmacopeia (USP), British Pharmacopeia (BP), International Organization for Standardization (ISO) and the American Society for Testing and Materials (ASTM). Sino-implant (II) samples tested met the quality requirements for all tests conducted (Table 1).

We conclude that Shanghai Dahua Pharmaceutical Co., Ltd continues to demonstrate the ability to consistently produce a contraceptive implant that meets international quality standards.

**Table 1. Summary of the quality assurance evaluation of Sino-implant (II)**

Test		Lot #	Results
<b>Quality Assurance Monitoring of Sino-implant (II)</b>			
Sino-implant (II): Commercial Lot Release Testing Verification <sup>a</sup>		07112001 05162012 06082012 06272012 07132012 08032012 09152012 10072012	Met requirements
<b>Annual Quality Assurance Evaluation of Sino-implant (II)</b>			
Levonorgestrel: Active Ingredient Quality Assurance Evaluation	Levonorgestrel: China Pharmacopeia Evaluation <sup>a</sup>	ZQ20120002 ZQ20110016 ZQ20110022	Met requirements
	Levonorgestrel: British Pharmacopeia Evaluation <sup>e</sup>		Met requirements
Sino-implant(II) : Final Product Quality Assurance Evaluation	Sample Lot Release Verification <sup>a</sup>	09022012 24022012 10032012	Met requirements
	Ethylene Oxide Residuals Evaluation <sup>b</sup>		Met requirements
	Inorganic Impurities Evaluation <sup>c</sup>		Met requirements
	Residual Solvents Evaluation <sup>d</sup>		Met requirements
	Bacterial Endotoxin Evaluation <sup>b</sup>		Met requirements
	Cytotoxicity Evaluation <sup>b</sup>		Met requirements
Sino-implant(II) : Packaging Material Evaluation	Packaging Physicochemical Evaluation <sup>b</sup>	11-071PA1-11-OP-22-1 11-071P-11-8-23-1 110117	Met requirements
	Sino-implant (II): Package Integrity Evaluation <sup>b</sup>	09022012 24022012 10032012	Met requirements

<sup>a</sup> Conducted by SGS Life Sciences Division, Shanghai, China

<sup>b</sup> Conducted by Nelson Laboratories, Inc., Salt Lake City, UT

<sup>c</sup> Conducted by EAG-Life Sciences, Maryland Heights, MO

<sup>d</sup> Conducted by Irvine Pharmaceutical Sciences, Irvine, CA

<sup>e</sup> Conducted by Lancaster Laboratories, Lancaster, PA