CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214032Orig1s000

PRODUCT QUALITY REVIEW(S)

Office of Pharmaceutical Quality

NDA 214032

Integrated Quality Assessment Template

Table of Contents

QUALITY ASSESSMENT

.Recommendation: ***Approval with PMC***

NDA [214032]

ILLUCCIX (kit for the preparation of gallium Ga 68 gozetotide injection)

Review #[FINAL]

Drug Name/Dosage Form	ILLUCCIX (kit for the preparation of gallium Ga68 gozetotide injection); dosage form (sterile solution)
Strength(s)	(b) (4) MBq/mL ((b) (4) mCi/mL)
Route of Administration	IV injection
Rx/OTC Dispensed	Rx
Applicant	Telix Pharmaceuticals (US), Inc., Fishers, IN 46038
US agent, if applicable	N/A

SUBMISSION(S) REVIEWED (seq. no.)	DOCUMENT DATE	DISCIPLINE(S) AFFECTED
Original NDA 214032	9/23/2020	OPQ-CMC, Microbiology, Process/Facilities

Quality Review Team

DISCIPLINE	PRIMARY REVIEWER	SECONDARY REVIEWER
Drug Substance	Monica Cooper	Su Tran
Drug Product	John Amartey	Danae Christodoulou
Process/Facilities	Andrew Idzior	Vidya Pai
Microbiology	Laura Wasil	Yeissa Chabrier-Rosello
Environmental	John Amartey	Danae Christodoulou
RBPM	Anika Lalmansingh	N/A
Application Technical Lead	Eldon E. Leutzinger	N/A

Quality Review Data Sheet

1. RELATED/SUPPORTING DOCUMENTS

A. DMFs:

A relatively large panel of DMF are involved in NDA 214032. The identity and purpose served by these DMF's is enumerated in the reviews by Dr. John Amartey (primary reviewer), and so will not be included here, except for that of DMF (b) (4) for drug substance precursor (PSMA-11), determined to be adequate (4/30/2019) in support of NDA 214032. Those for the $^{68}Ge/^{68}Ga$ generators, Eckert & Ziegler GallioPharm (DMF 28741) and IRE Elit Eo (DMF 31715) are adequate (10/15/2014 and 5/04/2017, respectively). That for the Telix kit (DMF 32631) is adequate (7/20/2018).

B. Other Documents: *IND, RLD, or sister applications*

DOCUMENT	APPLICATION NUMBER	DESCRIPTION
IND	144421	Kit for the Preparation of Ga 68 PSMA-11
IND	130725	Endocyte in support of Telix kit
IND	133661	MSKCC in support of Telix kit

2. CONSULTS

DISCIPLINE	RECOMMENDATION	DATE	REVIEWER
N/A			

Executive Summary

I. Overall Recommendation on Approvability

OPQ recommends [**APPROVAL WITH PMC**] of NDA [214032] for commercialization of [ILLUCCIX/kit for the preparation of Ga68 gozetotide injection/ (b) (4) MBq/mL ((b) (4) mCi/mL)] with an expiration dating period of [4] hours at CRT USP, 25^{0}C (77^{0}F) in proposed container closure system.

- The applicant [has] provided adequate information on the proposed drug product to ensure the identity, strength, purity, and strength of the proposed drug product.
- The Office of Process and Facility has made a recommendation of [approval] for all the facilities involved in this application. (b) (4)
- The proposed labeling and labels [have] adequate information to meet the regulatory requirements.

II. Product Quality Review Context

Indication and Intended Population:
After radiolabeling with Ga-68, ILLUCCIX is (b) (4)

Regulatory Context - Designations:

Classification Code for NDA 214032:
The whole **issue of Code rests on what is the active ingredient, and what is the active moiety**.

In NDA 214032, we are approving the Telix "kit." The "kit" contains PSMA-11 as an active ingredient (not an active moiety). Since this is the first kit version of this product, **PSMA-11 is considered a "new active ingredient**."

When the Telix kit is radiolabeled, Ga-68-PSMA-11 becomes the active moiety, but that is the same as in previously approved NDAs 212642 and 212643. So, the Code for NDA 214032 cannot be Type 1 (NME).

Based on MAPP 2018.2, **NDA 214032 best fits Type 2 (New Active Ingredient), 5 (New Formulation or other differences).**

Scientifically, PSMA-11 is also considered a precursor to ^{68}Ga-PSMA-11. **But, once the kit is radiolabeled, the HBED-CC chelation section of the ligand sequesters the $^{68}Ga^{3+}$ cation resulting in formation of a metal-ligand coordination entity (^{68}Ga-PSMA-11) that is the "active moiety."**

This metal-ligand coordination entity, ***HBED($^{68}Ga^{3+}$)-CC-Ahx-Lys(OH)-CO-Glu(OH))***, contains a Urea-Based PSMA inhibitor and thereby becomes the substance "*intended to furnish pharmacological activity or other direct effect in the diagnosis, cure, …of disease…*" (21 CFR 314.3)], in other words ^{68}Ga-PSMA-11 is the **Drug Substance**.

Based on this regulatory definition, 21 CFR 314.3, it is saying that ^{68}Ga-PSMA-11 is the Drug Substance. That it is indeed the Drug Substance is clear from the science, providing a sound basis upon which the regulatory definition can meaningfully be applied to ^{68}Ga-PSMA-11 (ATL).

(b) (4)

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(b) (4)

[redacted]

Regulatory Context - Regulatory Status of the Precursor:
Because the radiolabeled entity is produced *in situ* during production of the drug product, it is not isolated, purified (in isolated form) and characterized as such as it would be for a conventional drug. **Consequently, radiochemical identity in the analytical quality controls can be established only indirectly. This also impacts strength and specific activity determinations, outcomes that create a chain-effect ultimately transferred to the patient dose, consequently intensifying the criticality of the Precursor, PSMA-11**. Additionally, the short half-life of the radionuclide (^{68}Ga, 68 min) imposes challenges (b) (4)

[redacted]

The precursor is the nearest intermediate to the drug substance in the radiolabeling reaction scheme that is readily accessible. But, reliance on the precursor in this context greatly heightens its criticality because of its potential as a conduit for bringing into the final drug product impurity substances originating from the precursor synthesis pathway. **Hence, joint with all the foregoing considerations, this places the precursor into a pivotal role, raising the necessity for its scrutiny at the level of an API.**

Regulatory Context – Regulatory Status of the ^{68}Ge/^{68}Ga Generator and Cyclotron:
(**Generator**)

- Eckert & Ziegler GallioPharm (Radiopharma GmbH).

Determined previously to be adequate in another NDA (DMF 28741)

- IRE Elit Eo Ge-68/Ga-68 Generator (DMF 031715)

(**Cyclotron**)
GE FASTlab

Product Profile and Critical Quality Attributes (CQA's):
The NDA is for a Kit for the Preparation of Ga 68 PSMA-11. **The kit comes in 2 configurations, each of 3 vials**:

- [redacted] vial
- [redacted] Acetate Buffer vial
  [redacted] 150 mg of anhydrous sodium acetate [redacted]
- [redacted] (empty)

The kit can be used with $^{68}GaCl_3$ from either a generator or cyclotron and radiolabeled to contain up to 50 mCi of ^{68}Ga-activity.

Each final product vial contains up to 50 mCi of ^{68}Ga activity (^{68}Ga-PSMA-11), 25 µg of PSMA-11, 10 µg of D-Mannose, 150 mg of Sodium Acetate, [redacted]

The container closure system is a clear 10 mL USP [redacted] glass vial [redacted] and closed with a [redacted] rubber lyophilization stopper [redacted] and an aluminum seal with flip-off cap.

(**CQA's**)
The Critical Quality Attributes for the PSMA-11 (precursor) and kit are described in DMF [redacted]). Those for the final drug product are the standard package typical for all radiopharmaceuticals, and any that rise to the level of uniqueness for the PSMA-11 chemical system is addressed under the next section (Areas of Unique Focus).

Areas of Unique Focus:
The approved ^{68}Ga-radiopharmaceuticals built from Ga-ligand coordination entities are **ready-to-use drugs** provided in multidose vials and commercially produced. By comparison, this will be the first adaptation of ^{68}Ga-PSMA-11 to **kit-production** in the radiopharmacy, i.e. where PSMA-11 comes to the radiopharmacy as a **kit** and can be radiolabeled there (on demand) by either generator-derived or cyclotron-derived $^{68}GaCl_3$. For perspective, the following is a summary of the ground covered since the emergence of ^{68}Ga as a radionuclide in the radiopharmaceutical landscape, showing the relationships among the key players (^{68}Ge, ^{68}Ga, ^{68}Zn) in their various positions.

[redacted]

(b) (4)

[redacted]

III. Summary of Quality Assessments

Drug Substance

Recall that ***HBED($^{68}Ga^{3+}$)-CC-Ahx-Lys(OH)-CO-Glu(OH)*** is identified as the entity that furnishes the "action" expected of a **drug substance** in a radiopharmaceutical. However, because it is produced *in situ* and not isolated, it cannot be characterized as

in conventional drugs. As a result, the integrity of the drug substance (radiochemical identity and purity) can be established only indirectly through quality control of the final drug product and the precursor. These circumstances impact strength and specific activity determinations, outcomes that create a chain-effect ultimately transferred to the patient dose.

Hence, the Precursor (***HBED-CC-Ahx-Lys(OH)-CO-Glu(OH***) occupies a pivotal role because it is the nearest intermediate in the radiolabeling reaction scheme that is readily assessable, intensifying its criticality and, raising its controls to the level of scrutiny for an API (see Regulatory Context – Regulatory Status of the Precursor). These considerations have the effect of elevating the Precursor to drug substance to a prominent position within this section. **However, there were no issues identified for the precursor, as determined through review of DMF (b) (4) by Dr. Monica Cooper, 4/06/2021.**

Drug Product

Many of the issues identified for drug product are in relation to the validation batches (b) (4) Some of these issues also include specifications, analytical methods, and stability, summarized within the following categories.

(b) (4)

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(b) (4)

An amendment was received on 9/20/2021 (covering information requests of 9/17/2021 and 9/13/2021) to address the issues of (b) (4) content. This was determined to be a major amendment, extending the clock to 12/23/2021. Additionally, FDA requested CMC information on 12/10/2021 (email IR) to which Telix responded that the additional information ((b) (4) content determination (b) (4)) requested will be provided on 2/28/2022.

PMC:
In conjunction with this, completion of the request (b) (4) (b) (4) was made post-approval (PMC #1), along with PMC #2 (additional sterility data for product produced from $^{68}GaCl_3$ eluate from aged generators (within 1 month of expiry). The language for the PMC in the approval letter is as follows:

4176-1 Provide additional data for (b) (4) to show consistency in the values reported and perform 100% sampling of the manufactured batches

if inconsistencies are observed. Provide a validated method (b) (4)

The timetable you submitted on November 11, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 02/22

4176-2 Provide additional sterility data for gallium Ga 68 gozetotide injection product batches made with Ga 68 chloride eluate from aged generators (within 1 month of expiry) to demonstrate that eluates from aged generators do not impact the sterility of the final radiolabeled product.

The timetable you submitted on November 11, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 04/22

Labeling

Labeling comments were sent to the applicant on 11/23/2021 covering a several items including PI (flow charts for clarity, etc.), inclusion of missing information in the description of the process/flow charts, missing information in the Configurations (A and B), and the cartons (A and B). Reponses have been received and the applicant has agreed to make the requisite changes or additions. Label comments (vial, syringe went to the applicant on 12/06/2021, and an edited PI to the applicant on 11/30/2021.

Microbiology

Multiple issues were identified for microbiology during review of the NDA, and the overall evaluation is indicated as inadequate (Laura R. Wasil, Ph.D.), 3/29/2021, based on the remaining deficiencies (b) (4) as described in the microbiology review. Many of these issues have been resolved, but what remains pertains to minor issues (b) (4) Other issues include radiolabeling data that is currently under review.

The microbiology review of DMF (b) (4) (Laura R. Wasil, Ph.D.), 3/10/2020, found the (b) (4) There are no remaining microbiology issues (**Resolved**).

Manufacturing Facilities

Based on the review of Andrew Idzior, Ph.D., OPQ/OPMA, the facilities are determined to be adequate (12/06/2021). From this review, in summary the "**facilities are acceptable based on compliance status, inspection history, and experience with the proposed operations. The facilities review risks were mitigated by two 704(a)**

document reviews, a pre-approval inspection and a PMC agreement with the applicant."

The (b) (4) the details of which are discussed in the OPMA review of 12/08/2021 along with the remaining facilities involving the 740(a) document reviews and pre-approval inspections.

Biowaver

A bridging issue has arisen between the proposed drug in NDA 214032 and the reference listed drug. As a consequence, a Biopharm IR has been drafted to address this issue. Basically, what it relates is that **the bridging approach to the reference drug product (Gallium Ga 68 PSMA-11, NDA 212643) via 21 CFR 320.24(b)(6) has not been adequately established**. In summary, the IR is requesting (1) comparative physicochemical properties, (2) a formulation comparison and (3) any other information deemed reasonable to establish bridging. This IR was conveyed to the applicant 6/21/2021 (by email).

IV. Final Analysis of Product Quality Review Issues (~200 words per issue)

There are no outstanding issues remaining from the standpoint of CMC (precursor to the drug substance, drug product, microbiology, facilities). Based on the review of Andrew Idzior, Ph.D., OPQ/OPMA, the facilities are determined to be adequate (12/08/3021). From this review, in summary the "facilities are acceptable based on compliance status, inspection history, and experience with the proposed operations. The facilities review risks were mitigated by two 704(a) document reviews, a pre-approval inspection and a PMC agreement with the applicant."

V. Summary Basis for Product Quality Recommendation (150 words)

Together with a PMC (b) (4) the applicant has provided adequate information to ensure the identity, strength, and purity of the proposed drug product.

VI. Lifecycle Considerations. N/A

VII. **Draft Text for Postmarketing Commitment**

4176-1 Provide additional data for (b) (4) to show consistency in the values reported and perform 100% sampling of the manufactured batches if inconsistencies are observed. Provide a validated method (b) (4)

The timetable you submitted on November 11, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 02/22

4176-2 Provide additional sterility data for gallium Ga 68 gozetotide injection product batches made with Ga 68 chloride eluate from aged generators (within 1 month of expiry) to demonstrate that eluates from aged generators do not impact the sterility of the final radiolabeled product.

The timetable you submitted on November 11, 2021, states that you will conduct this study according to the following schedule:

Final Report Submission: 04/22

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Labeling Review (NDA214032)

R Regional Information

1.14 Labeling

The established name of the radiolabeled drug product is gallium Ga 68 gozetotide. Gozetotide is also known as PSMA-11.

#3: Dosage Form and Strengths

ILLUCCIX is supplied as a [redacted] kit for the preparation of gallium Ga-68 gozetotide for intravenous use. Each kit contains:

- **Vial 1** ([redacted] gozetotide vial) 25 mcg of gozetotide and 10 mcg of D-mannose.
- **Vial 2** (Acetate buffer vial) 150 mg anhydrous sodium acetate in HCl buffer, provided as either [redacted] depending on Ga-68 source used.
- **Vial 3:** (Vacuumed reaction vial) A sterile, evacuated vial [redacted] serves as the collection vial for Ga-68 chloride [redacted]

Ga-68 [redacted] is obtained from one of the following sources:

- Cyclotron [redacted] GE FASTlab [redacted]
- Eckert & Ziegler GalliaPharm Ge-68/Ga-68 generator.
- IRE Galli-Eo Ge-68/Ga-68 generator.

[redacted]

#11: Description

Gallium-68 gozetotide is a radioconjugate composed of a human prostate specific membrane antigen (PSMA) targeting ligand peptide conjugated via the acyclic radiometal chelator, N,N'-bis [2-hydroxy-5-(carboxyethyl)benzyl]ethylenediamine-N,N'-diacetic acid (HBED-CC) to the radioisotope Ga-68. The amino acid sequence of the gozetotide peptide is Glu-NH-CO-NH-Lys(Ahx), [redacted]

(b) (4)

(Ahx = 6-amino hexanoic acid). Ga-68 gozetotide has a molecular weight of 1011.9 g/mol and the chemical structure is shown in figure (b) (4)

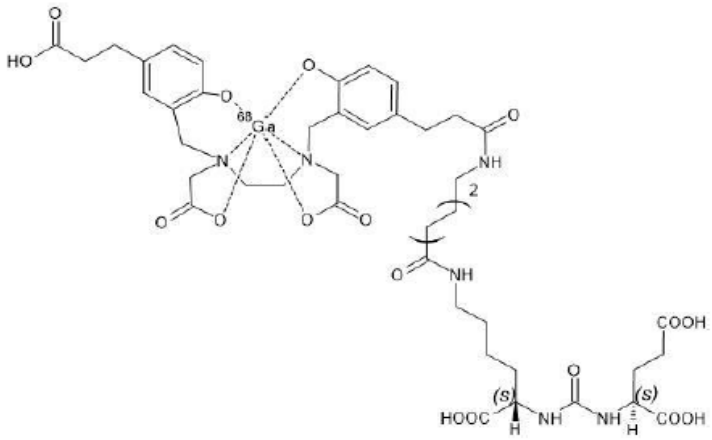

Figure (b) (4) Chemical Structure of gallium Ga 68 gozetotide

ILLUCCIX is supplied as a 3-vial kit which contains non-radioactive ingredients needed to produce Ga-68 gozetotide Injection. There are two (b) (4) configurations available for preparation of Ga-68 gozetotide using Ga-68 from different generators or cyclotron sources. The (b) (4) Ga-68 gozetotide Injection for intravenous use is a sterile, pyrogen free, clear, colorless solution with a pH between 4.0 to 5.0.

Table (b) (4) Principal Radiation Emission Data (>1%)

Radiation/ Emission	% Disintegration	Mean Energy (MeV)
beta+	88%	0.8360
beta+	1.1%	0.3526
gamma	178%	0.5110
gamma	3%	1.0770
X-ray	2.8%	0.0086
X-ray	1.4%	0.0086

Table (b) (4) Radiation Attenuation of 511 keV Photons by Lead (Pb) Shielding

Shield Thickness (Pb) mm	Coefficient of Attenuation

6	0.5
12	0.25
17	0.1
34	0.01
51	0.001

Table (b) (4) Physical Decay Chart for Gallium Ga-68

Minutes	Fraction Remaining
0	1.000
15	0.858
30	0.736
60	0.541
90	0.398
120	0.293
180	0.158
360	0.025

 # 16: How supplied/Storage and Handling (21CFR 201.57(c)(17)

ILLUCCIX is supplied as a (b) (4) kit for preparation of gallium Ga-68 gozetotide. There are two different kit configurations (b) (4), each containing three vials. The quantitative contents of the components are listed. The description of the components in general is adequate.

Comment: The applicant described the components of each of the configurations, however, the **Vial 3** (b) (4) is also the radiolabeling reaction vial and this should be described such as: " Sterile Vacuumed Reaction Vial"

Store gallium Ga-68 gozetotide injection upright (b) (4) at (b) (4) temperature. (25ºC (77ºF); excursions permitted to 15ºC to 30ºC (59ºF to 86ºF). Use gallium Ga 68 gozetotide injection within 4 hours after preparation. (b) (4) (b) (4)

Comment: Confirm that excursions permitted for the storage temperature of gallium Ga-68 PSMA-11 injection such as "25ºC (77ºF); excursions permitted to 15ºC to 30ºC (59ºF to 86ºF".

LABELS:

Labels with the respective NDC numbers are provided.

Carton and container labels are provided.

2.4 Drug Preparation

Comments: (resolved in the PI)

1. The generator elution, dilution and radiolabeling using the GalliaPharm generator should be separated from the use of the IRE ELIT Galli Eo generator. The flow charts should be revised and separated accordingly to show a complete reconstitution process for each generator. This is recommended for clarity and to avoid confusion of the processes since the buffer volumes for configuration A and B differ.

2. The eluent (0.1 M HCl) volumes for the GalliaPharm and IRE ELiT generators differ and should be indicated in the description of the elution process as well as in the flow charts.

3. Indicate the volume of acetate buffer used in configuration A and B in the flow chart.

4. In the revised flow chart indicate that **configuration A** is used for GalliaPharm generator and **configuration B** for the IRE ELIT generator.

5. Provide similar revision for the cyclotron sourced Ga-68 reconstitution process.

6. The flow chart for the cyclotron sourced Ga-68 should indicate the 5 mL volume of the $^{68}GaCl_3$ solution obtained from the FASTLab module and used for the reconstitution process. Explain clearly how the [^{68}Ga]$GaCl_3$ solution is transferred into Vial 3. Additionally, confirm that only the GE FASTlab will be utilized for the Gallium 68 chloride isolation process.

7. The applicant described the components of each of the configurations in **section 16,** however, the **Vial 3** (b) (4) is also the radiolabeling reaction vial and this should be described as **"Sterile Vacuumed Reaction Vial"** throughout the labeling.

8. Additionally, the Acetate buffer vial used for the cyclotron sourced Ga-68 should clearly be identified as **Configuration A** in the flow chart.

Specific comments and recommendations:

These comments are to be addressed by the applicant in the final labeling

Preparation:

- **step c.** Add specification for Ge-68 breakthrough for the generators (<0.001%) and testing on weekly basis. For the cyclotron produced Ga-68 test for Ga-67 and Ga-66 (with specification of <2% combined total) when a new Zn-68 lot is introduced for manufacturing.
- **Step d**: The radioactive label should include identify of the product with information such as lot#, date, etc.
- **Step g**: **see comment 10# above**.
- **Step j**: "continue with the dilution and [redacted] below".

Reconstitution:

- **Step 4**: for the E&Z generator should be moved to **step 1**: Prepare a syringe containing 5 mL, etc.
- The [redacted] should be combined to obtain **11-steps process**. The steps should follow the reconstitution with E&Z generator steps. These steps are common with the IRE generator and the cyclotron Ga-68 processes and can be referenced after description of the generator elution steps and transfer of the cyclotron sourced [redacted]a-68 solution into **Vial 3. *Such as: "repeat steps 1 through 11 of the Dilution and Radiosynthesis Procedure"*** for the IRE and cyclotron radiosynthesis processes.
- The **Dilution**: step 1 for E&Z, [redacted] should be revised to read (**Acetate Buffer Vial Configuration A**). The step should be repeated for the cyclotron Ga-68.
- The **Dilution**: step 1 for IRE, [redacted] should be revised to read (**Acetate Buffer Vial Configuration B**).

Radiosynthesis:

- **step** [redacted] revise and include the reaction temperature.
- **Step** [redacted] replace [redacted] with "Ga-68 gozetotide Injection"
- **Step** [redacted] After reconstitution and addition of Ga-68 chloride to the kit components in the reaction vial 3, use Ga-68 gozetotide within 4 hours. The final volume of the Ga-68 gozetotide Injection is 7.5 mL.

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CHAPTER VI: BIOPHARMACEUTICS

Product Information	The proposed product is a "Kit for the preparation of [redacted](b) (4)" which after radiolabeling with Ga-68 is a radioactive diagnostic agent indicated for use with PET for the evaluation of prostate cancer in men.
NDA Number	**214032**
Assessment Cycle Number	1
Drug Product Name/ Strength	Kit for the preparation of Ga-68 PSMA-11/ 5 mCi
Route of Administration	Intravenous
Applicant Name	Telix Pharmaceuticals US), Inc.
Therapeutic Classification/ OND Division	Division of Imaging and radiation Medicine (DIRM)
RLD/RS Number	**NDA 212643** (UCSF Ga-68-PSA-11)
Proposed Indication	Indicated for Positron emission tomography (PET) in men with suspected prostate cancer recurrence based on elevated blood prostate specific antigen (PSA) levels following prior treatment.

Assessment Recommendation: ADEQUATE

Assessment Summary:

On 23-Sep-2020, the Applicant submitted a 505(b)(2) new drug application (NDA 214032) to obtain approval to market a Kit for the Preparation of Ga-68 PSMA-11, which, after radiolabeling with Ga-68, acts as a radio-diagnostic agent [redacted](b) (4) The product, 68-Ga-PSMA-11, is a single-use, micro dose (≤[redacted](b) (4) µg) product.

In the original NDA, the Applicant intended to rely safety and efficacy of the proposed product based on literature evidence as well as MSKCC clinical trial data (under active IND [redacted](b) (4)). The proposed Kit was used as one of the Kits in MSKCC clinical study. Later the Applicant proposed to rely on safety and efficacy data from recently approved NDA 212643 UCSF Kit (Reference) for 68-Ga-PSMA-11 injection. To justify the use of the UCSF Kit's safety and efficacy data for the assessment of the proposed product, a biowaiver under 21 CFR 320.22(b)(1) is needed. Since the inactive ingredients in the proposed product and reference product (UCSF) are different, the biowaiver, however, is not applicable. The Agency recommended that a bridging between the proposed product and reference product under 21 CFR 320.24(b)(6) should be established. The proposed product contains D-mannose as a stabilizer and acetate as a buffer whereas the reference product contains 10% ethanol in 0.9% sodium chloride but no acetate or D-mannose. The Applicant indicated that the presence of D-mannose and acetate in the proposed product is not expected to affect the safety and efficacy of the product. The physiochemical properties like pH, osmolality and radiochemical purity are found to be similar or adequately controlled for both reference drug and proposed product. From a biopharmaceutics perspective, a scientific bridge (under 21 CFR 320.24(b)(6)) between the proposed product and the listed drug product has been established. However, as there are changes in inactive ingredients, we defer to

Pharmacology/Toxicology and Clinical Pharmacology for the final decision of this bridging if there are safety and efficacy concerns.

List Submissions Being Assessed (table):

Document(s) Assessed	Date Received
SN 0000 (Original NDA) SN 0016 (Response to IR) SN 0023 (CMC Response)	09/23/2020 06/28/2021 08/20/2021

Highlight Key Issues from Last Cycle and Their Resolution:

Concise Description of Outstanding Issues *(list bullet points with key information and update as needed)*:

B.1 BCS DESIGNATION
B.2 DISSOLUTION METHOD AND ACCEPTANCE CRITERIA
B.3 CLINICAL RELEVANCE OF DISSOLUTION METHOD & ACCEPTANCE CRITERIA *(e.g., IVIVR, IVIVC, In Silico Modeling, small scale in vivo)*
B.4 APPLICATION OF DISSOLUTION/IVIVC IN QbD
B.5 MODIFIED RELEASE ORAL DRUG PRODUCTS – *In-Vitro Alcohol Dose Dumping*
B.6 IN-VITRO SOFT-FOOD INTERACTION STUDY
B.7 IN-VITRO RELEASE TESTING (IVRT) FOR SEMI-SOLID PRODUCTS
B.8 IN-VITRO PERMEATION TESTING (IVPT) FOR TRANSDERMAL/TOPICAL PRODUCTS
B.9 IN-VITRO DISSOLUTION TESTING FOR ABUSE-DETERRENT PRODUCTS
B.10 IN-VITRO BE EVALUATION FOR PULMONARY PRODUCTS
B.11 EXTENDED-RELEASE DOSAGE FORMS –*Extended-Release Claim*
B.12 BRIDGING OF FORMULATIONS
Assessment: Sec B1-B12 are not Applicable for the assessment of NDA 241032.

B. 13 BIOWAIVER REQUEST
Assessment: *Adequate*
Based on several pre-NDA meetings with the Agency, the Applicant intended to reference clinical data generated under an active IND 130725 (Memorial Sloan Kettering Cancer Center, New York or MSKCC) which uses two formulations ((b) (4) µg PSMA-11 for the injection product and proposed Kit 25 µg PSMA-11 injection). Since the filing of this NDA, the Agency approved NDA 212642 (UCLA) and NDA 212643 (UCSF) Kits on 12/01/2020 for 68-Ga-PSMA-11 Injection as a radioactive diagnostic agent indicated for PET of prostate specific membrane antigen positive lesions in men with prostate cancer. Based on this information, the Applicant proposed to rely on data from FDA's findings of safety and effectiveness of the UCSF Kit (NDA 212643)(to support the efficacy and safety of proposed 68-Ga-PSMA-11 product. To use FDA's finding of safety and effectiveness of UCSF's product, a biowaiver or bridging study is required. In accordance with CFR 320.22(b)(1), a drug product's in vivo bioequivalence may be

considered self-evident if the product meets the following criteria: (1) the drug product (i) is a parenteral solution intended solely for administered by injection and (ii) contains the same active and inactive ingredients in the same concentration as a drug product that is the subject of an approved full NDA or ANDA. Since the amount of active and inactive ingredients are not in the same concentration in the proposed and approved drug product, biowaiver is not applicable and a bridging study to establish equivalency will be needed. In accordance with 21 CFR 320.24(b)(6), any other approach deemed adequate by FDA to measure bioavailability or establish bioequivalence can be used.
On 21-Jun-21, the Agency provided following comments to the Applicant:

> *Based on the information provided in the submission, the bridging approach to the reference drug product (GALLIUM GA 68 PSMA-11, N212643) via 21 CFR 320.24(b)(6) has not been adequately established. We recommend that you provide the following information to support the bridging to the listed drug product:*
>
> a) *Comparative physicochemical properties (e.g. osmolality, pH, radioactivity etc.) for the proposed drug product and listed drug product using at least three lots (if available) of the proposed drug product and available information for the listed drug product. The measurements should be done in triplicate for each lot tested.*
> b) *Formulation comparisons (for both before and after reconstitution or dilution if needed) between the proposed drug product and the listed drug product (side-by-side tabulated summary including the concentrations of active and inactive ingredients). For any differences observed, explain if such differences can lead to performance differences in pharmacokinetics, efficacy and safety.*
> c) *Any other information deemed reasonable to establish bridging.*

The Applicant submitted a response to the above information request on 06/29/2021 (Module 1.11.4, SN 0016). On 08/20/2021 (SN 0023), the Applicant provided a report on the test for osmolality and pH as additional information to the above response. The Applicant stated that the proposed product (ILLUCCIX[1], TEST) and reference product (UCSF's Kit, REF) use the same active ingredients in their final dosage form (Gallium 68-PSMA-11) and have similar physicochemical characteristics.

- Formulation Comparison:

The TEST kit includes the PSMA-11 drug substance precursor formulated with D-mannose, lyophilized in a sterile vial (Table 1), an acetate buffer solution in a sterile vial, and an empty sterile vacuum vial. Radiolabeling is performed using a 68Ge/68Ga generator or cyclotron-produced 68Ga and yields the active drug substance Ga-68-PSMA-11. The Kit is supplied in two configurations, which differ solely in the concentration and volume of solution provided in the (b) (4) Acetate Buffer (Configuration 1 and Configuration 2).

Table 1. Composition of PSMA-11 drug substance precursor in a Sterile vial

Component	Quantity/Vial	Function	Quality Standard
PSMA-11	25 µg	Precursor	In-house
D-mannose	10 µg	Stabilizer	In-house
(b) (4)			

[1] Proposed proprietary name

Table 2. Composition of [redacted] Acetate Buffer Vial, Configuration A

Component	Quantity/Vial	Function	Quality Standard
Anhydrous sodium acetate	150 mg	Buffer	USP
[redacted] % HCl	[redacted] mL	[redacted]	NF
[redacted]			

Abbreviations: NF = National Formulary; USP = United States Pharmacopeia.

Table 3. Composition of [redacted] Acetate Buffer Vial, Configuration B

Component	Amount	Function	Quality Standard
Anhydrous sodium acetate	150 mg	Buffer	USP
[redacted] % HCl	[redacted] mL	[redacted]	NF
[redacted]			

Abbreviations: NF = National Formulary; USP = United States Pharmacopeia.

Two different configurations are intended for use with different sources of 68Ga generators. The first (also referred to as Configuration A, Table 2) is for use with commercially available 68Ge/68Ga generator (EZAG GalliPharm®) or 68Ga produced by cyclotron. The second (also referred to as Configuration B, Table 3) is for use with commercially available 68Ge/68Ga generator IRE Galli-Eo™. After radiolabeling of the proposed Kit by the radiopharmacy site, the composition of the final drug product is shown in Table 4 (TEST).

Table 4. Composition of the proposed Drug Product 68-Ga-PSMA-11 used for clinical studies

Component	Quantity/Vial	Function	Quality Standard
Ga-68 PSMA-11	Up to 50 mCi	Drug substance	In-house
PSMA-11	25 µg[1]	Precursor	In-house
D-Mannose	10 µg	Stabilizer	In house
Hydrochloric acid [redacted]	[redacted] mL	[redacted]	NF
Sodium acetate	150 mg	Buffer	USP

Abbreviations: NF = National Formulary; USP = United States Pharmacopeia.

[1] A part of the drug substance PSMA-11 has been radiolabeled with Gallium-68 to form Ga-68 PSMA-11.

[2] [redacted]

Post-radiolabeling, the composition of the final drug product of TEST drug and REF drug is provided in Table 5.

Table 5. Post-radiolabeling Formulation Comparison

Component	ILLUCCIX Kit for the Preparation of Ga-68 PSMA-11			UCSF Ga-68 PSMA-11 Reference Product (Cyclotron Based)			UCSF Ga-68 PSMA-11 Reference Product (Generator Based)		
	Quantity/ Vial	Function	Quality Standard	Quantity/ Vial	Function	Quality Standard	Quantity/ Vial	Function	Quality Standard
Ga-68 PSMA-11	Up to (b) (4) mCi/mL	Drug substance	In-house	0.5–5 mCi/mL	Drug substance	In-house	0.5–5 mCi/mL	Drug substance	In-house
PSMA-11	25 µg[1]	Precursor	In-house	5 µg	Precursor	GMP	5 µg	Precursor	GMP
D-Mannose	10 µg	Stabilizer	In-house						
Hydrochloric acid, (b) (4) M[2]	(b) (4) mL	(b) (4)	NF						
Hydrochloric acid, 1 M[2]							5 mL	Generator eluent	GMP
Hydrochloric acid, 1.75 M[3]				4 mL	Ga-68 Purification	Ultrapure			
Sodium acetate, 0.5M[3]							0.1 mL	Buffering agent	Pharma grade
Sodium acetate, 1M[3]				1.3 mL	Buffering agent	Pharma grade			
Sodium acetate, anhydrous	150 mg	Buffer	USP						
Nitric acid, 0.1 M[3]				4 mL	Ga-68 purification	Trace metal basis			
Sodium Chloride, 2M[3]				4 mL	Ga-68 Purification	Trace metal basis			
Ethanol, 60%				1 mL	Product eluent	USP grade	1 mL	Product eluent	USP grade
Ultra-high purity water				50 mL	Solution preparation	Pharma grade	10 mL	Solution preparation	Pharma grade
Water for Injection USP				100 mL	Solution preparation	USP grade	4 mL	Solution preparation	USP grade
Sodium Chloride 0.9% Injection				5–10 mL	Isotonicity	USP grade	5–10 mL	Isotonicity	USP grade

[1] A part of the Drug Substance PSMA-11 has been radiolabeled with Gallium-68 to form Ga-68 PSMA-11.
[2] (b) (4)
[3] Removed during processing and not present in the final formulation of the UCSF Ga-68 PSMA-11 reference product.
(b) (4)

While both products contain the same active ingredient, 68-Ga-PSMA-11, there is a difference in inactive ingredients. The Applicant indicated that REF used 10% ethanol/saline (b) (4) (b) (4) However, TEST being a lyophilized product, used D-mannose as stabilizer and acetate as buffer but no ethanol. While both products used acetate as buffer, REF product removed acetate during the (b) (4) process. The Applicant indicated that acetate and D-mannose is routinely used in injectable products and the presence of these two excipients is not expected to have any impact on the safety, efficacy, or stability of the TEST product. The Applicant also indicated that based on literature data, the presence of D-mannose and acetate do not have any impact on image quality. Radiochemical purity, however, could be an important element for image quality. The radiochemical purity for TEST is high using the proposed method whereas REF product uses (b) (4) (b) (4) to ensure high radiochemical purity.

- Comparative Physicochemical Properties:

The Applicant provided comparative specifications for TEST and REF products (Table 6). The product specifications deemed comparable or equivalent for radiochemical purity, visual appearance, and pH over the shelf-life of the product. The pH and radiochemical purity specification are found to be tighter for the TEST formulation as compared to REF formulation.

Table 6. Comparative Specification for TEST and REF products

Test	Test method	Acceptance criteria UCSF	Acceptance criteria Telix
Radiochemical purity	Thin-layer chromatography	≥90%	Content of ^{68}Ga-PSMA-11: NLT 95% Content of free and colloidal Ga-68: NMT 5%
Appearance	Visual observation	Clear solution, free of particulates	Colorless to slightly yellow solution, practically free from visible particles
pH	pH paper	4.0–7.0	4.0 to 5.0

In SN 0023 (8/20/2021), the Applicant provided osmolality and pH testing report of non-radioactive TEST and REF kit preparations. The Applicant tested the osmolality of the TEST formulation (cold; without Ga-68) and EtOH/saline based formulation (no D-mannose or acetate[2] used) by REF in triplicate.

Following is the summary of pH and Osmolality values:

Sample ID	LAB ID	SAMPLE DESCRIPTION	pH	OSMOLALITY	SI UNITS
PL001-0032A	1008119	~9% Ethanol in 0.9% Saline	5.5	271	mmol/kg
PL001-0032B	1008120	~9% Ethanol in 0.9% Saline	5.5	267	mmol/kg
PL001-0032C	1008121	~9% Ethanol in 0.9% Saline	5.5	268	mmol/kg
PL001-0033A	1008122	PSMA in Acetate Buffer	4.0	479	mmol/kg
PL001-0033B	1008123	PSMA in Acetate Buffer	4.0	476	mmol/kg
PL001-0033C	1008124	PSMA in Acetate Buffer	4.0	481	mmol/kg

Osmolality is determined by USP<785>(Vapor pressure). The pH is determined by pH indicator strips. Based on above data, the TEST formulation exhibited higher osmolality compared to REF formulation. The higher osmolality value for TEST may have been due to the presence of D-mannose in TEST formulation. The normal range of osmolality of blood is 275-295 mOsm/Kg. Because of the low volume of injection (7.5-11 mL), the risk to patient (phlebitis or vascular damage) is low. Based on literature evidence[3] (submitted by the Applicant), the drug products intended for intravenous or intravascular injection, the recommended upper limit of osmolality should be generally controlled under 1,000 mOsm/kg for small-volume injections (≤ 100 mL). The pH of the product is also comparable. The acidic pH ensures [redacted] (b) (4)

[2] While acetate is present in the formulation of REF product, it is removed during the [redacted] (b) (4) [redacted] (b) (4) process.

[3] Wang, Wei. Tolerability of hypertonic injectables, Int J Pharm 2015 Jul 25:490(1-2)

From a biopharmaceutics perspective, a scientific bridge (under 21 CFR 320.24(b)(6)) between the proposed product and the listed drug product has been established. However, as there are changes in inactive ingredients, we defer to Pharmacology/Toxicology and Clinical Pharmacology for the final decision of this bridging in case there are safety and efficacy concerns. In a recent email communication (9/2/2021), August Hofling, Lead Physician, confirmed that "Clinical, nonclinical, and clin pharm all have no concerns with the inactive ingredients.

- Other information deemed reasonable for bridging:

The Applicant indicated cell binding and internalization studies to demonstrate equivalency of test and reference product. Literature evidence[4] (Carlucci et. al 2020) suggests 68-Ga-PSMA-11 prepared at ambient temperature using the proposed kit to 68-Ga-PSMA-11 prepared at elevated (95°C) temperature (as is done with UCSF's product) showed bioequivalence. Based on other studies[5], 68-Ga-PSMA-11 labeled at room temperature produces a mixture of diastereomers but at 95C, the main product is a thermodynamically stable isomer. However, a mixture of thermodynamically stable and less stable diastereomers showed similar binding profile. Literature evidence[6] also suggest less stable diastereomers interconverts to the most stable isomer with time. Since formation of a mixture of diastereomers is a function of pH and temperature, a slight change of pH or significant change of process temperature does not negatively influence the binding of the product. While peer-reviewed literature evidence is considered as supporting information to establish bridging, we defer the review of pharmacology studies to non-clinical/clinical pharmacology reviewers.

R. REGIONAL INFORMATION

Comparability Protocols

Assessment: *NA*

Post-Approval Commitments

Assessment: *None*

Lifecycle Management Considerations: None

BIOPHARMACEUTICS LIST OF DEFICIENCIES : None

Primary Biopharmaceutics Assessor's Name and Date:
Debasis Ghosh, Ph.D.
09/08/2021

Secondary Assessor Name and Date (and Secondary Summary, as needed):

I concur with the primary assessment.
Kimberly Raines, Ph.D.
09/09/2021

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[4] Carlucci, G et. al. J. Nucl. Med. 2021:62(2):149-55
[5] Eder, M. et. al, Pharmaceuticals (Basel), 2014;7(7):776-96.
[6] Schuhmacher, J. et. al. Cancer Res., 1995;55(1):115-23.

Debasis Ghosh

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Kimberly Raines

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CHAPTER VII: MICROBIOLOGY

Product Information	
NDA Number	214032
Assessment Cycle Number	MR01
Drug Product Name/ Strength	*ILLUCCIX® (kit for the preparation of gallium Ga -68 gozetotide injection)/ 5 mCi
Route of Administration	Intravenous injection
Applicant Name	Telix Pharmaceuticals (US) Inc.
Therapeutic Classification/ OND Division	PET products/ DIRM
Manufacturing Site	Grand River Aseptic Manufacturing (GRAM), 140 Front Avenue SW, Suite 3, Grand Rapids, MI 49504
Method of Sterilization	(b) (4)

Assessment Recommendation: **Adequate**

Assessment Summary:

List Submissions being assessed (table):

Document(s) Assessed	Date Received
eCTD Sequence 0000	**9/23/2020**
eCTD Sequence 0002	**1/29/2021**
eCTD Sequence 0007	**3/25/2021**
eCTD Sequence 0009	**4/8/2021**
eCTD Sequence 0011	**5/11/2021**
eCTD Sequence 0012	**5/19/2021**
eCTD Sequence 0013	**6/3/2021**
eCTD Sequence 0027	**11/12/2021**

Highlight Key Issues from Last Cycle and Their Resolution: N/A

Remarks: The drug product is a cold kit for the preparation of Ga-68 PSMA-11 Injection. The kit consists of three vials: (b) (4) (Vial 1), (b) (4) Acetate Buffer Vial (Vial 2), and an empty vacuum vial (Vial 3). The final drug product, Ga-68 PSMA-11, can be produced using Ga-68 produced from either

a cyclotron or one of two GMP Ge-68/Ga-68 generators [GalliaPharm generator (DMF 28741) or GalliEo generator (DMF 31715)]. Information requests dated 4 December 2020, 18 March 2021, 5 April 2021, and 14 May 2021 and the responses dated 29 January 2021, 25 March 2021, 8 April 2021, 11 May 2021, 19 May 2021 are covered in this review. Additionally, at a teleconference with the applicant on 27 May 2021, microbiological concerns regarding the use of eluates from aged generators to produce Ga-68PSMA-11 were discussed. In response on 3 June 2021, the applicant provided validation batch data from various clinical sites to support the sterility of the eluate; however, only one product batch was produced using eluate from a generator within 1 month of expiry. A Post-marketing Commitment (PMC # 4176-2) was negotiated with the sponsor on 8 November 2021 to obtain additional sterility and endotoxins data for Ga-68 PSMA-11 product batches produced with eluates from three lots each of Eckert and Ziegler (GalliaPharm®) and IRE (Galli Eo) generators that are within 1 month of expiry; sponsor agreement was obtained on 12 November 2021.

*The product name in the label is stated to be Illuccix® (kit for the generation of Gallium Ga-68 Gozetotide). However, the 356H form and the submission documents refer to the product as a "kit for the generation of Ga-68 PSMA-11." Since these names refer to the same drug product, for the purpose of this review, the product is called "Ga-68 PSMA-11", with the exception of the PMC section, where the product is referred to as Ga-68 gozetotide due to the use of this name in the PMC documentation.

Concise Description of Outstanding Issues
(List bullet points with key information and update as needed): N/A

Supporting Documents:
DMF 25912 (Grand River Aseptic Manufacturing) – for the manufacturing and facility information for production of the Telix kit. LOA from Grand River Aseptic Manufacturing, dated 3 September 2020, was provided. The facility information was reviewed and deemed adequate in D25912M01R01.docx, dated 14 March 2019. The environmental monitoring program was reviewed and deemed adequate in quality microbiology review D25912M02R01.docx, dated 2 March 2020. Validation of the sterilization/depyrogenation processes, (b) (4) (b) (4) and media fills was reviewed and deemed adequate in quality microbiology review D25912M03R01.docx, dated 13 May 2021.

DMF 28741 (Eckert and Ziegler) – for manufacturing and facility information related to production of the GalliaPharm® generator. LOA from Eckert and Ziegler Radiopharma GmbH, dated 21 September 2020, was provided. The most recent sterility assurance information was reviewed in D28741M04R01.docx, dated 1 November 2019. The endotoxins specification was reviewed in D28741M05R01.docx, dated 16 April 2021.

DMF 31715 (iRE ELiT) – for manufacturing and facility information related to production of the Galli Eo® generator. LOA from iRE ELiT Radiopharma, dated 21 September 2020, was provided. The most recent sterility assurance information was reviewed in D31715M01R01.docx, dated 26 December 2019, and D31715M02R01.docx, dated 1 July 2021.

(b) (4)

S DRUG SUBSTANCE

The (b) (4) quality microbiology review of the PSMA-11 drug substance is not applicable.

Ga-68 PSMA-11 is generated in the nuclear pharmacy via addition of Ga-68 chloride (eluate from Ge-68/Ga-68 generator or cyclotron) to PSMA-11 (reconstituted in sterile sodium acetate buffer). The applicant stated that two GMP Ge-68/Ga-68 generators can be used to generate Ga-68 PSMA-11: GalliaPharm generator (Eckert and Ziegler, DMF 28741) and Galli Eo generator (iRE ELiT, DMF 31715). Letters of authorization (LOA) were provided for DMF 28741, dated 21 September 2020, and DMF 31715, dated 21 September 2020.

Assessment: *Adequate*

For sterility assurance information associated with the GalliaPharm (Eckert and Ziegler) and Galli Eo (iRE ELiT) Ge-68/Ga-68 generators, DMF 28741 and DMF 31715, respectively, were reviewed and deemed adequate in product quality microbiology reviews D28741M04R01.docx, dated 1 November 2019, D28741M05R01.docx, dated 16 April 2021, D31715M01R01.docx, dated 26 December 2019, and D31715M02R01.docx, dated 1 July 2021, respectively. Please see these reviews for additional information.

P.1 DESCRIPTION OF THE COMPOSITION OF THE DRUG PRODUCT

(Module 3.2.P.1, Description and Composition of the Drug Product [Kit])

- **Description of the drug product –** the drug product is a kit consisting of 3 vials:
  - Vial 1- (b) (4)
  - Vial 2- (b) (4) Acetate Buffer Vial (supplied as Configuration A or B)
    - Configuration A – for use with the GalliaPharm generator or cyclotron-produced Ga-68
    - Configuration B – for use with Galli Eo produced Ga-68

- Vial 3- [redacted] (empty vial)

- **Drug product composition –**

Vial 1: [redacted]

Component	Function	Quantity/vial
PSMA-11	Precursor	25 µg
D-mannose	Stabilizer	10 µg
[redacted]		

Vial 2: [redacted] **Acetate Buffer Vial, Configuration A**

Component	Function	Quantity/vial
Anhydrous sodium acetate, USP	Buffer	150 mg
[redacted]		

Vial 2: [redacted] **Acetate Buffer Vial, Configuration B**

Component	Function	Quantity/vial
Anhydrous sodium acetate, USP	Buffer	150 mg
[redacted]		

- **Container Closure Systems –**

Vial 1: [redacted]

Component	Description	Manufacturer
Vial	10 mL [redacted] clear glass vial [redacted]	[redacted]
Stopper	20 mm Lyo gray rubber stopper, [redacted]	[redacted]
Cap	20 mm blue cap [redacted]	[redacted]

Vial 2: [redacted] **Acetate Buffer Vial, Configuration A**

Component	Description	Manufacturer
Vial	10 mL [redacted] clear glass vial [redacted]	[redacted]
Stopper	20 mm [redacted] gray rubber stopper, [redacted]	[redacted]
Cap	20 mm red cap [redacted]	[redacted]

Vial 2: (b) (4) **Acetate Buffer Vial, Configuration B**

Component	Description	Manufacturer
Vial	10 mL (b) (4) clear glass vial (b) (4)	(b) (4)
Stopper	20 mm (b) (4) gray rubber stopper, (b) (4)	(b) (4)
Cap	20 mm green cap (b) (4)	(b) (4)

Vial 3: Empty Vial

Component	Description	Manufacturer
Vial	10 mL (b) (4) clear glass vial (b) (4)	(b) (4)
Stopper	20 mm (b) (4) gray rubber stopper, (b) (4)	(b) (4)
Cap	20 mm white cap (b) (4)	(b) (4)

In the Information Request dated 4 December 2020, the following deficiency was issued:

We note that Module 1.14.1.1 contains (b) (4) (b) (4)

Applicant response dated 29 January 2021: The applicant confirmed (b) (4) (b) (4)

Assessment: ***Adequate***

The applicant provided an adequate description of the composition and container closure system of each kit component.

P.2 PHARMACEUTICAL DEVELOPMENT

P.2.5 MICROBIOLOGICAL ATTRIBUTES

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Yeissa Chabrier Rosello

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OTR-Short Form Report

Date: 2021-10-21

From: Jamie D. Mans, PhD, CDER/OPQ/OTR/DCDA
Daniel Weisz, PhD, CDER/OPQ/OTR/DCDA

Through: Alicia Hoover, PhD, CDER/OPQ/OTR/DPA
Cynthia Sommers, MS, (Lab Chief, Branch I) CDER/OPQ/OTR/DCDA

To: John Amartey, Review Chemist, CDER/OPQ/ONDP
Eldon Leutzinger, Review Chemist, CDER/OPQ/ONDP
Anika Lalmansingh, Sr. RBPM, CDER/OPQ/OPRO
Danae Christodoulou, Branch Chief, CDER/OPQ/ONDP

Subject: Review of NDA 214032 - Validation of Limit Test of PSMA-11 in finished product [(b) (4)] vial, 25 µg, Telix Pharmaceuticals (US), Inc.

Report file name: FY22-003-OTR-DCDA-M

Associated Protocols: N/A

Background: ONDP requested OTR to evaluate the method validation protocol (LCA-AN-032) and validation report (VR_limit test_PSMA-11_V02_EN) for the Validation of Limit Test of PSMA-11 in finished product [(b) (4)] vial, 25 µg submitted by Telix Pharmaceuticals (US), Inc. PSMA-II is a precursor which chelates to gallium and is provided as a kit. The validation guidelines provided in ICH Q2(R1) Validation of Analytical Procedures: Text and Methodology, USP <1225>, and the CDER Reviewer Guidance Validation of Chromatographic Method were used to evaluate the method.[1-3]

Conclusions:

- The validation of Limit Test of PSMA-11 for finished product [(b) (4)] Vial, 25 µg, is unacceptable for regulatory purposes.

[(b) (4)]

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