Frederick National Laboratory for
Cancer Research, Frederick, MD

Biopharmaceutical Development Program

Standard Operating Procedure

Title: Inspection of Unlabeled Vials of Finished Products

SOP Number: 15113

Revision Number: 09

Supersedes: Revision 08

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[redacted]

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1.0 Purpose

This SOP specifies Biopharmaceutical Development Program (BDP) requirements for the visual inspection of unlabeled vials of finished product produced under CGMP.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

2.0 Scope

All vials will have been filled with container closure in place prior to inspection. Inspection of vials is a joint effort by Manufacturing and Process Analytics/Quality Control (PA/QC) personnel with assistance by Biopharmaceutical Quality Assurance (BQA) personnel as indicated in the SOP.

The Manufacturing Department performs a 100% inspection of unlabeled vials of finished product. Vials with irregularities categorized as “minor”, “major” and “critical” are culled from the batch. A subsequent sampling of vials is screened by PA/QC to monitor the quality of the inspection performed by Manufacturing. This sampling is conducted according to ANSI/ASQC Z1.4, General Inspection Level II. Acceptable Quality Levels have been established for minor (AQL = 6.5), major (AQL = 1.5) and critical (AQL = 0.1) defects. After screening by PA/QC, any sublot exceeding the applicable alert limits will require the sublot to undergo a 100% screening by BQA. After the entire lot has been processed, defects detected by all phases of inspection (Manufacturing, PA/QC, and BQA) are tabulated and investigated if the total lot defect rate exceeds established limits.

For each lot, the complete cycle of inspection (Manufacturing inspection, PA/QC inspection, BQA inspection) is performed in sublots associated with pans of material so that individual pans can be cleared for labeling (to be performed at another location) while later sublots are simultaneously working through the unlabeled vial inspection process. This organization of the inspection process allows screened and acceptable sublots to proceed to labeling eliminating the need to wait for the unlabeled vial screening process to be completed for the entire lot before labeling can start. This reduces the interval that product is exposed to ambient conditions.

In addition, for products that are particularly labile and could likely be adversely affected during the inspection process, a focused inspection to detect critical defects is described. This focused inspection reduces the scope of inspection to detect critical defects only and therefore reduces the time required to complete the inspection. Focused inspections for labile products protect product identity, strength, quality, purity, and safety by minimizing the potential adverse impact to a product that could result from a prolonged standard inspection process.

Inspectors are trained on visual inspection of unlabeled vials by reviewing a training panel that contain both acceptable and unacceptable vials. When ready, inspectors then are tested by performing a vial inspection as they would for a final vialed product on a qualification panel that contains a mixture of acceptable and unacceptable containers. In order to pass the qualification, they must correctly detect 80% of acceptable vials and correctly detect 80% of unacceptable vials. Inspectors are recertified for visual inspection every two years.

3.0 Authority and Responsibility

3.1 The Director, Technical Operations, Biopharmaceutical Development Program, has the authority to define this procedure.

3.2 Manufacturing personnel are responsible for:

3.2.1 100% screening (and documentation) of unlabeled vials of finished product.

3.2.2 Calculation (and documentation) of total lot defects.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

3.2.3 Investigation for lots or sublots that exceed quality limits.

3.2.4 Successfully recertifying every two years for visual vial inspection using the Vial Inspection Qualification Panel.

3.3 Biopharmaceutical Process Analytics/Quality Control personnel are responsible for:

3.3.1 Screening of sublots (and documentation).

3.3.2 Calculation of total sublot defects from PA/QC screening.

3.3.3 Evaluating the disposition of each sublot (need for additional QA screening).

3.3.4 Successfully recertifying every two years for visual vial inspection using the Vial Inspection Qualification Panel.

3.4 Biopharmaceutical Quality Assurance personnel are responsible for:

3.4.1 Quality oversight of this procedure.

3.4.2 Performing 100% screening of each sublot that fails quality limits.

3.4.3 If quantity of rejects exceeds limits, and if requested, BQA will inspect each reject vial using enhanced vision (lighting and magnification) to confirm the PA/QC failure of the rejected vial.

3.4.4 Assisting in investigation for lots or sublots that exceed quality limits.

3.4.5 Successfully recertifying every two years for visual vial inspection using the Vial Inspection Qualification Panel.

4.0 Equipment

4.1 Black and white tiles with light source

4.2 Magnifier Illuminated (VWR #36935-100 or equivalent)

4.3 Microscope

4.4 Light boxes with black and white backgrounds

4.5 Inspection Station (Eisai)

5.0 Standard Procedure

5.1 Check that the lamp(s) used in the inspection equipment are working. Should any lamp not be illuminating, do not use that station until the lamp is repaired or the bulb replaced with another of the same output.

5.2 Manufacturing Screening

5.2.1 Designation of Sublots

5.2.1.1 Manufacturing will designate pans of material as specific sublots. The first pan of material will be designated as “Sublot A,” subsequent pans would be designated “Sublot B,” “Sublot C,” et cetera.

5.2.1.2 **Form 15113-01** is initiated by Manufacturing for each sublot of glass vials (See **Attachment 1**).

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

5.2.1.3 **Form 15113-03** is initiated by Manufacturing for each sublot of cryovials (See **Attachment 3**).

5.2.1.4 **Form 15113-05** is initiated by Manufacturing for each sublot or lyophilized product vials (See **Attachment 5**)

5.2.1.5 The number of vials contained in each pan/tray (sublot) is recorded on **Form 15113-01, 15113-03, or 15113-05**.

5.2.2 Examination and Culling of Vials

5.2.2.1 For each sublot, Manufacturing will conduct a visual inspection of all vials.

5.2.2.2 Choose an area that has good lighting and adequate counter space to perform the operation. In some instances, product may be light sensitive and special precaution should apply that may change illumination light type/source, duration of the inspection, et cetera. Any such special handling should be noted on the inspection forms.

5.2.2.3 Choose equipment as appropriate from Section 4.0 to perform the vial inspection.

5.2.2.4 Place each vial, illuminated from below, against the black and white backgrounds and inspect for defects. If an inspector is uncertain whether any vial is acceptable, the inspector may look at the vial using enhanced visual inspection.

5.2.2.5 Cull and segregate any vials possessing a minor, major, or critical defect.

5.2.2.5.1 Segregate culled vials by minor, major, and critical defects. If desired, additional categorized “cull boxes” can be used to categorize and segregate culled vials during the inspection process.

5.2.2.5.2 Retain culled vials until the need for an investigation has been determined.

5.2.3 Tabulation and Documentation of Results

5.2.3.1 For each sublot, Manufacturing will document the results of their inspection using **Form 15113-01, 15113-03, or 15115-05**.

5.2.3.2 A subtotal of minor, major and critical defects for each sublot is performed and recorded on **Form 15113–01, 15113-03, or 15113-05.**

5.2.4 Document Sign-off

5.2.4.1 Manufacturing inspectors will indicate the inspection equipment used and sign off on the document.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

5.3 Process Analytics/Quality Control Screening

5.3.1 Sampling

PA/QC will collect a random sampling of vials throughout the batch according to ANSI/ASQC Z1.4, General Inspection Level II. This sampling plan is reproduced in Table 1, below.

NOTE: Table 1 is not used when PA/QC is performing 100% inspection.

Table 1

Sublot (pan) Batch Size	Sample Size	ACCEPTANCE/REJECTION CRITERIA		
		Minor Defect AQL = 6.5	**Major Defect AQL = 1.5**	**Critical Defect AQL = 0.1**
2 to 8	2	Accept with 0, Reject with 1	Accept with 0, Reject with 1	Accept with 0, Reject with 1
9 to 15	3	Accept with 0, Reject with 1	Accept with 0, Reject with 1	Accept with 0, Reject with 1
16 to 25	5	Accept with 0, Reject with 1	Accept with 0, Reject with 1	Accept with 0, Reject with 1
26 to 50	8	Accept with 1, Reject with 2	Accept with 0, Reject with 1	Accept with 0, Reject with 1
51 to 90	13	Accept with 2, Reject with 3	Accept with 0, Reject with 1	Accept with 0, Reject with 1
91 to 150	20	Accept with 3, Reject with 4	Accept with 0, Reject with 1	Accept with 0, Reject with 1
151 to 280	32	Accept with 5, Reject with 6	Accept with 1, Reject with 2	Accept with 0, Reject with 1
281 to 500	50	Accept with 7, Reject with 8	Accept with 2, Reject with 3	Accept with 0, Reject with 1

5.3.2 Examination and Culling of Vials

5.3.2.1 Perform this operation in the same manner as Manufacturing, (See Section 5.2.2).

5.3.3 Tabulation and Documentation of Results

5.3.3.1 Perform this operation in the same manner as Manufacturing, (See Section 5.2.3).

5.3.4 Evaluation and Documentation of Screening Results

5.3.4.1 For each sublot, PA/QC will total the defects encountered by Manufacturing and PA for minor, major, and critical defects. PA/QC will evaluate and document the results of their inspection on **Form 15113-01, 15113-03, or 15113-05** according to Table 1 as:

5.3.4.1.1 Inspection results ACCEPTABLE, sublot may proceed to labeling (BQA inspection not required).

OR

5.3.4.1.2 100% BQA inspection and/or Investigation required of sublot before proceeding to labeling. PA/QC will indicate which Acceptable Quality Limit (AQL) has been exceeded (major, minor, or critical).

5.3.5 Document sign-off

5.3.5.1 PA/QC will sign off on **Form 15113-01, 11513-03, or 15113-05.**

5.4 Quality Assurance Screening

5.4.1 Quality Assurance (as requested) will inspect the rejected vials using enhanced vision (lighting and magnification) to confirm the correct classification of the rejects. QA may change the reject classification to another classification including acceptable. This change will be documented and justified.

5.4.2 Quality Assurance will perform a 100% screening of individual sublots when PA/QC inspection results exceed alert limits.

5.4.3 The screening process is conducted in a similar manner to Manufacturing Screening (See SOP Section 5.2)

5.4.4 QA Screening is documented on **Form 15113-02, 15113-04 or 15113-06**.

5.5 Summary of Results

5.5.1 **Form 15113-07** will be completed to capture inspection results for all sublots comprising the entire lot.

5.5.2 The overall lot defect rate (in %) will be calculated and evaluated against established limits (critical < 2%, major < 10%, minor <15%).

5.5.3 An investigation will be conducted for lots exceeding established limits.

5.6 Additional Inspection Criteria

NOTE: Depending on the product, additional inspection criteria may be appropriate.

5.6.1 Justification for Additional Inspection Criteria

5.6.1.1 The need for additional inspection criteria is indicated on **Form 15113-01, 15113-03, or 15113-05**, and will be justified in a memo attached to the screening forms signed by the Project Scientist and BQA.

5.6.1.2 The memo will specify how the additional inspection criteria will be documented and the acceptance/rejection criteria that will be applied.

6.0 Focused Procedure for Labile Products

NOTE: For labile products, where the time required to complete a standard inspection could affect the product's potency or integrity, a focused screening may be conducted at the initiation of the Project Scientist with approval from BQA.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

6.1 Justification for Focused Screening

6.1.1 The need for a focused screening is indicated on **Form 15113-01, Form 15113-05 or 15113-03** and will be justified in a memo attached to the screening forms and signed by the Project Scientist and BQA unless justification for focused inspection is included in the BPR.

6.1.2 Any screening performed by Manufacturing, PA/QC and BQA will be identical to that described in Section 5.0 except that the focus will be on critical defects only.

6.2 Acceptance/Rejection Criteria

6.2.1 Acceptance/rejection criteria for a focused inspection will apply only to results for critical defects.

7.0 Glass Vial Defects

NOTE: Glass vials and their closures may possess a variety of irregularities that may or may not affect a product's identity, strength, quality, and/or purity. Irregularities that may have a detrimental effect on a product are considered defects and are culled from the lot. Defects are categorized as minor, major and critical based on their potential to impact the product (See **Attachment 1 and 2**).

7.1 Vial Irregularities and Defects

7.1.1 Scuffing and scratches. Scuffing and minor scratches are not considered defects and are not culled from the lot.

7.1.2 Pitting. Pitting of the vial is considered as a defect and shall be culled from the lot.

7.1.3 Internal glass strands, fisheyes, glass particles. Internal glass strands, fisheyes, and glass particles are considered defects and shall be culled from the lot.

7.1.4 Cracks/Chips. Cracks and chips are considered defects and shall be culled from the lot.

7.1.5 Vial residue. Residue on the inside or outside of the vial is considered a defect and shall be culled from the lot.

7.2 Crimp Irregularities and Defects

7.2.1 Physical deformities. Dents and other physical deformities of the crimp are considered defects and shall be culled from the lot.

7.2.2 Inconsistent rounding-under. Crimps that are not consistently rounded under the neck of the vial are considered a defect and shall be culled from the lot.

7.2.3 Loose crimps. Crimps that are loose are considered a defect and shall be culled from the lot.

7.3 Product Irregularities and Defects

7.3.1 Particulate material. Particulate material including "floaters", "sinkers", fibers or other foreign material is considered a defect and shall be culled from the lot.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

7.3.2 Cloudiness. Atypical cloudiness is considered a defect and shall be culled from the lot.

NOTE: Certain products (e.g. emulsions, suspensions) which under normal conditions appear cloudy should not be rejected unless the cloudiness is atypical, as would be the result of contamination, et cetera.

7.4 Fill Irregularities and Defects

7.4.1 Overfills and underfills. Vials determined visually to be overfilled or underfilled are considered a defect and shall be culled from the lot.

8.0 Cryovial Defects

NOTE: Cryovials and their closures may possess a variety of irregularities that may or may not affect a product's integrity. Irregularities that may have a detrimental effect on a product are considered defects and are culled from the lot. Defects are categorized as minor, major and critical based on their potential to impact the product (see **Attachment 3 and 4**).

8.1 Cryovial Irregularities and Defects

8.1.1 Scuffing and scratches. Scuffing and minor scratches are not considered a defect and are not culled from the lot.

8.1.2 Physical deformities. Dents and other physical deformities are considered a defect and shall be culled from the lot.

8.1.3 Internal plastic strands or plastic particles. Internal plastic strands or plastic particles are considered a defect and shall be culled from the lot.

8.1.4 Cracks. Cracks are considered a defect and shall be culled from the lot.

8.1.5 Cryovial residue. Residue on the inside or the outside of the cryovial is considered a defect and shall be culled from the lot.

8.2 Cap Irregularities and Defects

8.2.1 Physical deformities. Caps missing gaskets, damaged threads or other physical deformities are considered a defect and shall be culled from the lot.

8.2.2 Loose caps. Caps that will not thread properly or are otherwise loose are considered a defect and shall be culled from the lot.

8.3 Product Irregularities and Defects

8.3.1 Particulate material. Particulate material including "floaters", "sinkers", fibers or other foreign material are considered a defect and shall be culled from the lot.

8.3.2 Cloudiness. Atypical cloudiness is considered a defect and shall be culled from the lot.

NOTE: Certain products (emulsions, suspensions) which under normal conditions appear cloudy should not be rejected unless the cloudiness is atypical as would be the result of contamination, et cetera.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

8.4 Fill Irregularities and Defects

8.4.1 Overfills and underfills. Cryovials visually determined to be overfilled or underfilled are considered a defect and shall be culled from the lot.

9.0 Lyophilized Products in Glass Vials

NOTE: Lyophilized products present inspection challenges that are not encountered with liquid filled vials. The product is usually in the form of a dry "cake" at the bottom of the vial. The Director of Manufacturing and QA shall be notified of any vials exhibiting discoloration, meltback/collapse, missing or shredded cakes, or other irregularities. An investigation may be necessary. Most cake related defects are considered critical.

Sample lyophilized vials should be provided by the Project Scientist as example vials for use by inspectors during inspection. Whenever possible, examples of acceptable cakes and non-acceptable cakes should be provided.

9.1 Vial Irregularities and Defects

9.1.1 Inspect vials as per Section 7.1 and 7.2 above.

9.2 Product Irregularities and Defects

9.2.1 Particulate material. Particulate material including "floaters" (visible on the top of the cake), "sinkers" (visible by looking through the bottom of the vial), and fibers or other foreign material that can be viewed through the sides of the vials are defects and shall be culled from the lot.

9.2.2 Discoloration and/or irregular cake appearance. Atypical appearance, such as cake discoloration, altered matrix/crystal structure, or irregular shape, thickness, etc., that differs from the expected appearance is considered a defect and shall be culled from the lot.

9.2.3 Meltback and collapse. Meltback/collapse usually results from insufficient water being removed from the product. If there was only a limited amount of moisture present, the cake can appear to be shorter, compressed, lopsided, or have depressions/holes in them. Greater amounts of moisture can result in what looks like dried amorphous material in the bottom of the vial. Occasionally, meltback can be expressed as small flat hard disks (buttons) at the bottom of the vial. The cake will usually appear dry. Any vials exhibiting meltback or collapse are defective and culled from the lot.

9.2.4 Missing or shredded cake. Some products require low solute concentration formulation buffers. Such products often have very light weight, "fluffy" or tenuous cakes that fail to hold together or stay in the vial. If it appears that all or part of the cake is missing and cannot be accounted for elsewhere in the vial, then such vials shall be culled from the lot. A missing cake may also be the result of product not being filled into the vial.

9.2.5 Irregular cake size. Vials determined visually to have a difference in cake height (too large or too small) are considered defective and shall be culled from the lot. Variation in cake size may be the result of overfilling the vial, under filling the vial and no product filled into the vial.

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

10.0 Documentation

10.1 Completed Forms **15113-01, 15113-02** (when needed for glass vials), **Forms 15113-03, and 15113-04** (when needed for cryovials), and **Forms 15113-05 and 15113-06** (when needed for lyophilized product vials). Form 15113-07 is completed for lyophilized products, glass and cryovials. All completed forms are attached to the BPR.

10.2 Any investigations required are to be documented and included as part of the BPR or a reference added as to where the investigation documentation is located

11.0 Attachments

11.1 **Attachment 1** Form 15113-01, Inspection of Unlabeled Vials of Finished Product Manufacturing and Process Analytics Inspection

11.2 **Attachment 2** Form 15113-02, Inspection of Unlabeled Vials of Finished Product Quality Assurance Inspection

11.3 **Attachment 3** Form 15113-03, Inspection of Unlabeled **Cryovials** of Finished Product Manufacturing and Process Analytics Inspection

11.4 **Attachment 4** Form 15113-04, Inspection of Unlabeled **Cryovials** of Finished Product Quality Assurance Inspection

11.5 **Attachment 5** Form 15113-05, Inspection of Unlabeled **Lyophilized** Vials Finished Product Manufacturing and Process Analytics Inspection

11.6 **Attachment 6** Form 15113-06, Inspection of Unlabeled **Lyophilized** Vials Finished Product Quality Assurance Inspection

11.7 **Attachment 7** Form 15113-07, Inspection of Unlabeled Containers of Finished Product Total Lot Defects

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

Attachment 1 – Form 15113-01
Inspection of Unlabeled Vials of Finished Product Manufacturing and Process Analytics Inspection

FNLCR, BDP
Form No.: 15113-01
SOP No.: 15113
Revision 09: JUN 08 2021

Product Description_____

Part #_____ Lot #_____

INSPECTION OF UNLABELED VIALS OF FINISHED PRODUCT
MANUFACTURING AND PROCESS ANALYTICS / QUALITY CONTROL INSPECTION

Inspection Type (Circle one) Standard Focused Additional Criteria - with attached memo

Pan Identification (Sub Lot ID)_____ Number of Vials Received from Fill Area_____		MANUFACTURING VIAL INSPECTION # Vials Inspected:_____			PROCESS ANALYTICS/ QUALITY CONTROL VIAL INSPECTION # Vials Inspected: _____					
		DEFECT CATEGORY			*DEFECT CATEGORY*					
VIAL DEFECT DESCRIPTION		*Minor*	*Major*	*Critical*	*Minor*	*Major*	*Critical*			
VIALS	Pitting - Significant	N/A		N/A	N/A		N/A			
	Internal Glass strands, particles ("fisheyes")	N/A	N/A		N/A	N/A				
	Cracks/ Chips	N/A	N/A		N/A	N/A				
	Vials – Residue outside		N/A	N/A		N/A	N/A			
	Vials – Residue inside	N/A	N/A		N/A	N/A				
CLOSURE	Crimps – Physical deformities		N/A	N/A		N/A	N/A			
	Crimps – inconsistent "rounding-under"		N/A	N/A		N/A	N/A			
	Crimps – loose	N/A		N/A	N/A		N/A			
PRODUCT	Particulate mat 'l– floaters, sinkers, fibers, foreign mat 'l	N/A	N/A		N/A	N/A				
	Cloudiness (atypical)	N/A	N/A		N/A	N/A				
FILL	Overfills		N/A	N/A		N/A	N/A	**Total PA/QC Rejects**	**PA/QC AQL Defect Limits**	**TOTAL DEFECTS** (Manuf. and PA/QC)
	Underfills	N/A		N/A	N/A		N/A			
VIAL INSPECTION TOTAL DEFECTS			N/A	N/A		N/A	N/A			
		N/A		N/A	N/A		N/A			
		N/A	N/A		N/A	N/A				

Equipment 1 - Black/White tiles w/ light source 2 - Magnifier with light 3 - Microscope 4 - Light Box w/ Black/White surface 5 - Eisai station

INSPECTED BY/DATE (Indicate inspection equipment used by number)	*Manufacturing Inspectors*
	PA/QC Inspectors

PA/QC Inspection AQL Defect Limits

Lot Size (circle)	Sample Size	Minor Defect AQL = 6.5	Major Defect AQL = 1.5	Critical Defect AQL = 0.1
2 to 8	2	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**
9 to 15	3	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**
16 to 25	5	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**
26 to 50	8	Accept with 1 Reject with **2**	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**
51 to 90	13	Accept with 2 Reject with **3**	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**
91 to 150	20	Accept with 3 Reject with **4**	Accept with 0 Reject with **1**	Accept with 0 Reject with **1**
151 to 280	32	Accept with 5 Reject with **6**	Accept with 1 Reject with **2**	Accept with 0 Reject with **1**
281 to 500	50	Accept with 7 Reject with **8**	Accept with 2 Reject with **3**	Accept with 0 Reject with **1**

PA/QC EVALUATION: by (name) _____ (date) _____

_____ Inspection results ACCEPTABLE, Sublot may proceed to labeling (QA inspection not required)

_____ 100% QA inspection of sublot required before labeling, investigation required. AQL was exceeded (Reject number reached or exceeded) for major / minor / critical defects (circle applicable) listed in table above.

COMMENTS:

_____

_____

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Attachment 2 – Form 15113-02
Inspection of Unlabeled Vials of Finished Product Quality Assurance Inspection

FNLCR, BDP
Form No.: 15113-02
SOP No.: 15113
Revision 09: JUN 08 2021

LOT:
SUBLOT:
NUMBER VIALS RECEIVED FROM INSPECTION AREA: ____

INSPECTION OF UNLABELED VIALS OF FINISHED PRODUCT
QUALITY ASSURANCE INSPECTION

GENERAL INFORMATION

PROJECT #	
PRODUCT DESCRIPTION	
INSPECTION TYPE	Standard / Focused / Additional Criteria (circle)

Inspection Equipment:
1 – Black / white tiles w/ light source
2 – Magnifier with light
3 – Microscope
4 – Light Box with Black / White surfaces
5 – Inspection Station (Eisai)

INSPECTION RESULTS

DEFECT DESCRIPTION		**QUALITY ASSURANCE INSPECTION** # Vials Inspected:_____		
		DEFECT CATEGORY		
		Minor	*Major*	*Critical*
VIALS	Pitting - Significant			
	Internal Glass strands, particles ("fisheyes")			
	Cracks/ Chips			
	Vials – Residue outside			
	Vials – Residue inside			
CLOSURE	Crimps – Physical deformities			
	Crimps – inconsistent "rounding-under"			
	Crimps – loose			
PRODUCT	Particulate mat'l– floaters, sinkers, fibers, foreign mat'l			
	Cloudiness (atypical)			
FILL	Overfills			
	Underfills			
DEFECTS	**Minor**			
	Major			
	Critical			
INSPECTED BY/DATE (Indicate inspection equipment used by number)				

COMMENTS:

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

Attachment 3 – Form 15113-03
Inspection of Unlabeled Cryovials of Finished Product Manufacturing and Process Analytics Inspection

FNLCR, BDP
Form No.: 15113-03
SOP No.: 15113
Revision 09: JUN 08 2021

Product Description_____

Part #_____ Lot #_____

INSPECTION OF UNLABELED CYROVIALS OF FINISHED PRODUCT MANUFACTURING AND PROCESS ANALYTICS / QUALITY CONTROL INSPECTION

Inspection Type (Circle one) Standard Focused Additional Criteria - with attached memo

		MANUFACTURING VIAL INSPECTION # Vials Inspected:_____			PROCESS ANALYTICS/ QUALITY CONTROL VIAL INSPECTION # Vials Inspected: _____					
Pan Identification (Sub Lot ID)_____ **Number of Vials Received from Fill Area_____**		*DEFECT CATEGORY*			*DEFECT CATEGORY*					
VIAL DEFECT DESCRIPTION		*Minor*	*Major*	*Critical*	*Minor*	*Major*	*Critical*			
VIALS	Pitting - Significant	N/A		N/A	N/A		N/A			
	Internal Glass strands, particles ("fisheyes")	N/A	N/A		N/A	N/A				
	Cracks/ Chips	N/A	N/A		N/A	N/A				
	Vials – Residue outside		N/A	N/A		N/A	N/A			
	Vials – Residue inside	N/A	N/A		N/A	N/A				
CLOSURE	Crimps – Physical deformities		N/A	N/A		N/A	N/A			
	Crimps – inconsistent "rounding-under"		N/A	N/A		N/A	N/A			
	Crimps – loose	N/A		N/A	N/A		N/A			
PRODUCT	Particulate mat 'l– floaters, sinkers, fibers, foreign mat 'l	N/A	N/A		N/A	N/A				
	Cloudiness (atypical)	N/A	N/A		N/A	N/A				
FILL	Overfills		N/A	N/A		N/A	N/A	**Total PA/QC Rejects**	**PA/QC AQL Defect Limits**	**TOTAL DEFECTS** (Manuf. and PA/QC)
	Underfills	N/A		N/A	N/A		N/A			
VIAL INSPECTION TOTAL DEFECTS			N/A	N/A		N/A	N/A			
		N/A		N/A	N/A		N/A			
		N/A	N/A		N/A	N/A				

Equipment 1-Black/White tiles w/ light source 2-Magnifier with light 3-Microscope 4-Light Box w/ Black/White surface 5-Eisai station

INSPECTED BY/DATE (Indicate inspection equipment used by number)	*Manufacturing Inspectors*
	PA/QC Inspectors

PA/QC Inspection AQL Defect Limits

Lot Size (circle)	Sample Size	Minor Defect AQL = 6.5	Major Defect AQL = 1.5	Critical Defect AQL = 0.1
2 to 8	2	Accept with 0 Reject with 1	Accept with 0 Reject with 1	Accept with 0 Reject with 1
9 to 15	3	Accept with 0 Reject with 1	Accept with 0 Reject with 1	Accept with 0 Reject with 1
16 to 25	5	Accept with 0 Reject with 1	Accept with 0 Reject with 1	Accept with 0 Reject with 1
26 to 50	8	Accept with 1 Reject with 2	Accept with 0 Reject with 1	Accept with 0 Reject with 1
51 to 90	13	Accept with 2 Reject with 3	Accept with 0 Reject with 1	Accept with 0 Reject with 1
91 to 150	20	Accept with 3 Reject with 4	Accept with 0 Reject with 1	Accept with 0 Reject with 1
151 to 280	32	Accept with 5 Reject with 6	Accept with 1 Reject with 2	Accept with 0 Reject with 1
281 to 500	50	Accept with 7 Reject with 8	Accept with 2 Reject with 3	Accept with 0 Reject with 1

PA/QC EVALUATION: by (name) _____ (date) _____

_____ Inspection results ACCEPTABLE, Sublot may proceed to labeling (QA inspection not required)

_____ 100% QA inspection of sublot required before labeling, investigation required. AQL exceeded (Reject number reached or exceeded) for major / minor / critical defects (circle applicable) listed in table above.

COMMENTS:

_____

_____

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

Attachment 4 – Form 15113-04
Inspection of Unlabeled Cryovials of Finished Product Quality Assurance Inspection

FNLCR, BDP
Form No.: 15113-04
SOP No.: 15113
Revision 09: JUN 08 2021

LOT:
SUBLOT:
NUMBER CRYOVIALS RECEIVED FROM INSPECTION AREA: _____

INSPECTION OF UNLABELED CRYOVIALS OF FINISHED PRODUCT QUALITY ASSURANCE INSPECTION

GENERAL INFORMATION

PROJECT #	
PRODUCT DESCRIPTION	
INSPECTION TYPE	Standard / Focused / Additional Criteria (circle)

Inspection Equipment:
1 – Black / white tiles w/ light source
2 – Magnifier with light
3 – Microscope
4 – Light Box with Black / White surfaces
5 – Inspection Station (Eisai)

INSPECTION RESULTS

DEFECT DESCRIPTION		**QUALITY ASSURANCE INSPECTION** # Vials Inspected:_____		
		DEFECT CATEGORY		
		Minor	*Major*	*Critical*
CRYOVIALS	Pitting - Significant			
	Internal Glass strands, particles ("fisheyes")			
	Cracks/ Chips			
	Vials – Residue outside			
	Vials – Residue inside			
CLOSURE	Caps – Physical deformities			
	Caps – loose			
PRODUCT	Particulate mat'l– floaters, sinkers, fibers, foreign mat'l			
	Cloudiness (atypical)			
FILL	Overfills			
	Underfills			
DEFECTS	**Minor**			
	Major			
	Critical			
INSPECTED BY/DATE (Indicate inspection equipment used)				

COMMENTS:

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

Attachment 5 – Form 15113-05
Inspection of Unlabeled Lyophilized Vials Finished Product Manufacturing and Process Analytics Inspection

FNLCR, BDP
Form No.: 15113-05
SOP No.: 15113
Revision 09: JUN 08 2021

Product Description_____

Part #_____ Lot #_____

INSPECTION OF UNLABELED LYOPHILIZED VIALS OF FINISHED PRODUCT MANUFACTURING AND PROCESS ANALYTICS / QUALITY CONTROL INSPECTION

Inspection Type (Circle one) Standard Focused Additional Criteria - with attached memo

Pan Identification (Sub Lot ID)_____

Number of Vials Received from Fill Area_____

VIAL DEFECT DESCRIPTION		MANUFACTURING VIAL INSPECTION # Vials Inspected:_____ DEFECT CATEGORY Minor	Major	Critical	PROCESS ANALYTICS/ QUALITY CONTROL VIAL INSPECTION # Vials Inspected: _____ DEFECT CATEGORY Minor	Major	Critical	Total PA/QC Rejects	PA/QC AQL Defect Limits	TOTAL DEFECTS (Manuf. and PA/QC)
VIALS	Pitting - Significant	N/A		N/A	N/A		N/A			
	Internal Glass strands, particles ("fisheyes")	N/A	N/A		N/A	N/A				
	Cracks/ Chips	N/A	N/A		N/A	N/A				
	Vials – Residue outside		N/A	N/A		N/A	N/A			
	Vials – Residue inside	N/A	N/A		N/A	N/A				
CLOSURE	Crimps – Physical deformities		N/A	N/A		N/A	N/A			
	Crimps – inconsistent "rounding-under"		N/A	N/A		N/A	N/A			
	Crimps – loose	N/A		N/A	N/A		N/A			
PRODUCT	Particulate mat 'l– floaters, sinkers, fibers, foreign mat 'l	N/A	N/A		N/A	N/A				
	Cloudiness (atypical)	N/A	N/A		N/A	N/A				
FILL	Overfills		N/A	N/A		N/A	N/A			
	Underfills	N/A		N/A	N/A		N/A			
VIAL INSPECTION TOTAL DEFECTS			N/A	N/A		N/A	N/A			
		N/A		N/A	N/A		N/A			
		N/A	N/A		N/A	N/A				

Equipment 1 - Black/White tiles w/ light source 2 - Magnifier with light 3 - Microscope 4 - Light Box w/ Black/White surface 5 - Eisai station

INSPECTED BY/DATE (Indicate inspection equipment used by number)

Manufacturing Inspectors

PA/QC Inspectors

PA/QC Inspection AQL Defect Limits

Lot Size (circle)	Sample Size	Minor Defect AQL = 6.5	Major Defect AQL = 1.5	Critical Defect AQL = 0.1
2 to 8	2	Accept with 0 Reject with 1	Accept with 0 Reject with 1	Accept with 0 Reject with 1
9 to 15	3	Accept with 0 Reject with 1	Accept with 0 Reject with 1	Accept with 0 Reject with 1
16 to 25	5	Accept with 0 Reject with 1	Accept with 0 Reject with 1	Accept with 0 Reject with 1
26 to 50	8	Accept with 1 Reject with 2	Accept with 0 Reject with 1	Accept with 0 Reject with 1
51 to 90	13	Accept with 2 Reject with 3	Accept with 0 Reject with 1	Accept with 0 Reject with 1
91 to 150	20	Accept with 3 Reject with 4	Accept with 0 Reject with 1	Accept with 0 Reject with 1
151 to 280	32	Accept with 5 Reject with 6	Accept with 1 Reject with 2	Accept with 0 Reject with 1
281 to 500	50	Accept with 7 Reject with 8	Accept with 2 Reject with 3	Accept with 0 Reject with 1

PA/QC EVALUATION: by (name) _____ (date) _____

_____ Inspection results ACCEPTABLE, Sublot may proceed to labeling (QA inspection not required)

_____ 100% QA inspection of sublot required before labeling, investigation required. AQL exceeded (Reject number reached or exceeded) for major / minor / critical defects (circle applicable) listed in table above.

COMMENTS:

_____

_____

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

Attachment 6 – Form 15113-06
Inspection of Unlabeled Lyophilized Vials Finished Product
Quality Assurance Inspection

FNLCR, BDP
Form No.: 15113-06
SOP No.: 15113
Revision 09: JUN 08 2021

LOT:

SUBLOT:

NUMBER VIALS RECEIVED FROM FILL AREA: _____

INSPECTION OF UNLABELED LYOPHILIZED VIALS OF FINISHED PRODUCT
QUALITY ASSURANCE INSPECTION

GENERAL INFORMATION

PROJECT #	
PRODUCT DESCRIPTION	
INSPECTION TYPE	Standard / Focused / Additional Criteria (circle one)

Inspection Equipment:
1 – Black / white tiles w/ light source
2 – Magnifier with light
3 – Microscope
4 – Light Box with Black / White surfaces
5 – Inspection Station (Eisai)

INSPECTION RESULTS

DEFECT DESCRIPTION		QUALITY ASSURANCE INSPECTION		
		DEFECT CATEGORY		
		Minor	*Major*	*Critical*
VIALS	Pitting - Significant			
	Internal Glass strands, particles ("fisheyes")			
	Cracks/ Chips			
	Vials – Residue outside			
	Vials – Residue inside			
CLOSURE	Crimps – Physical deformities			
	Crimps – inconsistent "rounding-under"			
	Crimps – loose			
PRODUCT	Particulate mat'l– floaters, sinkers, fibers, foreign mat'l			
	Cake – discoloration or irregular appearance			
	Cake – meltback or collapse			
	Cake – missing, partial or shredded			
	Cake – irregularly large or small compared to other vials			
DEFECTS	**Minor**			
	Major			
	Critical			
INSPECTED BY/DATE (Indicate inspection equipment used by number)				

COMMENTS:

_____
_____
_____

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.

Attachment 7 – Form 15113-07
Inspection of Unlabeled Containers of Finished Product Total Lot Defects

FNLCR, BDP
Form No.: 15113-07
SOP No.: 15113
Revision 09: JUN 08 2021

LOT:
SUBLOT:

INSPECTION OF UNLABELED CONTAINERS OF FINISHED PRODUCT TOTAL LOT DEFECTS

GENERAL INFORMATION

PROJECT #				
PRODUCT DESCRIPTION				
INSPECTION TYPE	Standard / Focused / Additional Criteria (circle one)			
LOT QUANTITY				
Received from filling	-	**Total Defects**	=	**Total Acceptable Vials**

SUMMARY OF UNLABELED VIAL INSPECTION PROCESS

SUBLOT ID	**DEFECTS** (From Form 15113-01 or Form 15113-03 or Form 15113-5) **(Manufacturing + PA Screening)**			**DEFECTS** (From Form 15113-02 or 15113-04 or Form 15113-06) **(QA Screening)**			**TOTAL**	**% of TOTAL LOT QUANTITY**	**ALERT LIMITS (Exceeding limit requires investigation)**
	MINOR	**MAJOR**	**CRITICAL**	**MINOR**	**MAJOR**	**CRITICAL**			
TOTAL: MINOR									15%
TOTAL: MAJOR									10%
TOTAL: CRITICAL									2%
RECORDED BY/DATE:						**TOTAL**			

EVALUATION:

_____ No alert limit exceeded for this lot
_____ Alert Limit(s) exceeded for minor, major, critical (circle appropriate) defects. (Investigation required).

COMMENTS: _____

_____

MANUFACTURING REVIEW: _____ Date: _____

QA REVIEW: _____ Date: _____

This procedure is made available through federal funds from the National Cancer Institute, NIH, under contract 75N91019D00024.