

**CBER/DMPQ CMC/Facility BLA Review Memorandum**

**BLA STN 125832/0**

**zopapogene imadenovec-drba**  
**[ PAPZIMEOS ]**

**Ou Olivia Ma, DMPQ**  
**Reviewer**

**1. BLA#: STN 125832/0**

**2. APPLICANT NAME AND LICENSE NUMBER**

Name: Precigen, Inc.  
US License #: 2364

**3. PRODUCT NAME/PRODUCT TYPE**

Proper name: zopapogene imadenovec-drba  
Proprietary name: PAPZIMEOS

**4. GENERAL DESCRIPTION OF THE FINAL PRODUCT**

- a. Pharmacological category: non-replicating adenoviral vector-based immunotherapy
- b. Dosage form: injection, suspension
- c. Strength/Potency:  $5 \times 10^{11}$  PU/mL
- d. Route of administration: subcutaneous injection
- e. Indication(s): for the treatment of adults with recurrent respiratory papillomatosis

**5. MAJOR MILESTONES**

- Application Receipt Date: December 27, 2024
- Filing Action: February 24, 2025
- Mid-Cycle Communication: May 6, 2025
- Late-Cycle Meeting with Applicant: June 12, 2025
- PDUFA Action Due Date: August 27, 2025

**6. DMPQ CMC/FACILITY REVIEW TEAM**

Reviewer/Affiliation	Section/Subject Matter
Ou Olivia Ma, OCBQ/DMPQ/MRB2	Drug substance, Drug Product, Facilities
Jana Highsmith, OCBQ/DMPQ/ARB	DMPQ RPM

**7. SUBMISSION(S) REVIEWED**

Date Received	Submission	Sequence #	Comments/ Status
Dec 27, 2024	125832/0.2	0003	Quality Module and completed submission of Rolling BLA
Aug 9, 2024	026884/43	N/A	Type-B meeting
Feb 7, 2025	125832/0.8	0009	Response to DMPQ IR #1, providing 3.2.A.1 (b) (4) facility information
Mar 24, 2025	125832/0.15	0016	Response to CMC IR regarding DP PPQ1
Apr 18, 2025	125832/0.25	0026	Response to DMPQ IR #2, a comprehensive IR regarding (b) (4) validation, CCIT, visual inspection, shipping studies, etc.

Date Received	Submission	Sequence #	Comments/ Status
May 23, 2025	125832/0.35	0036	Updated 3.2.A.1 Facilities and Equipment – Precigen, and updated report for DP engineering and pre-PPQ runs
Jun 17, 2025	125832/0.42	0043	DP release testing update

## 8. REFERENCED REGULATORY SUBMISSIONS (e.g., IND, BLA, 510K, Master File, etc.)

Submission Type & #	Holder	Referenced Item	Letter of Cross-Reference
IND 26884	Precigen, Inc	Entire IND	Provided
MF (b) (4)	(b) (4)	Facility Information	Provided
BB-MF (b) (4)	(b) (4)		Provided
BB-MF (b) (4)	(b) (4)		Provided
MF (b) (4)	(b) (4)		Provided
DMF (b) (4)	(b) (4)		Provided
DMF (b) (4)	(b) (4)	Analytical Procedure	Provided

## 9. REVIEWER SUMMARY AND RECOMMENDATION

### 1) EXECUTIVE SUMMARY

Precigen, Inc. (hereafter Precigen) submitted documentation to BLA STN 125832/0 to support licensure of zopapogene imadenovec-drba (PRGN-2012), an adenoviral vector gene therapy product indicated for the treatment of recurrent respiratory papillomatosis (RRP) in adults.

CBER/DMPQ reviewed and evaluated the drug substance (DS) and drug product (DP) manufacturing processes, and the facilities proposed for use for the manufacture of DS and DP. Information evaluated and documented in this memo includes data to validate and support the consistency of the manufacturing process and product quality; facility information which includes utilities, contamination prevention measures, maintenance of controlled environments, and equipment used during the manufacturing process.

As part of the BLA review, Pre-License Inspections (PLI) were conducted at the DS manufacturing facility Precigen Inc. from April 28 to May 2, 2025, and at the DP manufacturing facility (b) (4) from (b) (4). The PLIs were documented in establishment inspection reports (EIR). At the conclusion of the Precigen PLI, no FDA Form 483 was issued and this PLI is classified as no action indicated (NAI). At the conclusion of the (b) (4) PLI, an FDA Form 483 was issued on (b) (4), with six inspectional observations, to

which the firm responded on May 19, 2025. All inspectional 483 observations appear resolved, and this PLI is classified as voluntary action needed (VAI).


Facility inspections for DP testing facilities were waived based on the evaluations of the facilities' inspection histories and compliance status. The inspection waivers are documented in a separate inspection waiver memo.

## 2) RECOMMENDATION

Approval of the BLA is recommended from DMPQ perspective. Below is a listing of the Drug Substance and Drug Product facilities to be included in the approval letter:

- DS manufacturing facility:  
Precigen, Inc.  
20358 Seneca Meadows Pkwy  
Germantown, MD 20876  
FEI#: 3014429654  
DUNS#: 054652865
- DP manufacturing facility:

(b) (4)

A large rectangular area of the document is redacted with a solid grey fill, obscuring information related to the DP manufacturing facility.

### I. SIGNATURE BLOCK

Reviewer/Title/Affiliation	Concurrence	Signature and Date
Ou (Olivia) Ma Consumer Safety Officer OCBQ/DMPQ/MRB2	Concur	
Christine Harman Acting Branch Chief OCBQ/DMPQ/MRB2	Concur	
Anthony Lorenzo Acting Division Director OCBQ/DMPQ	Concur	

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## BACKGROUND of SUBMISSION

RRP is a rare, neoplastic disorder associated with chronic human papillomavirus (HPV) type 6 or 11 infection that manifests as recurrent papillomas in the upper aerodigestive tract that cause debilitating dysphonia and airway obstruction. There are no approved medical therapies, and the only available treatment for patients with RRP is repeat surgical debulking procedures which does not have curative intent and does not address the underlying disease.

PRGN-2012 is a non-replication competent gorilla adenovirus (GC46)-based gene therapy designed to express a fusion antigen comprising selected regions of HPV6/11 proteins. PRGN-2012 via subcutaneous injection results in the transduction of antigen-presenting cells (APCs), which in turn present small peptide segments of the protein/antigen on the human leukocyte antigen (HLA)/major histocompatibility complex (MHC) Class I complex located on the cell surface of APCs. The presentation of these small peptide segments by APCs leads to induction of T cell responses that are directed against papilloma cells that have been infected with HPV6 or HPV11. Precigen was granted Breakthrough Therapy Designation from the Agency on June 13, 2023.

### 3.2.S DRUG SUBSTANCE – PRGN-2012 DS

(b) (4)





6 pages have been determined to be not releasable: (b)(4)

(b) (4)

(b) (4)

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

### **3.2.P DRUG PRODUCT – PRGN-2012 DP**

#### **3.2.P.1 Description and Composition of the Drug Product**

The PRGN-2012 DP is a suspension for injection for subcutaneous use. The active ingredient in PRGN-2012 is the gorilla GC46 adenoviral vector, expressing an HPV

antigen under the control of a constitutive CMV promoter. PRGN-2012 DP is formulated in 10 mM Tris, 75 mM NaCl, 1 mM MgCl<sub>2</sub>, 5.5% trehalose dihydrate, 0.0025% polysorbate 80, pH (b) (4), and stored frozen at ≤ -60 °C. Each vial of PRGN-2012 DP is formulated to contain a recoverable dose of 5.0 X 10<sup>11</sup> adenoviral vector particles in a 1.0 mL suspension.

PRGN-2012 DP is filled in 2 mL, self-standing (b) (4) vials. Each vial is filled to a target volume of (b) (4) mL to deliver a minimum extractable volume of 1.0 mL. A (b) (4) storage box is used as the secondary container for PRGN-2012 vials. Boxes are sealed in protective (b) (4) pouches to prevent potential ingress of CO<sub>2</sub> gas when shipped on dry ice.

### **3.2.P.2.4 Container Closure System**

Refer to section 3.2.P.7 Container Closure System for the primary container closure system description, specifications, and qualification under DMPQ purview.

### **3.2.P.2.5 Microbiological Attributes**

Microbiological attributes of the DP are maintained via multiple levels of control, including the manufacturing process, release and stability testing, container closure suitability, and environmental controls.

DP is manufactured with an aseptic process after sterilizing (b) (4). (b) (4) is monitored as part of the manufacturing process and (b) (4) is tested (b) (4) (refer to section 3.2.P.3.4 and 3.2.P.3.5). The microbiological quality attributes are assessed by testing for sterility and bacterial endotoxins at release (refer to section 3.2.P.5.1). The microbiological suitability of the selected primary container closure system has been demonstrated through container closure integrity (CCI) characterization as described (refer to section 3.2.7). CCI is also monitored as part of the manufacturing process and (b) (4) as part of the stability testing program. Maintenance of an aseptic manufacturing environment is assured through facility controls at (b) (4) (refer to section 3.2.A.1).

### **3.2.P.3 Manufacture**

#### **3.2.P.3.1 Manufacturer(s)**

See section 3.2.A.1 for a complete list of facilities involved in the manufacturing and testing of PRGN-2012 DP.

#### **3.2.P.3.3 Description of Manufacturing Process**

The PRGN-2012 DP manufacturing process includes the following steps: (b) (4) filling, stoppering, and sealing of DP vials; 100% semi-automated visual inspection, freezing and storage of the vial DP; labeling and secondary packaging.

(b) (4)

(b) (4)

Filling: (b) (4)

Visual Inspection, Freezing, and Storage: (b) (4)

Shipping to the Labeling and Secondary Packaging Site: (b) (4)

Primary Labeling: (b) (4)

The nominal batch size for PRGN-2012 DP is approximately (b) (4) vials at (b) (4) mL/vial. Reprocessing is not performed for any process steps. Product shelf life is calculated based on the fill date.

**Reviewer's Comment:** *The process description appears acceptable. The PRGN-2012 (b) (4) does not require further formulation at the time of filling for PRGN-2012 DP. (b) (4) step is an open process that occurs in a Grade (b) (4).*

(b) (4)

### 3.2.P.3.4 Controls of Critical Steps and Intermediates

The in-process microbial quality controls during PRGN-2012 DP production are summarized below.

(b) (4)

(b) (4)

**Reviewer's Comment:** The in-process controls and hold times under DMPQ purview appear acceptable from microbial quality perspective. In addition to the testing performed in Table 4, the (b) (4) on the (b) (4) is subject to (b) (4) test, and the (b) (4) are subject to (b) (4) test. Assessment of other in-process controls and hold times from DP quality perspective is deferred to OTP reviewers.

### 3.2.P.3.5 Process Validation and/or Evaluation

(b) (4)

(b) (4)

(b) (4)

(b) (4)

(b) (4)

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(b) (4)

**3.2.P.5 Control of Drug Product****3.2.P.5.1 and 3.2.P.5.6 Specification(s) and Justification of Specification(s)**

The PRGN-2012 DP release specifications under DMPQ purview are summarized below.

Table 11. PRGN-2012 DP Release Specifications

<b>Attribute</b>	<b>Analytical Procedure</b>	<b>Release Specification</b>
Bacterial Endotoxins	(b) (4)	(b) (4)
Sterility	(b) (4)	No Growth
Particulate Matter	(b) (4)	(b) (4)
Deliverable Volume		(b) (4) 1 mL

Container closure integrity testing is performed on stability in lieu of sterility.

**Reviewer's Comment:** The DP release specifications associated with microbial quality attributes and the acceptance criteria appear acceptable. Assessment of the other release tests is deferred to OTP reviewers.

### 3.2.P.5.4 Batch Analyses

Batch analyses data from PPQ1, Pre-PPQ lot, (b) (4) engineering lots and (b) (4) clinical lots are provided. These lots were manufactured between (b) (4). All results met the bacterial endotoxin, sterility, particulate matter, and deliverable volume specifications as listed in Table 11.

**Reviewer's Comments:** Batch release testing results under DMPQ purview appear acceptable. For Engineering Lot (b) (4), CCIT was also performed during batch analysis. As CCIT is not considered a routine testing for DP release, refer to CCIT section below for evaluation of the Lot (b) (4) CCIT.

### 3.2.P.7 Container Closure System

#### Components of the Container Closure System (CCS)

The primary CCS for PRGN-2012 DP consists of a (b) (4) vial, a rubber stopper, and an aluminum seal.

Table 12. PRGN-2012 DP Primary Container Closure Components

	Vial	Rubber stopper	Cap
Description	(b) (4) serum vial, 2 mL	13-mm, (b) (4) grey chlorobutyl rubber stopper with (b) (4) barrier on product contact side, (b) (4) coating on non-product side	Aluminum seals with a flip-off plastic top, Red
Manufacturer	(b) (4) (Distributed by (b) (4))	(b) (4)	(b) (4)
Catalog	(b) (4)	(b) (4)	(b) (4)
Sterilization	RTU, (b) (4)	RTU, (b) (4)	RTU, (b) (4)
Particulates	Unspecified	(b) (4)	Not applicable
Bacterial Endotoxin (b) (4)	(b) (4)	(b) (4)	Unspecified

RTU = ready to use (received pre-sterilized by supplier)

**Reviewer's Assessment:** The selected primary CCS for PRGN-2012 is commonly used for cell and gene therapy products due to its performance



*properties of break resistance and structural integrity under cryogenic storage conditions. The cyclic olefin polymer (COP) (b) (4) material is more durable than glass at low temperature, and PRGN-2012 DP is stored at  $\leq -60^{\circ}\text{C}$ . Rubber stoppers and COP polymer have more similar coefficients (than glass) of thermal expansion, reducing the risk of ingress.*

*All components in the DP primary packaging components are received sterile and ready to use. The components of the CCS are released against vendor specifications based on the Certificate of Analysis (CoA) provided by the manufacturer. Incoming material testing and release was assessed during the (b) (4) PLI, and no objectionable findings were noted.*

#### Container Closure Integrity Test (CCIT)

(b) (4)



*The CCIT strategy, methods and results appear acceptable.*

### 3.2.P.8 Stability

#### 3.2.P.8.1 Stability Summary and Conclusion and 3.2.P.8.3 Stability Data

Engineering lot (b) (4), pre-PPQ lot (b) (4), and PPQ1 lot (b) (4) are placed on long-term stability study for storage at  $\leq -60^{\circ}\text{C}$  for up to (b) (4) months and accelerated stability study for storage at (b) (4) for up to (b) (4). Stability samples were stored (b) (4) in a controlled storage condition chamber.

Under DMPQ purview, CCIT is performed on (b) (4) vials each at 0-, 6-, 12-, 24-, (b) (4) months for the long-term stability study. CCIT is not performed for the accelerated stability study. Data is available for up to 9 months (for lot (b) (4)), and no leak was detected from samples tested.

The initial shelf-life claim is 24 months when stored at  $\leq -60^{\circ}\text{C}$ .

**Reviewer's Comment:** Available data supports container closure integrity for 6 months. In the post-approval stability protocol, the firm commits to perform CCIT (b) (4) until up to (b) (4) months.

### 3.2.A APPENDICES

#### Facilities Table

Manufacturing / Testing Activities	Inspection Waiver or Not Required?	Compliance Check Required for Approval?	RMS-BLA Entry Required ?	CMO ?	Comments
<b>Facility:</b> Precigen, Inc. 20358 Seneca Meadows Pkwy Germantown, MD 20876 <b>FEI#:</b> 3014429654  <i>Manufacture of DS, (b) (4)</i> <i>DS release, stability, in-process testing;</i> <i>DP release testing (volume in container and (b) (4))</i> <i>qualification and stability testing</i>	Inspection	Yes	Yes	No	PLI by CBER/DMPQ, NAI, Apr 28 – May 2, 2025
<b>Facility:</b> (b) (4)	Inspection	Yes	Yes	Yes	PLI by CBER/DMPQ VAI,

Manufacturing / Testing Activities	Inspection Waiver or Not Required?	Compliance Check Required for Approval?	RMS-BLA Entry Required ?	CMO ?	Comments
<b>FEI#:</b> (b) (4)  <i>Manufacture of DP; DP in-process testing</i> (b) (4)					(b) (4)
<b>Facility:</b> (b) (4)  <i>DP release testing (volume in container, (b) (4), particulates); Testing for (b) (4), PRGN-2012 (b) (4) (Adventitious agents)</i>	Waiver	Yes	Yes	Yes	Another address: (b) (4)  OII surveillance inspection, VAI, (b) (4)
<b>Facility:</b> (b) (4)  <i>DP primary labeling and secondary packaging</i>	Waiver	Yes	Yes	Yes	OII Surveillance Inspection, NAI, (b) (4)
<b>Facility:</b> (b) (4)  <i>DP release testing (sterility)</i>	Waiver	Yes	Yes	Yes	ORA surveillance inspection, VAI, (b) (4)
<b>Facility:</b> (b) (4)  	Not Required	Yes	Yes	Yes	PLI by CBER/DMPQ VAI, (b) (4)

Manufacturing / Testing Activities	Inspection Waiver or Not Required?	Compliance Check Required for Approval?	RMS-BLA Entry Required ?	CMO ?	Comments
<i>DS release testing</i> ((b) (4)) <i>Testing for</i> ((b) (4)) , PRGN-2012 <sup>(b) (4)</sup> (Adventitious agents)					
<b>Facility:</b> ((b) (4))  <i>DP stability testing (CCIT);</i> <i>Testing for</i> ((b) (4)) , PRGN-2012 ((b) (4)) (Sterility)	Not Required	Yes	Yes	Yes	ORA surveillance inspection, VAI, ((b) (4))
<b>Facility:</b> ((b) (4))   <i>DS release testing</i> ((b) (4))	Not Required	No	Yes	Yes	N/A
<b>Facility:</b> ((b) (4))   <i>Storage for DP, DS,</i> ((b) (4))	Not Required	No	Yes	Yes	N/A
<b>Facility:</b> ((b) (4))    	Not Required	No	Yes	Yes	N/A

Manufacturing / Testing Activities	Inspection Waiver or Not Required?	Compliance Check Required for Approval?	RMS-BLA Entry Required ?	CMO ?	Comments
<i>DP storage</i>					
<b>Facility:</b> (b) (4) (b) (4) <i>Manufacture of</i> (b) (4)	Not Required	No	Yes	Yes	N/A
<b>Facility:</b> (b) (4) (b) (4) <i>Storage of</i> (b) (4)	Not Required	No	Yes	Yes	N/A

NAI = No Action Indicated; VAI = Voluntary Action Indicated;  
 ORA = Office of Regulatory Affairs; OII = Office of Inspections and Investigations;  
 CBER = Center for Biologics Evaluation and Research; DMPQ = Division of Manufacturing and Product Quality;  
 (b) (4)

## Precigen – DS Manufacturing Facility

### Facility Design

Precigen, Inc facility, located in Germantown, Maryland (MD), is a single-product facility dedicated for the production of PRGN-2012 DS.

The manufacturing building is a single connected building covering two addresses (20374 & 20376 Seneca Meadows Parkway, Germantown, MD). The building consists of cleanroom space including areas for upstream and downstream manufacturing, staging, and preparation activities to support manufacturing operations. The manufacturing building also consists of quality control (QC) labs for GMP testing and EM, warehouse, and shipping and receiving. A second building at 20358 Seneca Meadows Parkway, Germantown, MD consists of QC microbiology and QC analytical labs.


Table 13. Facility Areas for PRGN-2012 DS Production

Room Number	Manufacturing Step	Process Step Type
-------------	--------------------	-------------------

(b) (4)

Room Number	Manufacturing Step	Process Step Type
<div data-bbox="190 302 1078 632">(b) (4)</div>		

(b) (4)



### Prevention of Contamination

Precigen is a single product facility, and PRGN-2012 is manufactured with a bioburden-controlled process.

The facility is constructed with clean-room appropriate materials and maintains area classifications in compliance with (b) (4). Processing rooms and airlocks maintain differentials pressure and are controlled with an interlocking system to maintain pressure differentials and minimize reverse airflow. HEPA-filtered air is supplied to the manufacturing areas.

Personnel, materials, equipment, waste flows, and changeover procedures are in place. Facility and equipment decontamination/cleaning, waste management, pest control, area clearance, and environmental and utility monitoring are designed to reduce risk of contamination. Approved standard operating procedures are established and maintained governing the manufacturing areas.

PRGN-2012 (b) (4) production only utilizes single-use, sterile, disposable materials.

**Reviewer's Comment:** *The contamination control features and procedures are reviewed and found acceptable. Facility cleaning and room changeover procedures were evaluated in detail during the Precigen PLI and no objectionable findings were noted.*

## Facility Cleaning

The disinfectants used at the facility includes (b) (4) [REDACTED]. The GMP manufacturing area cleaning protocol encompasses (b) (4) types:

(b) (4)

**Reviewer's Comment:** *The disinfectants used at the Precigen facility and the cleaning procedures appear suitable. The disinfectant efficacy study was not provided in the BLA but was reviewed during the Precigen facility PLI and found acceptable. Although facility-specific disinfectant virucidal studies haven't been performed, the disinfectants selected demonstrate effectiveness against adenovirus based on published literature and manufacturer's technical data sheets; additionally, these disinfectants, such as (b) (4) [REDACTED] are commonly used as effective disinfectants in facilities that manufacture adenovirus products.*

## Critical Utilities

The critical utilities at the Precigen facility includes heating, ventilation and air conditioning system (HVAC), (b) (4) [REDACTED] and compressed air.

**Reviewer's Comment:** (b) (4) [REDACTED] is the only product-contact utility at Precigen. Water used in the production process (e.g. (b) (4) [REDACTED] making) is purified water (b) (4) [REDACTED] water purchased from qualified vendors. Clean compressed air (CCA) used for (b) (4) [REDACTED] testing is also purchased from qualified vendors and distributed (b) (4) [REDACTED]. CCA is monitored (b) (4) [REDACTED] at the points of use.

(b) (4) [REDACTED]



(b) (4)

## HVAC

The classified areas are under the control of (b) (4) air handling system, which uses a (b) (4) air handling unit (AHU) / (b) (4) configuration employing a dedicated outside air system (DOAS) with an energy recovery exhaust system to reduce energy requirements while preventing intake and exhaust from mixing. The (b) (4) DOAS supplies all the (b) (4) units with fresh air which is mixed with the recirculating air from the given area. Conditioned air is circulated through terminal high efficiency particulate air (HEPA) filters to achieve the desired classification for each room.

The HVAC system controls the room temperature, humidity, pressure, and air exchange rates. Temperature and humidity are controlled via a (b) (4) building automation system and monitored by the Environmental Monitoring System (EMS). Air exchange rate is controlled at (b) (4) (b) (4) for ISO (b) (4) rooms and (b) (4) for ISO (b) (4) rooms. Pressure differential from higher to lower classification is controlled at (b) (4). Airlock room (b) (4) in the (b) (4) suite and room (b) (4) and (b) (4) in the (b) (4) suite are designed as (b) (4) to provide containment. Routine preventive maintenance including certification of the HEPA filtered air system and HEPA (b) (4) testing is in place.

**Reviewer's Comment:** HVAC design specifications appear acceptable. The pressure differential across rooms of different classifications is (b) (4) (b) (4), lower than the (b) (4) recommended in the Guidance for Industry – Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice. However, it is to be noted that PRGN-2012 (b) (4) is manufactured with a (b) (4) process instead of aseptic process. Additionally, during the Precigen facility PLI, no significant EM deviations involving total particulates were noted, indicating the current pressure differential is efficient in maintaining the desired room classifications.

HVAC qualification and requalification was also examined in detail during the Precigen facility PLI. (b) (4)

## Environmental Monitoring

Routine EM includes airborne viable (active air) particulate, non-viable particulate and viable surface sampling of (b) (4) rooms. Production-related EM includes passive viable air and personnel monitoring (b) (4). The sampling

locations and number of samples taken were selected based on risk assessment. EM alert and action levels are established for the classified areas.

Table 14 Clean Room EM Action Limits

(b) (4)	(4)
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Alert or action level EM excursions can trigger investigation or trend identification, (b) (4), additional cleaning, and additional EM sampling. EM data trend is evaluated (b) (4) and formal trending is performed (b) (4).

**Reviewer's Comment:** It was clarified during the Precigen facility PLI that 1) (b) (4) monitoring is also performed for dynamic/in-operation conditions and the action limit aligns with (b) (4) requirements, and that 2) EMPQ has been successfully completed. Refer to the Precigen PLI EIR for details. The EM program appears acceptable for a (b) (4) manufacturing facility.

## Equipment



Major equipment used in the PRGN-2012 (b) (4) manufacturing process includes (b) (4), freezers, refrigerators, (b) (4).

The PRGN-2012 (b) (4) manufacturing process exclusively uses single-use, disposable product contact equipment and materials, either received sterile and ready-to-use (RTU) from qualified suppliers or sterilized by qualified (b) (4) on site. All pieces of equipment, except freezers and refrigerators, are dedicated to a (b) (4) of PRGN-2012 manufacturing when in use and are not shared with other lots of PRGN-2012. Equipment calibration and maintenance is performed according to the schedule prescribed in the respective equipment SOP.

Cleaning of the (b) (4) is performed (b) (4) use with (b) (4) by manufacturing operators. Complete (b) (4) cleaning involves cleaning of the (b) (4) of equipment using (b) (4) is performed on the same schedule (every (b) (4) days) as the level (b) (4) facility cleaning. (b) (4) are cleaned (b) (4) (b) (4).

(b) (4) preventive maintenance is performed every (b) (4) months and includes certification of the (b) (4) air system and (b) (4) testing.

(b) (4)



**Reviewer's Comment:** The major equipment qualification appears acceptable to support the (b) (4) -controlled process of PRGN-2012 (b) (4) production. The equipment qualification was assessed during the Precigen facility PLI and no objectionable conditions were noted.

### Computer Systems



Initial Installation and Qualification of the computerized systems used at the Precigen facility was performed to ensure proper installation and verification of functionality within specified parameters. Data Integrity Assessment (DIA) procedural controls were implemented, verified, and approved to ensure compliance with 21CFR 11.

**Reviewer's Comment:** The computer systems were reviewed in detail during the Precigen facility PLI and no objectionable findings were noted.

(b) (4) – DP Manufacturing Facility

### Facility Design

(b) (4)



15 pages have been determined to be not releasable: (b)(4)