PROGRESSIVE SURGICAL Half Time

Keeping you "in the know" in the ASC industry

PRIMAPHARMA

PROGRESSIVE SURGICAL SOLUTIONS

COMPOUNDING PROBLEMS

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Compounding Problems Overview

- ASC regulations regarding medication management and drug compounding
- Compounders producing commercial quantities of sterile drugs
- Patient Safety – Numerous Deaths, Injuries
- Impacts of compounding on Product Safety & Efficacy
- Potential Subscriber Liability

ASC Regulations

- **CMS CfC 416.48** – The ASC must provide drugs and biological in a safe and effective manner, in accordance with accepted professional practice, and under the direction of an individual designated responsible for pharmaceutical services.
- **CMS CfC 416.48(a)** – Drugs must be prepared and administered according to established policies and acceptable standards of practice.
- **Exhibit 351** – Infection Control Surveyor Worksheet

Single-Dose Medication

- SDV will be used immediately upon opening, on one patient only and discarded appropriately after use
- SDVs shall be discarded:
  - After use on one patient
  - When suspected contamination occurs
  - When contamination/particulates are visible
- Opened single-dose vials/ampules shall not be stored for any period of time

Multiple-Dose Medication

- Dated upon opening
  - Date opened or the beyond-use date (28-days from opening, unless otherwise recommended by the manufacturer)
- The ASC has voluntarily adopted a policy that medications labeled for multi-dose use for multiple patients are nevertheless only used for one patient (Exhibit 351)
- MDVs and immediate patient care areas

USP 797

- United State Pharmacopeia Chapter 797, Pharmaceutical Compounding – Sterile Preparations
  - Applies to all personnel and facilities where Compounded Sterile Preparations (CSPs) occur
  - CSPs involve the pre-administration management and preparation of sterile compounds for application, implantation, infusion, inhalation, injection, insertion, instillation or irrigation, including preparation, storage and transportation.
  - Establishes criteria for low, medium and high risk CSPs

Immediate Use CSPs

- Intended for immediate use and emergency situations
- Cannot be stored for the purposes of anticipated need or batch compounding
- Must meet specific criteria
  - No more than 3 commercially available sterile products in original container and no more than 2 entries into any container /package/device
  - Continuous process completed w/in 1 hour
  - Adheres to aseptic technique
  - Administered w/in 1 hour or discarded

Best Practices for Immediate Use CSPs

- Quiet place free from distraction
- Prepare before you start
- Disinfect the area
- Hand hygiene
- PPE
- Disinfect entry points
- Mix accurately
- Shake to assure mixing
- Verify calculations and procedure
- Administer w/in 1 hour
- Proper labeling

Patient Safety: Death and Injury

- 2011 Avastin repackaged and distributed
  - > 15 patient injuries including blindness
- 2012 – NECC Fungal meningitis outbreak
  - > 700 patient injuries, > 60 deaths
- 2016-17 – Guardian Pharmacy Services, Dallas
  - > 30 patients lose visual acuity

Compounding Problems Overview

- New Regulations – Drug Quality & Security Act (DQSA)
- Explanation of 503A vs. 503B
- Definitions
  - cGMP
  - 483
  - EIR
  - Facility Differences
  - Statements of Procedures (SOP)
- Recommendations & Resources

Product Safety & Efficacy Issues: Causes

- Container closures - Avastin: repackaged into plastic or glass syringes with sprayed on silicon and/or prepared in unsanitary conditions
- Lack of sterile facilities and processes - NECC Fungal meningitis outbreak as an example of the impact of non-sterile compounding and inadequate processes for sterile fill
- Lack of sterile facilities and processes - Guardian Pharmacy Services, Dallas is another example of non-sterile compounding and inadequate processes for sterile fill

Compounding Problems

1. No previous statutory FDA authority to oversee compounding pharmacies
2. No FDA registration requirements for compounding pharmacies
3. Production of commercial quantities of sterile drugs (no FDA approval or oversight)

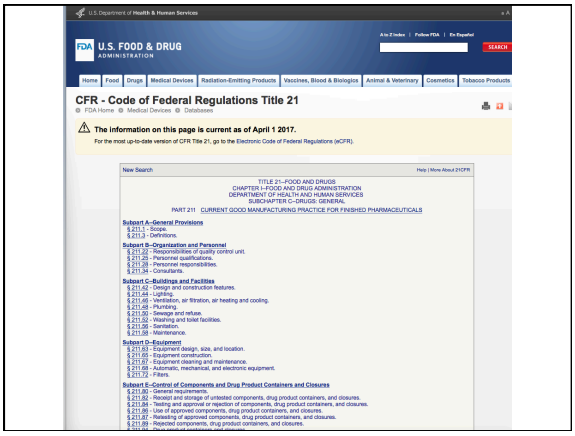
New Regulations under DQSA

Drug Quality & Security Act (DQSA)

- Created two classes of compounders
  - 503A – Traditional compounding pharmacies
  - 503B – Outsourcing Facility
- Granted FDA authority to regulate

New Regulations under DQSA

	503A Compounding Pharmacies	503B Outsourcing Facilities
Regulatory Authority	State Boards of Pharmacy FDA registration & inspection	FDA registration & inspection Additional State requirements
Applicable Standards	USP <797> FDA 503A Policy Guide	FDA cGMP (21CFR 210 & 211) Additional State requirements
FDA Inspection	Under authority to enforce 503A	FDA authority to enforce cGMP regulations
Licensing	State Boards of Pharmacy	FDA Registration
Inspection	FDA State Boards of Pharmacy	FDA & States IF additional State requirements
Limitation on Services	Individual prescription only. Limited anticipatory compounding	Batch processing. May maintain inventory. Must sell direct to prescriber



503A to 503B Conversion

Difficulty converting a 503A qualified facility into a 503B qualified Facility

Total FDA Registered 503B Facilities	71	100.00%
After inspection received a warning letter or other regulatory notice	26	36.62%
Inspected by the FDA, issues found but final outcome not determined	32	45.07%
Unaudited	13	18.31%
Inspected with no serious issues. NOT ONE HAS CLEARED THEIR AUDIT	0	0.00%

503A/503B Differences

503A

- Laminar flow hood
- Lack of aseptic technique
- No qualification of
  - API & excipient vendors
  - Container closure
  - Aseptic operators
  - Environmental controls

503B

- Full cGMP, qualified
  - API & Excipient vendors
  - Validated sterile procedures
  - Aseptic technique
  - Aseptic operators
  - Environmental controls
  - Environmental monitoring
  - Release assays
  - Stability testing

503A/503B Differences

503A

503A/503B Differences

503B

Prescriber/Physician Liability Exposure

- May rely on FDA approval for commercially available drug
- If prescribing a compounded drug due diligence is **REQUIRED**.
  - Licenses, certifications, safety record. Notification & recall process for safety issues
  - Source & grade of pharmaceutical ingredients, sterility of facility, equipment & other factors affecting safety and efficacy

Recommendations & Resources

1. Use FDA approved commercial product as first choice
2. If not available commercially use a cGMP 503B registered facility if product available
3. If not available at a 503B registered facility use a 503A facility and **DO YOUR DUE DILIGENCE**
4. Know the regulatory status of your provider (503A or 503B)
5. Qualify your provider
   Sample questionnaire from International Academy of Compounding Pharmacists

PRIMAPHARMA

INFORMATION RELEASE

Name of Company: PrimaPharma, Inc.

Address: 3443 Tripp Court
San Diego, CA 92121

Telephone 858 259 0969

Web Site PrimaPharma.net

Type of Operation: Contract Manufacturing & Product Development Drugs, Medical Devices and Diagnostics

Background: PrimaPharma, Inc. is a privately held manufacturer of drugs, devices, cosmetics and diagnostic products located in the North San Diego (Del Mar) area. PrimaPharma has been in business since 1992 operating in compliance with cGMP's and is an ISO certified (BSI) and FDA (Drug & Device) inspected facility. The company has full manufacturing capabilities in over 20,000 square feet including ISO Class 5 and ISO Class 7 clean room facilities. The management team has over 100 years combined experience in the manufacture and development of products for regulated industries worldwide. This experience includes injectable drugs, aseptic lyophilization, isolation of natural and biological products including enzymes, proteins and peptides. PPI customers include large Pharmaceutical and Device Companies, government agencies, as well as many "start-ups" and small to medium companies engaged in product and process development, both domestically and internationally.

Types of Products: Pharmaceuticals, Medical Devices and Diagnostics

Facility 20,000 Square Feet with administrative offices, production, clean rooms, packaging, laboratories, shipping and receiving

Quality System Compliant with cGMP's (21CFR210 & 211), QSR (21CFR820) and ISO 13485:2003 requirements

Registrations
> FDA Drug Establishment Registration DUNS #079699106
> FDA FEI# 1000135880
> FDA Device Establishment Owner Operator #9088899
> ISO Certification Quality Management System ISO 13485:2003 (BSI Certificate No: FM 59723, expires 4/30/16)
> CA State Food & Drug Branch Drug Mfg License # 76963
> CA State Food & Drug Branch Device Mfg License # 76963

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PRIMAPHARMA

FDA Inspections Most recent FDA Inspections:
>September 2009 (combination Drug cGMP & QSIT)
>September 2010 (cGMP & PAI)
>January 2011 (cGMP)
>January 2012 (cGMP)
>June 2013 (cGMP)
>October 2014 (cGMP)

Employees 37 full time employees
>18 employees in QC/QA

Clean Rooms ISO Class 5 Clean Room General Purpose
ISO Class 7 Clean Room General Purpose

Laboratories Micro Lab (Environmental Monitoring, Bioburden, PET, AME, Sterility, LAL)
QC Lab
Analytical Chemistry Lab
Research Lab

Other Equipment
>Autoclave
>USP Water Manufactured on Site
>Micro-emulsion
>Tube Filler
>-80°C Storage
>Bottle Filler (5 ml to 360 ml)
>Labelers
>Centrifuges
>Standard Pharmaceutical Process Equipment

Product Forms Liquids, Lyophilized Proteins, Lotions, Gels, Injectables, Creams, Emulsions, Small Volume Aseptic Liquids and Lyophilized Products (aseptic & preserved), Syringe Pre-Filling

Products & Services Custom Drug & Device Manufacturing, Drug & Device Product Development, Clinical Supplies Manufacturing, Process Development, Lyophilization Cycle Development, Formulation Development, Packaging & Distribution

Primary Contacts:
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Tony Dziabo
VP Development
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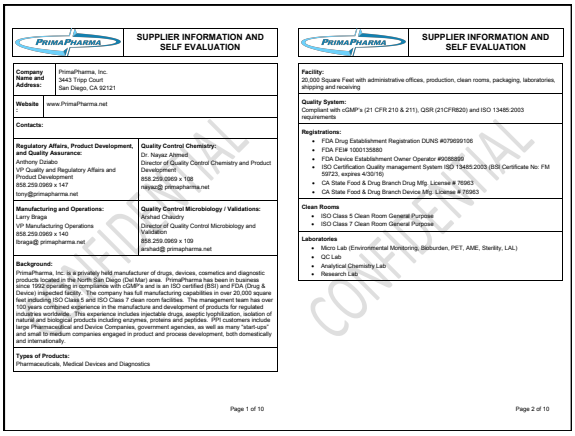
PRIMAPHARMA

SUPPLIER INFORMATION AND SELF EVALUATION

Appendix	Document Description
Appendix A	Supplier Information and Self Evaluation
Appendix B	PrimaPharma, Inc. Quality Manual
Appendix C	PrimaPharma, Inc. Organizational Chart
Appendix D	PrimaPharma, Inc. Facility Map
Appendix E	PrimaPharma, Inc. SOP Index
Appendix F	ISO 13485 Certificate



SUPPLIER INFORMATION AND SELF EVALUATION

Company Name and Address:	PrimaPharma, Inc. 3443 Tripp Court San Diego, CA 92121
Website	www.PrimaPharma.net

Contacts:

Regulatory Affairs, Product Development, and Quality Assurance:
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Manufacturing and Operations:
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VP Manufacturing Operations
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Quality Control Microbiology / Validations:
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Director of Quality Control Microbiology and Validation
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arshad@ primapharma.net

Background:
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Pharmaceuticals, Medical Devices and Diagnostics

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SUPPLIER INFORMATION AND SELF EVALUATION

Facility:
20,000 Square Feet with administrative offices, production, clean rooms, packaging, laboratories, shipping and receiving

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Registrations:
- FDA Drug Establishment Registration DUNS #075699106
- FDA FEI# 1000135880
- FDA Device Establishment Owner Operator #9088886
- ISO Certification Quality management System ISO 13485:2003 (BSI Certificate No: FM 59723, expires 4/30/16)
- CA State Food & Drug Branch Drug Mfg. License # 76963
- CA State Food & Drug Branch Device Mfg. License # 76963

Clean Rooms
- ISO Class 5 Clean Room General Purpose
- ISO Class 7 Clean Room General Purpose

Laboratories
- Micro Lab (Environmental Monitoring, Bioburden, PET, AME, Sterility, LAL)
- QC Lab
- Analytical Chemistry Lab
- Research Lab

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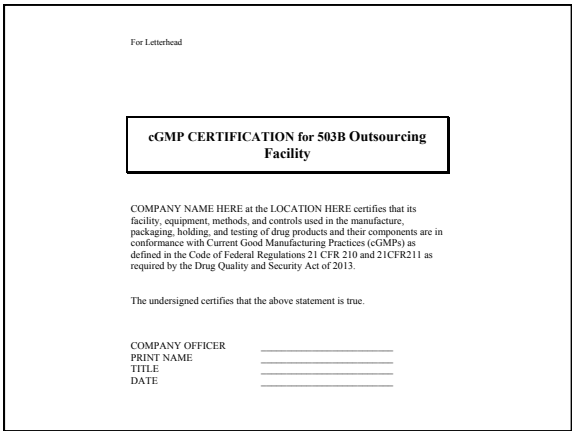

For Letterhead

cGMP CERTIFICATION for 503B Outsourcing Facility

COMPANY NAME HERE at the LOCATION HERE certifies that its facility, equipment, methods, and controls used in the manufacture, packaging, holding, and testing of drug products and their components are in conformance with Current Good Manufacturing Practices (cGMPs) as defined in the Code of Federal Regulations 21 CFR 210 and 21CFR211 as required by the Drug Quality and Security Act of 2013.

The undersigned certifies that the above statement is true.

COMPANY OFFICER _____
PRINT NAME _____
TITLE _____
DATE _____

Recommendations & Resources

6. An ancillary contract should be executed
7. Supplemental information will be obtained:
   - Proof of PCAB Accreditation for Sterile Compounding
   - Copy of, and verification of, state licensure in the state where they are compounded
   - Query results of the receiving state's Board of Pharmacy for any regulatory infractions
   - Copy of malpractice face sheet
8. Contract and services provided will be reviewed annually with rest of ancillary contracted services
9. Reported to the Governing Body

Questions?

info@pss4asc.com

mark@primapharma.net

Continued Education Credit

- 1 CE contact hour per attendee.
- Complete course evaluation by Friday September 1.
- Allow 2 weeks for processing of your certificate.
- Any questions regarding continued education contact courtney@pss4asc.com

PROGRESSIVE SURGICAL eSupport

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Mark Your Calendars

PROGRESSIVE SURGICAL Huddle

September 18, 2017 11am PT/ 2am ET
MINIMIZING THE RISK OF LEGAL CLAIMS AND LIABILITY
Will Miller
Higgs, Fletch & Mack

November 20, 2017 11am PT/ 2am ET
ANNUAL SURVEY WATCH REPORT
Crissy Benze
Progressive Surgical Solutions

Mark Your Calendars

PROGRESSIVE SURGICAL Half Time

November 27, 2017 11am PT/ 2am ET

ASK THE CLINICAL DIRECTOR PANEL

Denise Carpenter

Alison Galloway

Progressive Surgical Half Time

COMPOUNDING PROBLEMS

August 25, 2017

GUARDIAN PHARMACY SERVICES, DALLAS, TX
https://www.dallasnews.com/business/health-care/2017/04/27/patients-lose-vision-routine-cataract-surgeries-dallas-key-whitman-center

All COMPOUNDING PHARMACIES REGULATORY STATUS
https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm339771.htm

CFR TITLE 21 PART 211
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=211

503B REGISTERED OUTSOURCING FACILITIES & REGULATORY STATUS
https://www.fda.gov/drugs/guidancecomplianceregulatoryinformation/pharmacycompounding/ucm378645.htm

PHYSICIANS & COMPOUNDING PHARMACIES: LIABILITY ISSUES
http://m.grayreed.com/portalresource/Physicians%20and%20Compounding%20Pharmacies%20Article.pdf

COMPOUNDING PHARMACY ASSESSMENT QUESTIONNAIRE FROM INTERNATIONAL ACADEMY OF COMPOUNDING PHARMACISTS
http://faculty.mercer.edu/strom_jg/pha529/iacp_cpaq.pdf

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