FPI-2068-101 PHARMACY MANUAL

Investigational Products:	FPI-2053 Infusion [cold antibody] [^{111}In]-FPI-2017 Injection [imaging agent] [^{225}Ac]-FPI-2068 Injection [therapeutic agent]
Study Title:	A Phase 1, First-in-human, Multicenter, Open-label, Dose-escalation Study of [^{225}Ac]-FPI-2068 in Adult Participants with Advanced Solid Tumors
Protocol Number:	FPI-2068-101
Sponsor:	Fusion Pharmaceuticals Inc. 270 Longwood Road South Hamilton, ON L8P 0A6 Canada
IMP Manual:	Version 3.0 15-FEB-2024
US IND Number:	[^{225}Ac]-FPI-2068: 161011 [^{111}In]-FPI-2107: 161010

Version History		
Pharmacy Manual Version Number	**Pharmacy Manual Version Date**	**Pharmacy Manual Updates**
V3.0	15Feb2024	1. Appendix 3: Added FPI-2053 and IVBP French labels
V2.0	19Dec2023	2. Section 2: updated FPI-2068 dose levels 3. Section 3.1: added equipment and ancillary list 4. Section 3.2: updated IMP Receipt instructions 5. Section 3.4: updated FPI-2053 information 6. Section 4.1: updated [^{111}]-FPI-1547 and [^{225}Ac]-FPI-2068 ordering instructions 7. Section 4.2: added Withdrawing request for and order instructions 8. Section 4.3: updated [^{111}]-FPI-1547 and [225Ac]-FPI-2068 receipt process 9. Section 4.6 updated [^{111}]-FPI-1547 preparation 10. Section 4.6, 4.7, 4.11 and 4.12: added Drug Administration Worksheet instructions 11. Section 4.8: Added Imaging Standard information 12. Updated FPI-2053 Drug Administration Worksheet
V1.0	29Nov2023	New Document

SPONSOR SIGNATURE PAGE

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Director, Clinical Operations
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CONTACT INFORMATION:

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Fusion Pharmaceuticals Inc.: FPI-2068-101@fusionpharma.com

AstraZeneca: FPI2068101@astrazeneca.com

Product complaints:

Fusion email: clinicalcomplaints@fusionpharma.com

Table 1: Abbreviations

Abbreviation	Full Name
^{111}In or In-111	Indium-111
^{225}Ac or Ac-225	Actinium-225
FPI-2068	[^{225}Ac]-FPI-2068 (radioimmuno-therapeutic agent [hot antibody])
FPI-2107	[^{111}In]-FPI-2107 (the radioimmuno-SPECT agent) [hot antibody]
FPI-2053	Unconjugated / unlabelled bispecific antibody (cold antibody)
AZ	AstraZeneca
CPM	Counts per minute
DTPA	Diethylenetriaminepentaacetic Acid
eCRF	Electronic Case Report Form
Fusion	Fusion Pharmaceuticals Inc.
GCP	Good Clinical Practice
IMP	Investigational Medicinal Product
ISF	Investigator Site File
IV	Intravenous
IVBP	IV Bag Protectant
MBq	Megabecquerel
mCi	Millicurie
SOP	Standard Operating Procedure
SNMMI NMCTG	Society of Nuclear Medicine and Molecular Imaging Nuclear Medicine Clinical Trials Group
SRC	Safety Review Committee
TOC	Time of Calibration
WFI	Water for Injection

1. PURPOSE AND OVERVIEW

FPI-2068-101 is a first-in-human, Phase 1, multicenter, open-label dose escalation study designed to investigate the safety, tolerability, dosimetry, biodistribution, and pharmacokinetics (PK) of [^{225}Ac]-FPI-2068, [^{111}In]-FPI-2107, and the effect of pre-dose administration of FPI-2053 on the PK and biodistribution of [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107. In addition, the pharmacodynamics, preliminary anti-tumour activity, and recommended Phase 2 dose (RP2D) of a [^{225}Ac]-FPI-2068 regimen in participants with advanced, metastatic and/or recurrent solid tumours (HNSCC, NSCLC, mCRC, PDAC) that demonstrate uptake of the imaging agent as determined by SPECT/computed tomography (CT) will be evaluated.

[^{225}Ac]-FPI-2068 does not emit radiation that is readily amenable for clinically useful image acquisition, therefore, the imaging agent [^{111}In]-FPI-2107 will be used as a radioimmuno-Single Photon Emission Computed Tomography (SPECT) imaging agent to identify participants for treatment with [^{225}Ac]-FPI-2068.

This pharmacy manual is a reference manual for the pharmacist, pharmacy personnel, site staff, and clinical trial team involved in the use of Investigational Medicinal Products (IMPs). The following is a guidance of minimum acceptable procedures and does not replace an understanding of, or adherence to the requirements contained in the approved protocol, applicable regulation, guidelines, good clinical practices, aseptic preparation techniques, or Standard Operating Procedures (SOPs) governing this study.

The purpose of this manual is to:

- Outline the procedures for ordering, management, preparation, administration, accountability, and disposal of the following IMPs:
  - FPI-2053 – Investigational Medicinal Drug, cold antibody
  - [^{111}In]-FPI-2107 – Investigational Medicinal Drug, imaging agent
  - [^{225}Ac]-FPI-2068 – Investigational Medicinal Drug, targeted alpha therapeutic agent
- Provide consistent direction across all clinical sites for preparing a dose of study intervention.

The Pharmacy Manual will be updated and revised as needed. The most recent approved version will take precedence over any previous version(s). The Protocol, Investigator's Brochure, Certificate of Analysis, and product labelling should be consulted for further information regarding the use of these materials in the FPI-2068-101 study.

2. INVESTIGATIONAL PRODUCTS INFORMATION

[^{225}Ac]-FPI-2068 is a targeted alpha therapeutic agent. [^{225}Ac]-FPI-2068 is manufactured using FPI-2053, a bifunctional chelate (FPI-1784), and actinium-225 (^{225}Ac or Ac-225), an alpha particle emitting radionuclide. [^{225}Ac]-FPI-2068 is intended to be developed for the treatment of participants with advanced solid tumors. [^{225}Ac]-FPI-2068 has not previously been studied in humans.

[^{111}In]-FPI-2107 is an imaging agent and is manufactured using FPI-2053, a bifunctional chelate (FPI-1784), and indium-111 (^{111}In or In-111). The biodistribution of [^{111}In]-FPI-2107 is used as a surrogate for the biodistribution of the therapeutic agent [^{225}Ac]-FPI-2068. [^{111}In]-FPI-2107 has not been previously studied in humans.

[^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107 are supplied for parenteral administration as sterile, non-pyrogenic, injectable, clear, colorless solutions in sterile 20 mL glass vials capped with chlorobutyl rubber stoppers and secured with aluminum seals. The contents of the vials are radioactive and will be supplied in a lead pot packaged within a shipping container. Vials are individually produced for each participant. Each vial is single-use and should only be used for one participant and should not be used for multiple administrations. The IMPs are ready-to-use solutions and should not be diluted or mixed with any other solutions. There are no guarantees that [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107 are latex free. [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107 are manufactured by SpectronRX.

FPI-2053 is a targeting human bispecific monovalent antibody that is given prior to [^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068. FPI-2053 vials are single-use and should only be used for one participant and should not be used for multiple administrations. The IMP is provided as a lyophilized powder and will require reconstitution with sterile water for injection (WFI) onsite. FPI-2053 is to be used in conjunction with the supplied IV Bag Protectant (IVBP).

FPI-2053 and the IVBP are supplied by Fisher Clinical Services based in Mt. Prospect, IL, US and FPI-2053 is manufactured by AstraZeneca (AZ).

Any manufacturing related inquiries should be relayed to Fusion Pharmaceuticals Inc. (Fusion) at FPI-2068-101@fusionpharma.com.

Table 2: Investigational Products Information

IMP Name:	**FPI-2053**	**[^{111}In]-FPI-2107**	**[^{225}Ac]-FPI-2068**
Dose Formulation:	Concentrate for Infusion After reconstitution with 2.3 mL sterile WFI, the vial contains 50 mg/mL FPI-2053 in 20 mM L-histidine/L-histidine-HCl, 240 mM sucrose, 0.02% (w/v) polysorbate-80, pH 6.0.	Solution for Injection Sodium acetate (0.41% w/w, buffer), polysorbate 80 (0.01% w/w, surfactant), diethylenetriamine pentaacetic acid (DTPA, 0.05% w/w, metal chelating agent), and sodium ascorbate (0.20% w/w, radioprotectant)	Solution for Injection Sodium acetate (0.41% w/w, buffer), polysorbate 80 (0.01% w/w, surfactant), diethylenetriamine pentaacetic acid (DTPA, 0.05% w/w, metal chelating agent), and sodium ascorbate (0.20% w/w, radioprotectant)
Nominal Concentration(s)	50 mg/mL once reconstituted with sterile WFI	74 – 111 MBq/mL at TOC 0.29 – 0.67 mg/mL protein	0.407 – 0.629 MBq/mL at TOC 0.2 – 0.5 mg/mL protein
Appearance:	Lyophilized, white to off white powder	Clear, colorless solution, free of visible particulates.	Clear, colorless solution, free of visible particulates.
Route of Administration:	IV infusion	IV injection	IV injection
Dosing Instructions:	Administered as a single dose, IV infusion in an IV bag that has been pretreated with the IVBP solution. FPI-2053 is administered to the	Administered as a single dose, IV injection 185 MBq (5 mCi). The injection is to be administered undiluted as a slow (3-5 minutes) IV injection	Administered as a single dose, IV injection at the following doses: 15, 25, 40, 70, kBq/kg depending on the study cohort and SRC decision. The injection is to be

IMP Name:	FPI-2053	[^{111}In]-FPI-2107	[^{225}Ac]-FPI-2068
	participant via a 60- minute IV infusion.		administered undiluted as a slow (3-5 minutes) IV injections.

Time of Calibration (TOC) 12:00 ET 2 days post manufacture

3. INSTRUCTIONS FOR FPI-2053 (COLD ANTIBODY)

FPI-2053 is an EGFR-cMET targeting bispecific humanized monoclonal antibody that is given prior to [^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068.

FPI-2053 is provided as a lyophilized, white to off-white powder to be reconstituted with sterile water for injection (WFI) on the day of use.

FPI-2053 is to be used only with the supplied IV Bag Protectant (IVBP).

3.1. FPI-2053 and IVBP Ordering

The FPI-2053 and IVBP ordering process will be initiated once all required start-up activities are completed and the site has communicated that they have a potential participant. Once the site has communicated a potential participant, the first shipment of FPI-2053, IVBP, and ancillary supplies will be triggered.

- 1 kit: 10 vials FPI-2053 and 3 vials IVBP
- Saline bags (250 mL, 100 mL, and 50 mL)
- Syringes (3 mL and 1 mL)
- 0.22 Micron Filtered Tubing
- PhaSeal CSTD vial adaptor
- PhaSeal CSTD syringe adaptor
- PhaSeal CSTD bag adaptor
- PhaSeal CSTD Luer-Lock adaptor
- Fluid Dispensing Connector

Sites are to monitor and track their supply and request additional FPI-2053 and IVBP Kits, and/or ancillary supplies (kits) as needed by emailing an order request to FPI-2068-101@fusionpharma.com and provide the following:

- Anticipated date shipment is needed by.
- Pharmacy address and contact personnel for shipment.
- Contact details:
  - Name(s)
  - Telephone
  - Email

Fusion will confirm receipt of the order within 3 business days and will inform the site of the estimated date of delivery.

Please note the date of delivery may take up to around 10 business days from the confirmation of order received (depending on site location).

3.2. FPI-2053 and IVBP Kit Receipt

The Investigator or designee must confirm that appropriate conditions have been maintained during transit and receipt and that any discrepancies are reported and resolved before use of the IMP.

The Investigator or designee are to complete the following procedures upon receipt of the FPI-2053 and IVBP Kit:

- Examine the entire shipping packaging for damage.
  - If damage is identified throughout the inspection, **DO NOT OPEN THE PACKAGE, place the package in Quarantine status** and contact Fusion immediately at clinicalcomplaints@fusionpharma.com. Fusion will provide additional instructions.
- Inspect the outer and ancillary labels for consistency and to confirm the correct product has been received.
- Visually inspect the vials and vial contents.
- If there are any concerns regarding damage to the vials (e.g., leakage, breakage) or the appearance of the product, the **FPI-2053 and IVBP MUST NOT BE ADMINISTERED**. Contact Fusion immediately at clinicalcomplaints@fusionpharma.com. Note that the temperature logger, storage, and receipt instructions (below) should be performed for product that is damaged or that there are concerns about. Hold the "Stop" button on the TempTale® **(the temperature logger found inside of the shipper) for approximately three seconds to stop the temperature reading.** Follow the instructions found inside the shipper to upload the TempTale® data. Confirm there has been no temperature excursion(s).
  - Please see table below for the temperature range and appropriate actions the site should take upon review of the TempTale® data:

Table 3: Temperature Range and Actions

Temperature Range	Action
2-8°C	Acceptable for use
<2°C	Contact Fusion
>8°C	Contact Fusion

Please note, if there was a temperature excursion at any point during transit, the site should contact Fusion prior to dosing a participant. Fusion will provide additional instructions as to how the site should proceed.

- Immediately transfer the cartons containing the vials to a 2 to 8 °C refrigerator. Both Quarantine status and Acceptable for Use status cartons should be placed in the 2 to 8 °C refrigerator

- Email the signed IMP package receipt and the Temperature Logger data PDF to ipreceipt@fusionpharma.com
  - Complete any other required local standard operating procedures.
  - If the shipment does not arrive at the site at or before the expected delivery date and time, the site should contact Fusion at FPI-2068-101@fusionpharma.com immediately so the Fusion team can investigate the delay.
- Relevant sections of the FPI-2053 and IVBP Investigational Product Receipt and Dispensing Accountability Log should be completed upon receipt of FPI-2053 kits:
  - The Lot number and expiry date (both are provided on the outer label)
  - "Date received" refers to the date that FPI-2053 was received at the clinical trial site.
  - Quantity of vials received.

3.3. FPI-2053 and IVBP Kit Storage

FPI-2053 and IVBP Kits must be stored in a secure, controlled, and monitored area in accordance with the labelled storage conditions and the Investigator's Brochure. Access to the kits must be limited to the Investigator and appropriately trained authorized site staff.

The FPI-2053 and IVBP vials and kits should be stored at 2 to 8 °C. The kits must not be frozen or shaken and should be protected from direct sunlight. The refrigerator temperature must be checked and recorded when the materials are placed in the refrigerator, and daily while they are stored.

The refrigerator temperature must be checked and recorded when the materials are removed from the refrigerator for dose preparation.

Notify Fusion immediately if the refrigerator temperature is outside of the specified 2-8 °C.

3.4. FPI-2053 Preparation

FPI-2053 is provided as a sterile lyophilized powder and contains no preservatives. Each single use, vial contains 100 mg of FPI-2053.

Doses of FPI-2053 for administration must be prepared by qualified staff members using aseptic techniques and following local regulations and site requirements.

Total time from needle puncture of FPI-2053 vial to the start of administration must not exceed 24 hours. Of this time, not more than 4 hours may be at room temperature (up to 25°C), with the remaining time at 2°C to 8°C, otherwise a new dose must be prepared from new vials.

FPI-2053 does not contain preservatives; any unused portion of the vial must be discarded immediately after use.

During preparation of FPI-2053, the following should be documented on the *FPI-2053 Drug Administration Worksheet*:

- Calculated volume
- Actual volume in the syringe pre-infusion

3.5. FPI-2053 Dose Calculation

FPI-2053 lyophilized powder is reconstituted with 2.3ml sterile Water for Injection (WFI). The volume of reconstituted FPI-2053 to be added to the IV bag (dose volume) is dependent upon the participant's weight and the target dose level (mg/kg) of FPI-2053. See below for calculations.

Weight-based doses will be calculated using the following formula:

$$\text{Dose volume (mL)} = \frac{\text{Dose Level (mg/kg)} \times \text{Body Weight (/kg)}}{\text{FPI} - 2053 \text{ Concentration (mg/mL)}}$$

FPI-2053 Concentration = 50 mg/mL

The participant's weight at screening (baseline) will be used to calculate the initial dose. If the participant's weight changes by ± 10% from the general screening weight, please contact Fusion for next steps.

EXAMPLE:

Example of dose calculation with 50 mg/mL reconstituted FPI-2053, assuming a participant weight of 80 kg and 1.0 mg/kg dose level

$$\text{Dose volume (mL)} = \frac{1.0 \text{ (mg/kg)} \times 80 \text{ (kg)}}{50 \text{ mg/mL}} = 1.6 \text{ mL}$$

The calculated volume of FPI-2053 should be rounded to the nearest tenth of a mL (0.1 mL). Therefore, in the example above the dose volume (1.6 mL) does not require additional rounding.

Example calculation of number of vials needed to supply this dose is as follows:

$$\text{\# Vials} = \frac{\text{calc. dose volume (mL)}}{\text{Label claim volume (mL)}}$$

The post-reconstitution label-claim volume for FPI-2053 is 2.0 mL

$$\text{Example: \# Vials} = \frac{1.6 \text{ (mL)}}{2.0 \text{ (mL)}} = \sim 0.8 \text{ vials}$$

The calculated number of vials is ~0.8 vials, which should be rounded up to the next whole number; therefore, 1 vial of FPI-2053 is needed to supply this volume of drug for a single dose.

3.6. FPI-2053 Reconstitution Instructions

Slowly add 2.3 mL of sterile WFI by tilting the vial to one side such that the liquid stream is directed along the vial wall and not directly onto the lyophilized product to minimize product foaming.

Gently swirl the solution until all solids are dissolved.

DO NOT SHAKE OR VIGOROUSLY AGITATE THE VIAL.

Visually inspect the solution to ensure that the entire content is completely reconstituted.

The reconstituted solution should appear clear to opalescent. A thin layer of bubbles on the liquid surface is considered normal.

After reconstitution, FPI-2053 vial will contain a label-claim volume of 2.0 mL drug solution.

If a closed system transfer device (CSTD) must be used for reconstitution, then a new syringe and syringe adapter must be used to withdraw the reconstituted product, i.e., do not re-use the same syringe and syringe adapter that was used for reconstitution to withdraw the product. This will prevent additional dilution resulting from the addition of residual WFI contained in the syringe and syringe adapter.

Note: An IVBP solution is supplied to ensure compatibility of FPI-2053 to the IV infusion components and diluent solution. The lyophilized FPI-2053 product must not be reconstituted with the IVBP solution.

FPI-2053 at 0.03 to 8.9 mg/mL in 0.9% sodium chloride for injection when used with IVBP:

- BD PhaSeal CSTDs
- Polyolefin (PO) IV Bags
- Polyvinylchloride (PVC) lines
- 0.2 or 0.22 µm PES filters

If a CSTD must be used and less than 3 mL of FPI-2053 is to be added through the IV bag adapter, then it is required to flush the IV bag adapter with approximately 2 mL of 0.9% sodium chloride for injection using a new syringe and syringe adapter in order to ensure that the full dose has been added to the IV bag.

Doses will be prepared using an IV bag containing 0.9% sodium chloride for injection.

Add 1 mL of IVBP solution to the IV bag and gently mix by inverting to ensure homogeneity and pre-treat the IV bag.

Add the calculated volume of FPI-2053 to the IV bag. The IV bag size should be selected such that the final concentration is between 0.03 to 8.9 mg/mL; however, the selected IV bag size must not be >250 mL. Mix the bag gently by inverting to ensure homogeneity of the dose in the bag. Do not shake the prepared IV bag.

3.7. FPI-2053 Dose Administration

FPI-2053 infusions are to be administered through an IV administration set with a 0.2 or 0.22 µm in-line filter; acceptable configurations include an IV set containing an in-line filter or the attachment of a separate filter to the distal end of the IV tubing.

The FPI-2053 dose should not be administered with any other IV fluids, combined with other drugs, or administered through an infusion set used at the same time for any purpose other than study dose administration. Neither implanted venous access devices, e.g., Port-a-Cath, nor peripherally inserted central catheter (PICC) lines should be used for IMP administration.

FPI-2053 infusion time is 60 minutes; however, the total allowed time must not exceed 4 hours with the infusion bag kept at room temperature, otherwise a new dose must be prepared from new vials.

Do not co-administer other drugs through the same infusion line.

The IV line will be flushed with a volume equal to the IV-line volume, according to local practices, to ensure the full dose is administered. Infusion time does not include the final flush time.

Investigational Product Receipt and Dispensing Accountability Logs should be completed for both FPI-2053 and IVBP:

- Quantity of vials dispensed
- Balance/Forward Balance
- Participant ID
- Dose Administered
- Administration Date/Time
- Confirmation vial discarded
- Staff Initials

After administration of FPI-2053 the following should be documented on the *FPI-2053 Drug Administration Worksheet* (Appendix 7):

- Infusion site
- Infusion start date/time
- Infusion end date time
- Infusion interruption (yes/no, reason and time)
- Infusion restart (yes/no and time)
- Confirmation flush with normal saline
- Total volume infused

4. INSTRUCTIONS FOR [^{111}IN]-FPI-2107 AND [^{225}AC]-FPI-2068:

4.1. Ordering of Radioactive IMP [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107

Once a potential participant is identified at a site, the delegated site staff completes and submits a Slot Request and Allocation Form to Fusion at FPI-2068-101@fusionpharma.com before participant signs consent. Fusion will communicate with Manufacturing to confirm injection dates with the site and the doses will be ordered at risk. Once the slot is assigned, and the participant signs consent, the participant will enter the General Screening Period. During the General Screening Period [^{111}In]-FPI-2107 will be ordered:

- Fusion will initiate the IMP Order Form by completing Sections 1 through 3
- Fusion will then forward IMP Order Form to the site for review of Sections 1 through 3 and completion of Section 4 (dosing information) and Section 5 (AU signature)
- Once complete, the site will follow the manufacturer's instructions for submission that is located in Section 2.
- IMP Order Forms must be submitted by end of day the Monday of the week prior to injection
- For Part A: Both [^{111}In]-FPI-2107 can be submitted at the same time
- Fusion will confirm with the site that manufacturing has received the IMP Order Form

During Imaging Screening, [^{225}Ac]-FPI-2068 will be ordered following the above instructions.

Should the participant not be eligible for treatment, Fusion will notify the manufacturer to cancel the dose.

4.2. Withdrawing a Request for an Order

If there is a need to change a previously requested shipment of [^{111}In]-FPI-2107 and/or [^{225}Ac]-FPI-2068 or permanently hold the shipment of [^{111}In]-FPI-2107 and/or [^{225}Ac]-FPI-2068, the Investigator or the designated clinical trial site personnel must immediately notify Fusion via email at FPI-2068-101@fusionpharma.com. The email must clearly specify that the request for the [^{111}In]-FPI-2107 and/or [^{225}Ac]-FPI-2068 has been withdrawn and include the following information:

- The participant number
- The original scheduled date of injection
- Reason for cancelation and/or rescheduling
- If rescheduled, Fusion will place a new order on behalf of the site should the participant remain eligible and if the manufacturing schedule allows.

4.3. Receipt of Radioactive IMP

The site will receive each of [^{225}Ac]-FPI-2068 (1 vial) and [^{111}In]-FPI-2107 (1 vial) for administration per participant. Site Standard Operating Procedures (SOPs) for the receipt of radioactive materials must be followed. The appropriate delegated site personnel must complete the following procedures upon receipt of [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107.

NOTE: All handling of radioactive material must be in compliance with Country, Federal, State, and Local regulations, and site procedures.

- Examine the entire shipping packaging for damage.
  - If damage is identified throughout the inspection, DO NOT OPEN THE PACKAGE, place the package in Quarantine status and contact Fusion immediately at clinicalcomplaints@fusionpharma.com. and Fusion will provide additional instructions. Note that the temperature logger, storage, and receipt instructions (below) should be performed for product that is damaged or that there are concerns about.
- Inspect the outer and ancillary labels affixed to the outer shipping container and lead pot, respectively (Appendix 3), for consistency and to confirm the correct IMP has been received.
  - Please see table below for the temperature range and appropriate actions the site should take upon review of the TempTale® data by Fusion:

Table 4: Temperature Range and Actions

Temperature Range	Action

2-8°C	Acceptable for use
<2°C	Fusion to contact site
>8°C	Fusion to contact site

- SpectronRx uses a temperature logger Aegis that will be accessed by Fusion. Fusion will monitor transit and be alerted should the temperature goes outside the specified 2-8°C.
- Please note, if there was a temperature excursion at any point during transit, Fusion will contact the site immediately prior to the site preparing the dose for administration. Fusion will provide additional instructions as to how the site should proceed. This includes whether the IMP may be administered. Participants should not be dosed until the excursion is discussed with Fusion and you receive written approval to administer.
- Transfer the lead container to a suitably shielded area to open it and remove the [^{225}Ac]-FPI-2068 or [^{111}In]-FPI-2107 vial. Compare the vial label to the outer label to confirm that the correct IMP has been received and that the label information is consistent.
- Visually inspect the vial and vial contents.
  - If damage is identified during the inspection, whether it be damage to the outer carton, the vial, or the appearance of the IMP (e.g., particulate matter, discoloration), [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107 **MUST NOT BE ADMINISTERED.** Follow the site's SOPs for receiving damaged radioactive materials and contact Fusion immediately at clinicalcomplaints@fusionpharma.com for additional instructions.
- Immediately transfer the vial to a 2 to 8 °C refrigerator. Both quarantine status and Acceptable for Use status cartons should be placed in the 2 to 8 °C refrigerator
- Complete the IMP Receipt Form, file the form in the site records, and email a copy of the form to ipreceipt@fusionpharma.com.
- Once Fusion has received the IMP Receipt Form, Fusion will forward the Temperature logger report along with the Certificate of Analysis (CoA)

All shipping materials must be stored, decayed, and disposed of safely in accordance with Country, Federal, State and Local regulations and site procedures. All shipping materials are intended for single use and are not to be returned.

- **If the shipment does not arrive at the site at or before the expected delivery date and time, the site should contact FPI-2068-101@fusionpharma.com immediately so the Fusion team can investigate the delay.**

Relevant sections of the [^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068 Injection Accountability Log should be filled upon receipt of [^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068:

- The Lot number, expiry date and time are provided on the [^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068 outer label.
- "*Date received*" refers to the date that [^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068 was received at the clinical trial site.

- The amount of activity received and the time of measurement [^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068 outer label.

4.4. Handling Radioactive IMP

- All handling of radioactive material must be in compliance with Country, Federal, State, and Local regulations and site procedures.
- Suitable radiation protection measures must be taken to minimize the exposure to the participants, site staff, and other persons that may be in the vicinity.
- Radiopharmaceuticals should be handled by individuals trained and authorized in the safe use, handling, and administration of radiopharmaceuticals to humans.
- Individuals who are handling the FPI-2068-101 radiopharmaceuticals ([^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107) must be listed on the study Delegation of Responsibilities (DOR) Log.
- Note that any changes to individuals listed on the DOR Log must be recorded and filed according to the Investigator Site File (ISF) Index and notify Fusion.
- Care must be taken to minimize contamination of clothing and skin of site personnel through the use of disposable gloves and protective clothing.
- Hands must be washed after handling any radioactive materials.
- For further information on [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107 please refer to the FPI-2068-101 study protocol and Investigator's Brochure.

4.5. Storage of Radioactive IMP

- Radioactive materials must be stored in a designated and secure area suitable for storage of radioactive IMP and accessible only by authorized personnel.
- The vials of [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107 must be stored upright in a refrigerator at a temperature of 2-8 °C in a lead shielded container and must be used before the expiry date and time designated on the labels.
- **The refrigerator temperature must be checked and recorded when the Radioactive materials are placed in the refrigerator, and daily while they are stored.**
- **Notify Fusion immediately if the refrigerator temperature is outside of the specified 2-8 °C.**
- The shelf life of [^{225}Ac]-FPI-2068 is ten (10) days (240 hours) post-manufacturing.
- The shelf life of [^{111}In]-FPI-2107 is nine (9) days (216 hours) post-manufacturing.
- The vials must be protected from light and must not be shaken or frozen. [^{225}Ac]-FPI-2068 and [^{111}In]-FPI-2107 must be prepared and administered within 6 hours of removing the vial from the refrigerator.

4.6. Preparation of [^{111}In]-FPI-2107, Radioactive Imaging IMP

Dose calibrators should be calibrated prior to performing any study related procedures. Please refer to the Invicro Technical Operations Manual (TOM) procedure and forms for more information on the calibration settings.

- **Note: The dose calibrator used for dose administration measurement should be the same machine which was utilized during the dose calibrator calibration process during study start-up. Please notify Fusion immediately at FPI-2068-101@fusionpharma.com if any equipment changes have occurred since study start-up (i.e., new calibrator, new hardware, change of location, etc.)**

[^{111}In]-FPI-2107 must be prepared aseptically for administration under the site's standard environmental conditions and SOPs. Follow the below procedures for preparing for administration:

- Ensure the area of preparation is cleaned prior to dispensing [^{111}In]-FPI-2107. Prior to donning gloves, hands must be washed, or sanitized using an alcohol-based hand sanitizer. Once gloves are donned, it is recommended that they are sprayed with 70% isopropyl alcohol (IPA), if possible.
- The vial septum must be wiped with a sterile IPA pad. Allow the wiped septum to dry before piercing the septum.
- A sterile disposable syringe and needle must be used to prepare the injection and assembled immediately before preparing the injection. Syringes must be assembled with needles in a clean environment (or aseptic environment if possible). Aseptic connections must not be handled directly. The volume to be administered of [^{111}In]-FPI-2107 to a given participant should be calculated using the:
  - Radioactivity concentration of the product at the Time of Calibration (TOC). TOC is the date and time when the supplied radionuclide corresponds to the stated activity of the radionuclide. After the TOC, the activity is lower than stated. The activity concentration, and time and date of calibration, is stated on the Certificate of Analysis (CoA).
  - The CoA will be emailed to the site by Fusion once the IMP Receipt Form has been received and the temperature data has been reviewed.
  - Decay correction factor for In-111 to the nearest hour to correct for physical decay (see Appendix 1).

The estimated volume to be administered to a participant for [^{111}In]-FPI-2107 is calculated as follows:

[^{111}In]-FPI-2107:

$$Volume\ (mL) = \frac{185\ MBq}{Decay\ Correction\ Factor\ \underline{In\text{-}111} * Activity\ Concentration\ at\ TOC\ \left(\frac{MBq}{mL}\right)}$$

- Record the calculated volume and have a second person verify the calculation.
- Draw up the calculated volume into a syringe using aseptic techniques. Do not inject air into the vial.
- Before administration, the syringe should be assayed in a dose calibrator to measure the radioactivity.
    - Be sure to use a valid calibration setting for In-111 and note the measurement on the provided dosing worksheet.
- **If the measured activity does not correlate with the calculated volume, DO NOT administer and contact the Fusion at FPI-2068-101@fusionpharma.com**

Of note, the radioactivity reading immediately after the participant dose is withdrawn from the vial into the syringe for administration can be used for activity measurement as the equilibrium is not disturbed when pulling up the syringe from the vial (*Syringe Transfer Study of [^{225}Ac]-FPI-1434, report on file).*

The Investigational Products administered to each participant must be documented to show the net activity administered to the participant. During the preparation of the participant dose, the following should be documented on the [^{111}In]-FPI-2107 Drug Administration Worksheet:

- Calculated Volume
- Dial setting of dose calibrator
- Pre-injection assay (Activity, date, and time)
- Actual volume in the syringe (pre-injection)

4.7. Administration of the [^{111}In]-FPI-2107, Radioactive Imaging IMP

Prior to administration of the [^{111}In]-FPI-2107, the Investigator or delegated site personnel must verify that the participant continues to meet protocol eligibility criteria. Written directives from an authorized user shall be obtained. Follow the below procedures for administering [^{111}In]-FPI-2107 to the participant:

- The participant must be adequately hydrated, according to site/departmental practice, prior to administration. The participant will be asked to void their bladder prior to the injection.
- **The IMP should not be diluted or administered with any other IV fluids, combined with other drugs, or administered through an infusion set used at the same time for any purpose other than study IMP administration. Neither implanted venous access devices, e.g., Port-a-Cath, nor peripherally inserted central catheter (PICC) lines should be used for IMP administration.**
- The injection tubing should be primed with an adequate volume of normal saline prior to use.
- The IMP will be administered by slow intravenous injection (IV, 3-5 minutes).
    - For [^{111}In]-FPI-2107, a single dose of 185 MBq (5 mCi) [^{111}In]-FPI-2107 will be administered. All Participants receive the same dose.

- The use of a 3-way stopcock is recommended for injection to ensure intravenous delivery of the IMP.
- After administration, the tubing and syringe will be thoroughly flushed with an adequate volume of normal saline.
- The syringe and all contaminated tubing should be assayed in the same dose calibrator to determine the net dose administered. The volume injected, date and time of administration, and participant net dose should be recorded.
- The injection site will be assessed just prior to, during, and immediately after injection for local irritation, and during and after injection for radiopharmaceutical extravasation. Following administration, the injection line should be removed from the participant and not used for any other procedures.
- After administration the following should be documented on the [^{111}In]-FPI-2107 Drug Administration worksheets:
  - Injection site:
  - Injection Start Date/Time
  - Injection End Time
  - Injection interruption (yes/no, reason and time)
  - Injection restarted (yes/no and time)
  - Confirmation of flush with normal saline
  - Dial setting post-injection
  - Post-injection assay (activity, date, and time)
  - Net activity injected (pre-injection activity minus post-injection activity)
  - Total volume injected
  - Participant void prior to imaging (yes/no, volume, aliquot assay activity, date/time, volume)
  - Imaging Standard (activity, date/time, placement)

Note: [^{111}In]-FPI-2107 Drug Administration Worksheet should be completed in its entirety and forwarded to FPI-2068-101@fusionpharma.com within 24 hours post administration.

NOTE: Please provide the Participant Hygiene/Precaution Instructions located in Appendix 9 of this Manual to the participant and discuss prior to injection.

4.8. [^{111}In]-FPI-2107 Imaging Standard

For each participant cycle, a reference standard must be prepared prior to their first scan and included within the field of view of each subject scan. The reference standard must be prepared in a syringe with a barrel diameter no greater than approximately 1 cm (e.g., a standard 3 mL syringe) with an activity of approximately 50 µCi of ^{111}In in an approximate volume of 1.5 to 2.5 mL.

NOTE: Please refer to Invicro Technical Operation Manual (TOM) for full details regarding the imaging standard.

4.9. Accountability of the [^{111}In]-FPI-2107, Radioactive Imaging IMP

After IMP is administered to a participant, the remaining sections of the [^{111}In]-FPI-2107 Accountability Logs must be recorded:

- The participant ID number
- Date and time of administration of IMP
- Quantity of IMP administered in MBq and mL

4.10. Disposal of [^{111}In]-FPI-2107, Radioactive Imaging IMP

[^{111}In]-FPI-2107 should be stored, decayed, and disposed of in accordance with site Country, Federal, State and Local regulations, and site procedures. Typically, waste must be stored for a minimum of four months (> 10 half-lives) before disposal. Please refer to Appendix 1 for specific decay requirements for [^{111}In]-FPI-2107.

All materials associated with the preparation and administration of the radiopharmaceutical must be checked for residual contamination after use. The materials that contain contamination from the radiopharmaceutical must be monitored by a low-level radiation monitor and may be disposed of as ordinary waste once the levels of radiation are found to be below regulatory and license limits for radioactive waste. If the site has radiation waste disposal, this may not be necessary.

The used syringe containing residual amounts of [^{111}In]-FPI-2107 must be placed into a biohazard sharps container, labelled as radioactive, and placed in a designated area for decay. Syringes are not required for drug accountability purposes. The identification label and tag should be removed and destroyed before disposing of the waste, when possible.

“Discard date” (disposal) should be documented on the [^{111}In]-FPI-2107 Accountability Logs.

4.11. Preparation of [^{225}Ac]-FPI-2068 Radioactive IMP

Dose calibrators should be calibrated prior to performing any study related procedures. Please refer to the Invicro Technical Operations Manual (TOM) procedure and forms for more information on the calibration settings.

- **Note: The dose calibrator used for dose measurement should be the same machine which was utilized during the dose calibrator calibration process during study start-up. Please notify Fusion immediately at FPI-2068-101@fusionpharma.com if any equipment changes have occurred since study start-up (i.e., new calibrator, new hardware, change of location, etc.)**

[^{225}Ac]-FPI-2068 must be prepared aseptically for administration under the site’s standard environmental conditions and SOPs. Follow the below procedures for preparing for administration:

- Ensure the area of preparation is cleaned prior to dispensing [^{225}Ac]-FPI-2068. Prior to donning gloves, hands must be washed, or sanitized using an alcohol-based hand sanitizer. Once gloves are donned, it is recommended that they are sprayed with 70% isopropyl alcohol (IPA), if possible.
- The vial septum must be wiped with a sterile IPA pad. Allow the wiped septum to dry before piercing the septum.

- A sterile disposable syringe and needle must be used to prepare the injection and assembled immediately before preparing the injection. Syringes must be assembled with needles in a clean environment (or aseptic environment if possible). Aseptic connections must not be handled directly. The volume to be administered of [^{225}Ac]-FPI-2068 to a given participant should be calculated using the:
  - Radioactivity concentration of the product at the Time of Calibration (TOC). TOC is the date and time when the supplied radionuclide corresponds to the stated activity of the radionuclide. After the TOC, the activity is lower than stated. The activity concentration, and time and date of calibration, is stated on the Certificate of Analysis (CoA).
  - The CoA will be emailed to the site by Fusion once the IMP Receipt Form has been received and the temperature data has been reviewed.
  - Decay correction factor for Ac-225 to the nearest day to correct for physical decay (see Appendix Appendix 1).
  - For [^{225}Ac]-FPI-2068 administration, the actual body weight from **the participant's general screening visit**, which is also the weight recorded on the Imaging Screening Notification Form, must be used to calculate the [^{225}Ac]-FPI-2068 dose.
  - If the participant's current body weight has changed by 10% or more (plus or minus) from the general screening visit body weight, contact Fusion at FPI-2068-101@fusionpharma.com. The [^{225}Ac]-FPI-2068 dose MAY be adjusted by Fusion.
  - For [^{225}Ac]-FPI-2068 administration, the prescribed dosage level (in kBq/kg) per study cohort is recorded on the Slot Request and Allocation Form (Appendix 5).

The estimated volume to be administered to a participant for [^{225}Ac]-FPI-2068 is calculated as follows:

[^{225}Ac]-FPI-2068:

$$\textbf{Volume (mL)} = \frac{\textbf{Dose Level (kBq/kg) x Body weight in kg}}{\textbf{Decay Correction Factor Actinium} * \textbf{Activity Concentration at TOC (kBq/mL)}}$$

- Record the calculated volume and have a second person verify the calculation.
- Draw up the calculated volume into a syringe using aseptic techniques. Do not inject air into the vial.
- Before administration, the syringe should be assayed in a dose calibrator to measure the radioactivity.
  - Be sure to use a valid calibration setting for Ac-225 and note the measurement on the provided dosing worksheet.
- **If the measured activity does not correlate with the calculated volume, DO NOT administer and contact Fusion at FPI-2068-101@fusionpharma.com.**

Of note, the radioactivity reading immediately after the participant dose is withdrawn from the vial into the syringe for administration can be used for activity measurement as the equilibrium is not

disturbed when pulling up the syringe from the vial (*Syringe Transfer Study of [^{225}Ac]-FPI-1434, report on file).*

During the preparation of the participant dose, the following should be documented on the [^{225}Ac]-FPI-2068 Drug Administration Worksheet:

- Calculated Volume
- Dial setting of dose calibrator
- Pre-injection assay (Activity, date, and time)
- Actual volume in the syringe (pre-injection)

4.12. Administration of [^{225}Ac]-FPI-2068 Radioactive IMP

Prior to administration of [^{225}Ac]-FPI-2068 the Investigator or delegated site personnel must verify that the participant continues to meet protocol eligibility criteria. Follow the below procedures for administering [^{225}Ac]-FPI-2068 to the participant:

- The participant must be adequately hydrated, according to site/departmental practice, prior to administration.
- The injection tubing should be primed with an adequate volume of normal saline prior to use.
- The IMP will be administered by slow intravenous injection (IV, 3-5 minutes).
  - The [^{225}Ac]-FPI-2068, dose to be administered will depend on participant weight and study cohort assignment.
- **The FPI-2053 dose should not be diluted or administered with any other IV fluids, combined with other drugs, or administered through an infusion set used at the same time for any purpose other than study dose administration. Neither implanted venous access devices, e.g., Port-a-Cath, nor peripherally inserted central catheter (PICC) lines should be used for IMP administration.**
- The use of a 3-way stopcock is recommended for injection to ensure intravenous delivery of the IMP.
- After administration, the tubing and syringe will be thoroughly flushed with an adequate volume of normal saline.
- Following administration and flush, the injection line should be removed from the participant and not used for any other procedures.
- The syringe and all contaminated tubing should be assayed in the same dose calibrator to determine the net dose administered. The volume injected, time of administration, and participant net dose should be recorded.
- The injection site will be assessed just prior to, during, and immediately after injection for local irritation, and during and after injection for radiopharmaceutical extravasation.
- After administration the following should be documented on the [^{225}Ac]-FPI-2068 Drug Administration Worksheets:
  - Injection site:

- Injection Start Date/Time
- Injection End Time
- Injection interruption (yes/no, reason and time)
- Injection restarted (yes/no and time)
- Confirmation of flush with normal saline
- Dial setting post-injection
- Post-injection assay (activity, date, and time)
- Net activity injected (pre-injection activity minus post-injection activity)
- Total volume injected

Note: [^{225}Ac]-FPI-2068 Drug Administration worksheet should be completed in its entirety and forwarded to FPI-2068-101@fusionpharma.com within 24 hours post administration.

NOTE: Please provide the Participant Hygiene/Precaution Instructions located in Appendix 9 of this Manual to the participant and discuss prior to injection.

4.13. Accountability of [^{225}Ac]-FPI-2068 Radioactive IMP

After IMP is administered to a participant, the remaining sections of the [^{225}Ac]-FPI-2068 Accountability Logs must be recorded:

- The participant ID number
- Date and time of administration of IMP
- Quantity of IMP administered in MBq and mL

4.14. Disposal of [^{225}Ac]-FPI-2068 Radioactive IMP

[^{225}Ac]-FPI-2068 should be stored, decayed, and disposed of in accordance with site Country, Federal, State and Local regulations, and site procedures. Typically, waste must be stored for a minimum of four months (> 10 half-lives) before disposal. Please refer to Appendix 2 for specific decay requirements for [^{225}Ac]-FPI-2068.

All materials associated with the preparation and administration of the radiopharmaceutical must be checked for residual contamination after use. The materials that contain contamination from the radiopharmaceutical must be monitored by a low-level radiation monitor and may be disposed of as ordinary waste once the levels of radiation are found to be below regulatory and license limits for radioactive waste. If the site has radiation waste disposal, this may not be necessary.

The used syringe containing residual amounts of [^{225}Ac]-FPI-2068 must be placed into a biohazard sharps container, labelled as radioactive, and placed in a designated area for decay. Syringes are not required for drug accountability purposes. The identification label and tag should be removed and destroyed before disposing of the waste, when possible.

“Discard date” (disposal) should be documented on the [^{225}Ac]-FPI-2068 Accountability Logs.

5. TREATMENT COMPLIANCE

Participants are to receive IMPs in accordance with dosages specified in the protocol and under the direct supervision of the Authorized User. In the case of overdosing of an IMP, even if asymptomatic or not fulfilling the seriousness criterion, the overdose is to be reported immediately (**within 24 hours of the time the Investigator becomes aware of it**) andthe Investigators or other site personnel indicate an AE is serious in the electronic data capture (EDC) system, an automated email alert is sent to the designated Sponsor. If the EDC system is not available, then the Investigator or other study site staff reports an SAE to the appropriate Sponsor representative by telephone.

[^{111}In]-FPI-2107 and [^{225}Ac]-FPI-2068 will be reported as an overdose if the administered dose differs by 20% from the prescribed dose.

FPI-2053 will be reported as an overdose if the administered dose differs by 10% from the prescribed dose.

6. CLINICAL MONITORING

The study monitor will perform accountability of the [^{225}Ac]-FPI-2068, [^{111}In]-FPI-2107, FPI-2053 and IVBP during the monitoring visit(s). The IMP and documentation, on site storage and supply will be routinely monitored by a Site Monitor soon after the first study participant is dosed and periodically thereafter by onsite or remote monitoring visits (as per the Monitoring Plan). The site will be notified in advance by the Site Monitor as to the date and time of each monitoring visit.

7. INVESTIGATIONAL PRODUCT RECALL PLAN

In the case of any recall, Fusion will distribute information accordingly and will alert all clinical sites immediately, via telephone and email.

8. DOCUMENTATION

All forms, logs, and study documentation must be kept in a secure location in the Investigator site file (ISF) and/or the local nuclear medicine department documentation. Site should follow International Conference on Harmonization-GCP guidelines and all local policies.

The study monitor will review the documents during monitoring visits and regulatory authorities or Fusion, or designees, may review, as required. At the end of the study any documentation not held in the ISF must be incorporated into the ISF and archived according to current procedures.

APPENDIX 1. IN-111 DECAY CORRECTION TABLE

No correction is required for changes to Daylight Saving Time. To select the correct factor for decay correction of In-111, calculate the number of hours the date/time of IMP preparation and the reference date and time which is stated on the In-111 vial label.

In-111 Decay Correction Table-
based on **hours** from Time of Calibration (TOC)

Day 1 0-23h		Day 2 24-47h		Day 3 48-71h		Day 4 72-95h		Day 5 96-119h		Day 6 120-143h		Day 7 144-167h		Day 8 168-191h		Day 9 192-215h	
Hrs	DK factor	Hrs	DK factor	Hrs	DK factor	Hours	DK factor	Hours	DK factor	Hours	DK factor	Hours	DK factor	Hours	DK factor	Hours	DK factor
0	1.000	24	0.781	48	0.610	72	0.476	96	0.372	120	0.291	144	0.227	168	0.177	192	0.138
1	0.990	25	0.773	49	0.604	73	0.472	97	0.368	121	0.288	145	0.225	169	0.175	193	0.137
2	0.980	26	0.765	50	0.598	74	0.467	98	0.365	122	0.285	146	0.222	170	0.174	194	0.136
3	0.970	27	0.757	51	0.591	75	0.462	99	0.361	123	0.282	147	0.220	171	0.172	195	0.134
4	0.960	28	0.750	52	0.585	76	0.457	100	0.357	124	0.279	148	0.218	172	0.170	196	0.133
5	0.950	29	0.742	53	0.579	77	0.453	101	0.353	125	0.276	149	0.216	173	0.168	197	0.132
6	0.940	30	0.734	54	0.573	78	0.448	102	0.350	126	0.273	150	0.213	174	0.167	198	0.130
7	0.930	31	0.727	55	0.568	79	0.443	103	0.346	127	0.270	151	0.211	175	0.165	199	0.129
8	0.921	32	0.719	56	0.562	80	0.439	104	0.343	128	0.268	152	0.209	176	0.163	200	0.128
9	0.911	33	0.712	57	0.556	81	0.434	105	0.339	129	0.265	153	0.207	177	0.162	201	0.126
10	0.902	34	0.705	58	0.550	82	0.430	106	0.336	130	0.262	154	0.205	178	0.160	202	0.125
11	0.893	35	0.697	59	0.545	83	0.425	107	0.332	131	0.260	155	0.203	179	0.158	203	0.124
12	0.884	36	0.690	60	0.539	84	0.421	108	0.329	132	0.257	156	0.201	180	0.157	204	0.122
13	0.875	37	0.683	61	0.534	85	0.417	109	0.325	133	0.254	157	0.199	181	0.155	205	0.121
14	0.866	38	0.676	62	0.528	86	0.412	110	0.322	134	0.252	158	0.197	182	0.153	206	0.120
15	0.857	39	0.669	63	0.523	87	0.408	111	0.319	135	0.249	159	0.195	183	0.152	207	0.119
16	0.848	40	0.662	64	0.517	88	0.404	112	0.316	136	0.246	160	0.193	184	0.150	208	0.117
17	0.839	41	0.656	65	0.512	89	0.400	113	0.312	137	0.244	161	0.191	185	0.149	209	0.116
18	0.831	42	0.649	66	0.507	90	0.396	114	0.309	138	0.241	162	0.189	186	0.147	210	0.115
19	0.822	43	0.642	67	0.502	91	0.392	115	0.306	139	0.239	163	0.187	187	0.146	211	0.114
20	0.814	44	0.636	68	0.496	92	0.388	116	0.303	140	0.237	164	0.185	188	0.144	212	0.113
21	0.806	45	0.629	69	0.491	93	0.384	117	0.300	141	0.234	165	0.183	189	0.143	213	0.112
22	0.797	46	0.623	70	0.486	94	0.380	118	0.297	142	0.232	166	0.181	190	0.141	214	0.110
23	0.789	47	0.616	71	0.481	95	0.376	119	0.294	143	0.229	167	0.179	191	0.140	215	0.109

APPENDIX 2. AC-225 DECAY CORRECTION TABLE

No correction is required for changes to Daylight Saving Time. To select the correct factor for decay correction of Ac-225, calculate the number of days between the date of IMP preparation and the Time of Calibration (TOC) which is stated on the Ac-225 vial label.

Ac-225 Decay Correction Table
based on **days** from Reference Date

Days from Reference day (0)	Decay factor Ac-225
0	1.000
1	0.933
2	0.871
3	0.812
4	0.758
5	0.707
6	0.660
7	0.616
8	0.574
9	0.536
10	0.500

APPENDIX 3. INVESTIGATIONAL PRODUCT LABELS

[^{225}Ac]-FPI-2068 US Label

^{225}Ac-FPI-2068

Rx Only – In U.S.
Do not use if cloudy or contains particulate matter.

Sterile solution for infusion.
For intravenous use only. Single-dose vial. Discard unused portion.

Store at 2-8ºC

CAUTION

RADIOACTIVE MATERIAL

Protocol No: _____ Subject ID: _____
Batch No: _____ Volume (mL): _____
Date/Time of Calibration (TOC): _____. (*DDMMMYYYY hh:mm ET*)
Radioactive Concentration at TOC (µCi/mL): _____.
Expiry Date/Time: _____ (*DDMMMYYYY hh:mm ET*)

Sponsor: Fusion Pharmaceuticals Inc. 270 Longwood Rd. S. Hamilton, ON L8P 0A6
Manufactured By: SpectronRx 9550 Zionsville Rd. Suite 1, Indianapolis, IN 46268-1063, US.
Caution: New Drug – Limited by Federal (or US) Law to Investigational Use.

[^{225}Ac]-FPI-2068 CAD (English)/AUS Label

^{225}Ac-FPI-2068

Do not use if cloudy or contains particulate matter.

Sterile solution for infusion.
For intravenous use only. Single-dose vial. Discard unused portion.

Store at 2-8ºC

CAUTION

RADIOACTIVE MATERIAL

Protocol No: _____ Subject ID _____
Batch No: _____ Volume (mL): _____
Date/Time of Calibration (TOC): _____. (*DDMMMYYYY hh:mm ET*)
Radioactive Concentration at TOC (µCi/mL): _____.
Expiry Date/Time: _____ (*DDMMMYYYY hh:mm ET*)

Sponsor: Fusion Pharmaceuticals Inc. 270 Longwood Rd. S. Hamilton, ON L8P 0A6
Manufactured By: SpectronRx 9550 Zionsville Rd. Suite 1, Indianapolis, IN 46268-1063, US.
Investigational Drug to be used only by qualified investigator.

[^{225}Ac]-FPI-2068 CAD (French)

^{225}Ac-FPI-2068

Ne pas utiliser si l'apparence est trouble trouble ou en présence de particules.

Solution stérile pour injection.
Voie intraveineuse uniquement.
Flacon a dose unique. disposer de tout résidu..

Conserver à 2-8ºC

RAYONNEMENT

DANGER RADIATION

Protocole No: _____
N. de lot: _____ Volume (mL): _____
Heure de calibration: _____. (*DDMMMYYYY hh:mm ET*)
Concentration de l'activité à l'heure de calibration (µCi/mL): _____.
Expiration Date/ Heure: _____ (*DDMMMYYYY hh:mm ET*)

Commanditaire de l' étude: Fusion Pharmaceuticals Inc. 270 Longwood Rd. S. Hamilton, ON L8P 0A6
Fabriqué par: SpectronRx 9550 Zionsville Rd. Suite 1, Indianapolis, IN 46268-1063, US.
Mise en garde - nouveau médicament limité par la loi fédérale à l'utilisation expérimentale

[^{111}In]-FPI-2107 US Label

^{111}In-FPI-2107

Rx Only – In U.S.
Do not use if cloudy or contains particulate matter.

Sterile solution for infusion.
For intravenous use only. Single-dose vial. Discard unused portion.

Store at 2-8°C

CAUTION

RADIOACTIVE MATERIAL

Protocol No: _____ Subject ID: _____
Batch No: _____ Volume (mL): _____
Date/Time of Calibration (TOC): _____. *(DDMMMYYYY hh:mm ET)*
Radioactive Concentration at TOC (µCi/mL): _____.
Expiry Date/Time: _____ *(DDMMMYYYY hh:mm ET)*

Sponsor: Fusion Pharmaceuticals Inc. 270 Longwood Rd. S. Hamilton, ON L8P 0A6
Manufactured By: SpectronRx 9550 Zionsville Rd. Suite 1, Indianapolis, IN 46268-1063, US.
Caution: New Drug – Limited by Federal (or US) Law to Investigational Use.

[^{111}In]-FPI-2107 CAD (English)/AUS Label

^{111}In-FPI-2107

Do not use if cloudy or contains particulate matter.

Sterile solution for infusion.
For intravenous use only. Single-dose vial. Discard unused portion.

Store at 2-8°C

CAUTION

RADIOACTIVE MATERIAL

Protocol No: _____ Subject ID _____
Batch No: _____ Volume (mL): _____
Date/Time of Calibration (TOC): _____. *(DDMMMYYYY hh:mm ET)*
Radioactive Concentration at TOC (µCi/mL): _____.
Expiry Date/Time: _____ *(DDMMMYYYY hh:mm ET)*

Sponsor: Fusion Pharmaceuticals Inc. 270 Longwood Rd. S. Hamilton, ON L8P 0A6
Manufactured By: SpectronRx 9550 Zionsville Rd. Suite 1, Indianapolis, IN 46268-1063, US.
Investigational Drug to be used only by qualified investigator.

[^{111}In]-FPI-2107 CAD (French)

^{111}In-FPI-2107

Ne pas utiliser si l'apparence est trouble trouble ou en présence de particules.

Solution stérile pour injection.
Voie intraveineuse uniquement.
Flacon a dose unique. disposer de tout résidu..

Conserver à 2-8°C

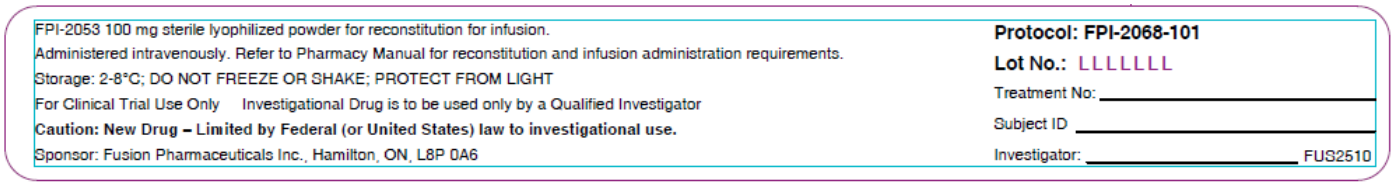
RAYONNEMENT

DANGER RADIATION

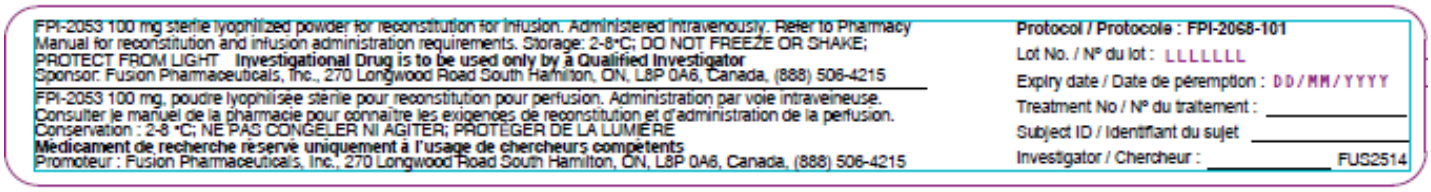
Protocole No: _____
N. de lot: _____ Volume (mL): _____
Heure de calibration: _____. *(DDMMMYYYY hh:mm ET)*
Concentration de l'activité à l'heure de calibration (µCi/mL): _____.
Expiration Date/ Heure: _____ *(DDMMMYYYY hh:mm ET)*

Commanditaire de l' étude: Fusion Pharmaceuticals Inc. 270 Longwood Rd. S. Hamilton, ON L8P 0A6
Fabriqué par: SpectronRx 9550 Zionsville Rd. Suite 1, Indianapolis, IN 46268-1063, US.
Mise en garde - nouveau médicament limité par la loi fédérale à l'utilisation expérimentale

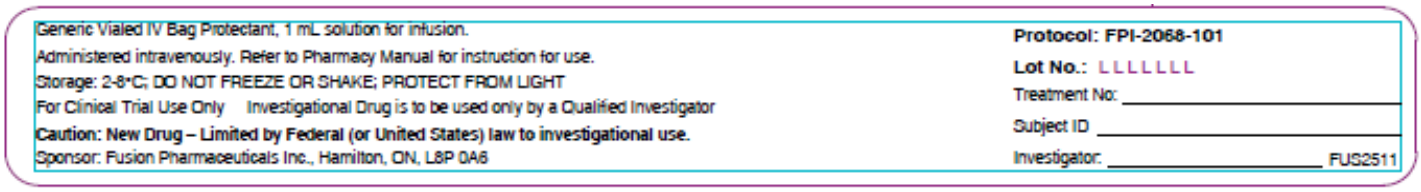
FPI-2053-English



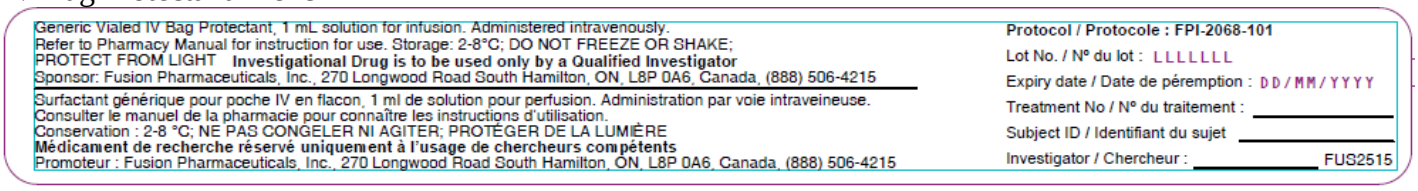
FPI-2053-French



IV Bag Protectant-English



IV Bag Protectant-French



APPENDIX 4. SLOT ALLOCATION AND ELIGIBILITY FORMS

AstraZeneca	Fusion Pharmaceuticals Inc. FPI-2068-101 Study	Fusion

Slot Request and Allocation Form

FORM COMPLETION INSTRUCTIONS

This form is to be completed and emailed to {HYPERLINK "mailto:FPI-2068-101@fusionpharma.com"} and {HYPERLINK "mailto:FPI2068101@astrazeneca.com"}_before consenting a participant to the FPI-2068-101 study. The site should complete this form as soon as possible when a participant candidate is identified. Cohort slots are limited, and screening approvals are subject to cohort slot availability. Please consult participant on injection dates prior to submitting form and please do not consent a participant until slot is assigned.

Name the file with the following naming convention: "FPI-2068-101_Site ####_Slot Request and Allocation Form_DDMMMYYYY".

For completion by the site to request a slot prior to participant signing the Informed Consent Form. Please note for Part A [^{111}In]-FPI-2107 and FPI-2053 + [^{111}In]-FPI-2107 should be dosed one week apart.

Site Number		**Principal Investigator**	
Planned Date of Informed Consent (dd/mmm/yyyy)		**Date of Request** (dd/mmm/yyyy)	
***For Part A only - Preferred [^{111}In]-FPI-2107 Injection Date** (dd/mmm/yyyy)		***For Part A only - Backup [^{111}In]-FPI-2107 Injection Date** (dd/mmm/yyyy)	
[^{111}In]-FPI-2107 Injection Date (dd/mmm/yyyy)		***Backup [^{111}In]-FPI-2107 Injection Date** (dd/mmm/yyyy)	
***Preferred [^{225}Ac]-FPI-2068 Injection Date** (dd/mmm/yyyy)		***Backup [^{225}Ac]-FPI-2068 Injection Date** (dd/mmm/yyyy)	
Signature of Person Completing Form		**Name of Person Completing Form**	
Diagnosis			

**Please provide preferred and back up injection request at least one week apart. Please note, only one set of injection dates (preferred or backup) will be approved.*

FPI-2068-101 Slot Request and Allocation Form - Version 1.0
Page { PAGE } of { NUMPAGES }

AstraZeneca	**Fusion Pharmaceuticals Inc.** **FPI-2068-101 Study**	Fusion

For completion by the Fusion Trial Manager, or designee, to approve and assign a cohort slot:

☐ **Screening Slot Approved** ☐ **Added to Wait List** ☐ **Screening Slot NOT Approved**

Comments:

Slot Allocation	**Dose Level**
Cohort: _____ ☐ **Part A1** ☐ **Part A2** ☐ **Part A3** **Cohort:** _____ ☐ **Part B0** ☐ **Part B1** ☐ **Part B2** ☐ **Part B3**	• **[^{111}In]-FPI-2107 (MBq):** _____ • **[^{225}Ac]-FPI-2068 (kBq/kg):** _____ • **FPI-2053 (mg/kg):** _____

Name/Title: **Signature:** **Date:** ____ / _____ /_____
(dd/mmm/yyyy)

Note: Fusion MM, or designee, will return the Slot Request and Allocation Form within 3 business days of receipt of the request and assign a cohort slot if the participant is approved for a slot.

AstraZeneca	Fusion Pharmaceuticals Inc. FPI-2068-101 Study	Fusion

General Screening Eligibility Form

FORM COMPLETION INSTRUCTIONS

This form is to be completed and emailed to FPI-2068-101@fusionpharma.com and FPI2068101@astrazeneca.com once the participant satisfies all General Screening eligibility criteria for the FPI-2068-101 study.

Name the file with the following naming convention: "FPI-2068-101_Site ####_General Screening Eligibility Form_DDMMMYYYY".

Please note that the participant weight at general screening is required to order [^{111}In]-FPI-2107, and [^{225}Ac]-FPI-2068.

For completion by the site once the participant satisfies all General Screening eligibility criteria. Form must be completed prior to administering [^{111}In]-FPI-2107:

Site Number		**Principal Investigator**	
Date of Notification (to Fusion) (dd/mmm/yyyy)		**Participant ID**	
Participant Weight at General Screening (kg)		**Diagnosis and initial date of diagnosis**	
For Part A only - Planned [^{111}In]-FPI-2107 Injection Date (dd/mmm/yyyy)		**Planned [^{225}Ac]-FPI-2068 Injection Date** (dd/mmm/yyyy)	
Planned FPI-2053 + [^{111}In]-FPI-2107 Injection Date (dd/mmm/yyyy)			

Participant General Screening Inclusion Criteria Verification
Does the participant satisfy all protocol inclusion criteria except for the TBR ≥ 2:1, relative to paravertebral spinal muscle, in at least one measurable extrahepatic lesion, as determined by SPECT/CT scan imaging criterion? ☐ Yes No ☐ **If No, please provide comment:**

FPI-2068-101 General Screening Eligibility Form - Version 1.0

Page 1 of 2

AstraZeneca	Fusion Pharmaceuticals Inc. FPI-2068-101 Study	Fusion

Participant General Screening Exclusion Criteria Verification
Please confirm prior EBRT limits do not exceed 1.7 Gy to the kidney, 17 Gy to the liver, and 0.5 Gy to the lung; Prior radiation > 20 Gy to more than one-third of the pelvis **Please confirm none of the remaining exclusion criteria are met ☐ Yes No ☐**
Investigator Signature
_____ _____ _____ **Investigator (or designee) Name** **Signature** **Date**

FPI-2068-101 General Screening Eligibility Form - Version 1.0

Page 2 of 2

AstraZeneca	Fusion Pharmaceuticals Inc. FPI-2068-101 Study	Fusion

Image Screening Eligibility Form

FORM COMPLETION INSTRUCTIONS

This form is to be completed and emailed to FPI-2068-101@fusionpharma.com and FPI2068101@astrazeneca.com once the participant completes imaging screening for the FPI-2068-101 study.

Name the file with the following naming convention: "FPI-2068-101_Site ####_Imaging Eligibility Form _DDMMMYYYY".

For completion by the site once the participant satisfies all- imaging eligibility criteria. Form must be completed prior to administration of [^{111}In]-FPI-2107.

Site Number		**Principal Investigator**	
Date of Notification to Fusion (dd/mmm/yyyy)		**Participant ID**	
Participant Weight at General Screening (kg)		**Planned [^{225}Ac]-FPI-2068 Injection Date** (dd/mmm/yyyy)	

Participant Imaging Eligibility Verification

Did the participant have TBR ≥ 2:1 uptake read ☐ **Yes** **No** ☐

If No, please provide reason:

If Yes, was TBR ≥ 2:1 relative to paravertebral spinal muscle, in at least one measurable extrahepatic lesion?

☐ **Yes** **No** ☐

If No, please provide comment:

FPI-2068-101 Image Screening Eligibility Form – Version 1.0 Page 1 of 2

AstraZeneca	Fusion Pharmaceuticals Inc. FPI-2068-101 Study	Fusion

For all participants, does the participant satisfy ALL protocol inclusion and exclusion criteria for treatment with [^{225}Ac]-FPI-2068?

☐ Yes No ☐

If No, please provide comment:

Reminder: participant's lab values (CBC, reticulocyte count, and chemistry) should be confirmed within protocol treatment requirements (48 hours prior to [^{225}Ac]-FPI-2068).

Investigator (or designee) Name	Signature	Date

FPI-2068-101 Image Screening Eligibility Form – Version 1.0 Page 2 of 2

APPENDIX 5. PHARMACY ORDER FORM

Form

Title: **In-111 IP Order Form**

1. Protocol Information (Fusion to Complete)	
Target	
Protocol Number	

2. Manufacturer Information (Fusion to Complete)	
Manufacturer	
Address	
Instructions	

3. Site Information (Fusion to Complete)	
Site Number	
Site Name	
Principal Investigator	
Site Contact Name	
Site Contact Address	
Site Contact Email	
Site Contact Phone	

4. Investigational Product (Site to Complete)					
Isotope Requested					
Participant ID	Anticipated Date of Intravenous Injection (DD/MMM/YYYY)	Estimated Intravenous Injection Time (24 hour clock and time zone)	Dose Level (kBq/kg)	Patient General Screening Visit Weight (kg)*	Prescribed Dose (MBq)**
					185
*If the participant's current body weight has changed by 10% or more from the general screening visit body weight, please contact Fusion.					
**In-111 dose will be 185 MBq					

Form

Title: **In-111 IP Order Form**

5. Authorized User (Site to Complete)		
Name (Print):	Signature:	Date:

6. Batch Information (Manufacturer to Complete)	
Product Number	
Batch/Lot Number	
Date of Manufacturer	

7. Vial Fill Details for Patient Injection (Manufacturer to Complete)			
Patient ID	Activity Dispensed (MBq)	Time of Calibration (DD/MMM/YYYY); 24 hour clock with time zone	Expiry (DD/MMM/YYYY); 24 hour clock with time zone

8. Personnel Submitting Order (Manufacturer to Complete)		
Name (Print):	Signature:	Date:

Form

Title: **Ac-225 IP Order Form**

1. Protocol Information (Fusion to Complete)	
Target	
Protocol Number	

2. Manufacturer Information (Fusion to Complete)	
Manufacturer	
Address	
Instructions	

3. Site Information (Fusion to Complete)	
Site Number	
Site Name	
Principal Investigator	
Site Contact Name	
Site Contact Address	
Site Contact Email	
Site Contact Phone	

4. Investigational Product (Site to Complete)					
Isotope Requested					
Participant ID	Anticipated Date of Intravenous Injection (DD/MMM/YYYY)	Estimated Intravenous Injection Time (24 hour clock and time zone)	Dose Level (kBq/kg)	Patient General Screening Visit Weight (kg)*	Prescribed Dose (MBq)**
*If the participant's current body weight has changed by 10% or more from the general screening visit body weight, please contact Fusion.					
**Prescribed Dose (MBq) = (Dose Cohort Level (kBq/kg)×Patient General Screening Visit Weight (kg)/1000					

Form

Title: **Ac-225 IP Order Form**

5. Authorized User (Site to Complete)		
Name (Print):	Signature:	Date:

6. Batch Information (Manufacturer to Complete)	
Product Number	
Batch/Lot Number	
Date of Manufacturer	

7. Vial Fill Details for Patient Injection (Manufacturer to Complete)			
Patient ID	Activity Dispensed (MBq)	Time of Calibration (DD/MMM/YYYY); 24 hour clock with time zone	Expiry (DD/MMM/YYYY); 24 hour clock with time zone

8. Personnel Submitting Order (Manufacturer to Complete)		
Name (Print):	Signature:	Date:

APPENDIX 6. IMP RECEIPT FORM

Investigational Medicinal Product (IMP) Receipt Form			
Site Name:	Site Address:		
Site Number:	Participant ID:		
Date of Receipt:	Time of Receipt:		
Manufacturer Information			
Manufacturer:			
Protocol:	IMP Name:		
Lot Number:	Number Vials Received:		
Temperature Logger Serial Number:			
Activity Received			
Measured Activiy (MBq):	Date:	Time:	

	Yes	No
Was there any physical damage to the shipment box?		
Was there any radioactive contamination present on the shipment box?		
Were the documents included with the shipment box?		
Was the TempTale data logger included with the shipment? *(If SpectronRx is the manufacturer, note NA)*		
Was the temperature of the shipment witin specification during transit?		
Copy of the TempTale data emailed to Fusion and Manufacturer? *(If SpectronRx is the manufacturer, note NA)*		
Was the lead container placed immediately in a refrigerator or freezer immediately after unpacking and receipt measurement?		
Has sufficient activity been received to conduct the trial procedures? *(If no, please contact Fusion immediately)*		
Were there any concerns with the quality of the IMP? *(If yes, DO NOT administer. Contact Fusion immediately)*		

Print Name of Site Personnel Receiving IMP:	
Signature:	Date:

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

APPENDIX 7. DRUG ACCOUNTABILITY LOGS

[^{111}In]-FPI-2107 Injection Drug Accountability Log

Protocol	A Phase 1, First-in-human, Multicentre, Open-label, Dose-escalation Study of [^{225}Ac]-FPI-2068 Injection in Patients with Advanced Solid Tumours		
Protocol Number	FPI-2068-101	**Investigational Product**	[^{111}In]-FPI-2107 Injection
Investigator		**Site Number**	

Lot #	**Date Received (dd/mmm/yyyy)**	**Activity Received**		**Sign off**	**Expiration**		**Participant ID**	**Administered to Subject**		**Quantity Administered**	
		MBq Received	**TOC (on label) hh:mm**	**Site Staff Dated Initials**	**Date (dd/mmm/yyyy)**	**Time hh:mm**		**Date (dd/mmm/yyyy)**	**Time hh:mm**	**MBq[1]**	**mL**
								Start Decay Date:	**Stop Decay Date:**	**Discard Date:**	**Initials:**
								Monitor Check	**Date:**	**Initials:**	

Lot #	**Date Received (dd/mmm/yyyy)**	**Activity Received**		**Sign off**	**Expiration**		**Participant ID**	**Administered to Subject**		**Quantity Administered**	
		MBq Received	**TOC (on label) hh:mm**	**Site Staff Dated Initials**	**Date (dd/mmm/yyyy)**	**Time hh:mm**		**Date (dd/mmm/yyyy)**	**Time hh:mm**	**MBq[1]**	**mL**
								Start Decay Date:	**Stop Decay Date:**	**Discard Date:**	**Initials:**
								Monitor Check	**Date:**	**Initials:**	

[1] Amount to be recorded on this form is the net activity administered (pre-injection activity minus post-injection activity) (two decimal places required)

Site Staff Name/Title: _____ **Signature:** _____ **Date:** _____

Monitor Review Name: _____ **Signature:** _____ **Date:** _____

[225Ac]-FPI-2068 Injection Drug Accountability Log

Protocol	A Phase 1, First-in-human, Multicentre, Open-label, Dose-escalation Study of [225Ac]-FPI-2068 Injection in Patients with Advanced Solid Tumours		
Protocol Number	FPI-2068-101	**Investigational Product**	[225Ac]-FPI-2068 Injection
Investigator		**Site Number**	

Lot #	**Date Received (dd/mmm/yyyy)**	**Activity Received**		**Sign off**	**Expiration**		**Participant ID**	**Administered to Subject**		**Quantity Administered**	
		MBq Received	**TOC (on label) hh:mm**	**Site Staff Dated Initials**	**Date (dd/mmm/yyyy)**	**Time hh:mm**		**Date (dd/mmm/yyyy)**	**Time hh:mm**	**MBq[2]**	**mL**
								Start Decay Date:	**Stop Decay Date:**	**Discard Date:**	**Initials:**
								Monitor Check	**Date:**	**Initials:**	

Lot #	**Date Received (dd/mmm/yyyy)**	**Activity Received**		**Sign off**	**Expiration**		**Participant ID**	**Administered to Subject**		**Quantity Administered**	
		MBq Received	**TOC (on label) hh:mm**	**Site Staff Dated Initials**	**Date (dd/mmm/yyyy)**	**Time hh:mm**		**Date (dd/mmm/yyyy)**	**Time hh:mm**	**MBq[1]**	**mL**
								Start Decay Date:	**Stop Decay Date:**	**Discard Date:**	**Initials:**
								Monitor Check	**Date:**	**Initials:**	

[1] Amount to be recorded on this form is the net activity administered (pre-injection activity minus post-injection activity) (two decimal places required)

Site Staff Name/Title: _____ **Signature:** _____ **Date:** _____

Monitor Review Name: _____ **Signature:** _____ **Date:** _____

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

FPI-2053 Investigational Product Receipt and Dispensing Accountability Log

Sponsor:	Fusion	**Site Number:**	
Inv. Product:	FPI-2053 Administration	**PI Name:**	
Protocol Number:	FPI-2068-101	**Pharmacy:**	
		Address/Phone:	

Date Received	**Lot #**	**Expiry date Or N/A**	**Quantity of vials received/dispensed**	**Balance/ Forward Balance**	**Participant ID**	**Dose Administered**	**Administration Date/Time**	**Confirmation vial discarded**	**Recorder Initials**	**Checked by**	
										Monitor Initials	**Date**
				/							
				/							
				/							
				/							
				/							
				/							
				/							
				/							
				/							
				/							
***Monitor Signature:**						**Date:**					
***Investigator &/or Staff Signature:**						**Date:**					

*Both signatures required when the entire page is full, all patients listed have completed treatment AND accountability is complete.

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

FPI-2053 IVBP Investigational Product Receipt and Dispensing Accountability Log

Sponsor:	Fusion	**Site Number:**	
Inv. Product:	FPI-2053 IVBP Administration	**PI Name:**	
Protocol Number:	FPI-2068-101	**Pharmacy:**	
		Address/Phone:	

Date Received	Lot #	Expiry date Or N/A	Quantity of vials received/dispensed	Balance/ Forward Balance	Participant ID	Dose Administered	Administration Date/Time	Confirmation vial discarded	Recorder Initials	Checked by	
										Monitor Initials	Date
				/							
				/							
				/							
				/							
				/							
				/							
				/							
				/							
				/							
				/							

***Monitor Signature:**		**Date:**	
***Investigator &/or Staff Signature:**		**Date:**	

*Both signatures required when the entire page is full, all patients listed have completed treatment AND accountability is complete.

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

APPENDIX 8. DRUG ADMINISTRATION FORMS

Instructions:
Form to be completed by Investigator Site <u>within 24 hours post administration</u> and emailed to:
FPI-2068-101@fusionpharma.com and FPI2068101@astrazeneca.com

Fusion Protocol FPI-2068-101				
[^{111}In]-FPI-2107 Drug Administration Worksheet				
Site Name:	**Participant ID #:**	**PI:**		
Participant Information				
1. Assigned Therapy Dose Level [^{225}Ac]-FPI-2068 dose level:				
Please check one:				
Part A				
☐ 15 kBq/kg Dose Level				
Part B				
☐ 15 kBq/kg Dose Level Part B0	☐ 40 kBq/kg Dose Level Part B2			
☐ 25 kBq/kg Dose Level Part B1	☐ 70 kBq/kg Dose Level Part B3			
☐ Other (kBq/kg):				
Cold antibody (FPI-2053) dose level:	☐ 0.3 mg/kg	☐ 1.0 mg/kg	☐ 3.0 mg/kg	☐ NA
Part A and Part B: [^{111}In]-FPI-2107 Dose Level 185 MBq				
☐ Dose #1	☐ Dose #2 (Part A only)			
2. Participant's Sex at Birth (please check): ☐ Male ☐ Female				
3. Participant's Age (yrs)**:**				
4. Participant's General Screening Visit Height (cm)**:**				
5. Participant's General Screening Visit Weight (kg)**:**				

Injection Information
Planned Dose of [^{111}In]-FPI-2107:
The volume to be administered to a given participant should be calculated using the: • Radioactivity concentration of the product at the time of calibration (TOC). TOC is the date and time when the supplied radionuclide corresponds to the stated activity of the radionuclide. The activity concentration, and the time and date of calibration, is stated on the Certificate of Analysis (CoA) • Decay correction factor for Indium-111 to correct for physical decay of Indium-111 to the nearest hour (see Pharmacy Manual Indium-111 Decay Correction Table) • The estimated volume to be administered to a participant is calculated as follows: $$\textbf{The Estimated Volume to be administered (mL)} = \frac{\textbf{185 MBq}}{\textbf{Decay Correction Factor In-111} * \textbf{Activity Concentration at TOC} \left(\frac{\textbf{MBq}}{\textbf{mL}}\right)}$$ [^{111}In]-FPI-2107 dose should be within 20% of the prescribed dose.

Fusion Pharmaceuticals Inc.

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

The dose will be administered by slow intravenous injection (IV, 3-5 minutes) [^{111}In]-FPI-2107 should not be diluted or administered except as instructed in the Study Pharmacy Manual, or administered through an injection set that was used for any purpose other than study IMP administration. Do Not use a PICC line or Port.		
6. Calculated Volume**:**		
7. Dial setting of dose calibrator before injection**:**		
8. Activity in syringe **before** injection (MBq)**:**		
9. Assay Date/Time of Syringe **before** injection**:**		
(DD/MMM/YYYY):	HH:MM (24 hr):	Time Zone**:**
10. Actual volume in syringe **before** injection (mL)**:**		
11. Injection Site**:**		
12. Injection Start Date/Time:		
(DD/MMM/YYYY):	HH:MM (24 hr):	Time Zone**:**
13. Injection End Time: HH:MM (24 hr):		
14 Was injection interrupted? Yes☐ No ☐		
If Yes: Reason why**:**		
Interruption start time (HH:MM 24 hr)		
15. Was injection restarted? Yes☐ No ☐		
If Yes: Injection restart time HH:MM (24 hr): N/A ☐		
16. Was the line flushed with normal saline after injection: Yes☐ No ☐		
17. Dial setting of dose calibrator after injection:		
18. Activity in the syringe and tubing **after** injection (MBq):		
19. Assay Date/Time of Syringe and tubing post injection:		
DD/MMM/YYYY:	HH:MM (24 hr):	Time Zone:
20. Net [^{111}In]-FPI-2107 dose administered (Please subtract post-injection activity (#18) from pre-injection activity (#8)) (MBq):		
21. Total volume injected (mL):		
22. Did the participant void after the [^{111}In]-FPI-2107 injection and before the scan?		
Yes☐ No ☐		
If Yes: Total volume of urine void (mL):		
Urine aliquot activity assay Date/Time:		

Fusion Pharmaceuticals Inc.

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

DD/MMM/YYYY:	HH:MM (24 hr):	Time Zone:
Urine aliquot assay result (MBq):		
Volume of urine aliquot (mL):		

Planar and SPECT Imaging Standard		
23. In-111 Planar Reference Source Net Activity Assay Result (MBq):		
Assay Date (DD/MMM/YYYY):	Time of Assay HH:MM (24 hr):	Time Zone:
The Imaging Standard should be placed completely in the field of view of every Whole-Body Planar image, near the feet, at least 5 cm away from the participant.		
24. The Planar Imaging Reference Source was positioned at what location and orientation?		
25. In-111 SPECT Imaging Standard Net Activity Assay Result (MBq):		
Assay Date (DD/MMM/YYYY):	Time of Assay HH:MM (24 hr):	Time Zone
The Imaging Standard should be placed completely in the field of view of every SPECT/CT scan at least 2 cm away from the participant.		
26. The SPECT Imaging Reference Source was positioned at what location and orientation?		

Signatory	
Person completing this form (Please print):	Title:
Signature:	Date:
Person performing second check (Please print):	Title:
Signature:	Date:

Place [^{111}In]-FPI-2107 Dose Label

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

Instructions:
Form to be completed by Investigator Site <u>within 24 hours post administration</u> and emailed to:
FPI-2068-101@fusionpharma.com and FPI2068101@astrazeneca.com

Fusion Protocol FPI-2068-101				
[^{225}Ac]-FPI-2068 Drug Administration Worksheet				**Cycle #:**
Site Name - #:	**Participant ID:**	**PI:**		
Participant Information				
1. Assigned Therapy Dose Level [^{225}Ac]-FPI-2068 dose level:				
Please check one:				
Part A				
☐ 15 kBq/kg Dose Level				
Part B				
☐ 15 kBq/kg Dose Level Part B0	☐ 40 kBq/kg Dose Level Part B2			
☐ 25 kBq/kg Dose Level Part B1	☐ 70 kBq/kg Dose Level Part B3			
☐ Other (kBq/kg):				
Cold antibody (FPI-2053) dose level:	☐ 0.3 mg/kg	☐ 1.0 mg/kg	☐ 3.0 mg/kg	☐ NA
2. Participant's Sex at Birth (please check): ☐ Male ☐ Female				
3. Participant's Age (yrs)**:**				
4. Participant's General Screening Visit Height (cm)**:**				
5. Participant's General Screening Visit Weight (kg)**:**				

Injection Information
Planned Dose of [^{225}Ac]-FPI-2068:

The volume of [^{225}Ac]-FPI-2068 to be administered to a given participant should be calculated using the:
• Participant's body weight (kg)
  ○ Please use general screening visit body weight (this is also the weight recorded on the Imaging Screening Period Request and Approval Form).
  ○ If the participant's current body weight has changed by 10% or more from the general screening visit body weight, please contact the Sponsor at FPI-2068-101@fusionpharma.com and FPI2068101@astrazeneca.com
• Radioactivity concentration of the product (RAC) at reference date. The RAC at the reference date is stated on the Certificate of Analysis (CoA).
• Dose level of [^{225}Ac]-FPI-2068 in kBq/kg body weight
• Decay correction factor for Actinium-225 (DC-Actinium) to correct for physical decay of Actinium-225 to the nearest day (see Appendix 2. Actinium-225 Decay Correction Table)
• The total volume to be administered to a participant is calculated as follows:
$$\textbf{Volume to be administered (mL)} = \frac{\textbf{Dose Level (kBq/kg) x Body weight in kg}}{\textbf{Decay Correction Factor Actinium} * \textbf{RAC (kBq/mL)}}$$

Fusion Pharmaceuticals Inc.

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

[^{225}Ac]-FPI-2068 dose should be within 20% of the prescribed dose.

The dose will be administered by slow intravenous injection (IV, 3-5 minutes)

[^{225}Ac]-FPI-2068 should not be diluted or administered except as instructed in the Study Pharmacy Manual, or administered through an injection set that was used for any purpose other than study IMP administration. Do Not use a PICC line or Port

6. Calculated Volume**:**		
7. Dial setting of dose calibrator before injection**:**		
8. Activity in syringe **before** injection (MBq)**:**		
9. Assay Date/Time of Syringe **before** injection**:**		
(DD/MMM/YYYY):	HH:MM (24 hr):	Time Zone**:**
10. Actual volume in syringe **before** injection (mL)**:**		
11. Injection Site**:**		
12. Injection Start Date/Time:		
(DD/MMM/YYYY):	HH:MM (24 hr):	Time Zone**:**
13. Injection End Time: HH:MM (24 hr):		
14 Was injection interrupted? Yes☐ No ☐		
If Yes: Reason why**:**		
Interruption start time (HH:MM 24 hr)		
15. Was injection restarted? Yes☐ No ☐		
If Yes: Injection restart time HH:MM (24 hr): N/A ☐		
16. Was the line flushed with normal saline after injection: Yes☐ No ☐		
17. Dial setting of dose calibrator after injection:		
18. Activity in the syringe and tubing **after** injection (MBq):		
19. Assay Date/Time of Syringe and tubing post injection:		
DD/MMM/YYYY:	HH:MM (24 hr):	Time Zone:
20. Net [^{225}Ac]-FPI-2068 dose administered (Please subtract post-injection activity (#18) from pre-injection activity (#8)) (MBq):		
21. Total volume injected (mL):		

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

Signatory	
Person completing this form (Please print):	Title:
Signature:	Date:
Person performing second check (Please print):	Title:
Signature:	Date:

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

Instructions:
Form to be completed by Investigator Site within 24 hours post administration and emailed to:
FPI-2068-101@fusionpharma.com and FPI2068101@astrazeneca.com

Fusion Protocol FPI-2068-101				
FPI-2053 Drug Administration Worksheet				
Site Name - #:	**Participant ID #:**	**PI:**		
Visit: Day of Imaging Injection ☐ Day of Treatment Injection ☐ Cycle #:				
Participant Information				
1. Assigned Therapy Dose Level ([^{225}Ac]-FPI-2068) dose level (kBq/kg):				
Please check one:				
Part A				
☐ 15 kBq/kg Dose Level				
Part B				
☐ 15 kBq/kg Dose Level Part B0		☐ 40 kBq/kg Dose Level Part B2		
☐ 25 kBq/kg Dose Level Part B1		☐ 70 kBq/kg Dose Level Part B3		
☐ Other (kBq/kg):				
Cold antibody (FPI-2053) dose level:	☐ 0.3 mg/kg	☐ 1.0 mg/kg	☐ 3.0 mg/kg	☐ NA
2. Participant's Sex at Birth (please check): ☐ Male ☐ Female				
3. Participant's General Screening Visit Weight (kg):				

Infusion Information

- The volume of FPI-2053 to be infused to a given participant should be calculated using the:
  - Participant's general screening body weight (this is also the weight recorded on the Imaging Screening Period Request and Approval Form)
    - If the participant's current body weight has changed by 10% or more from the general screening visit body weight, please contact the Sponsor at FPI-2068-101@fusionpharma.com and ***FPI2068101@astrazeneca.com***
  - Dose level of FPI-2053 in mg/kg
  - Reconstituted FPI-2053 solution concentration = 50 mg/mL
  - The total volume to be administered to a participant is calculated as follows:

$$\textbf{The Estimated Volume to be infused (mL)} = \frac{\textbf{Dose Level } \left(\frac{\textbf{mg}}{\textbf{kg}}\right) \textbf{ x Body Weight (kg}}{\textbf{FPI} - \textbf{2053 Solution Concentration } \left(\frac{\textbf{mg}}{\textbf{mL}}\right)}$$

The final concentration is between 0.03 to 8.9 mg/mL in the saline bag

FPI-2053 should be administered over 60 minutes (+/- 5 minutes)

FPI-2053 dose should be within 10% of the prescribed dose.

Form

Title: **[^{225}Ac]-FPI-2068 Injection Drug Accountability Log**

FPI-2053 should not be diluted or administered except as instructed in the Study Pharmacy Manual, or administered through an injection set that was used for any purpose other than study IMP administration. Do Not use a PICC line or Port.		
4. Calculated Volume:		
5. Actual volume in syringe **before** injection into 500 ml IV Bag (mL):		
6. Infusion Site:		
7. Infusion Start Date/Time:		
DD/MMM/YYYY:	HH:MM (24 hr):	Time Zone:
8. Infusion End Date/Time:		
DD/MMM/YYYY:	HH:MM (24 hr):	Time Zone:
9. Was infusion interrupted? Yes ☐ No ☐		
If Yes: Reason why:		
Interruption start time (HH:MM 24 hr/Time Zone):		
10.. Was infusion restarted? Yes ☐ No ☐		
Infusion restart time (HH:MM 24 hr/Time Zone): N/A ☐		
11. Was the line flushed with normal saline after infusion: Yes ☐ No ☐		
12. Total volume infused (mL):		

Signatory	
Person completing this form (Please print):	Title:
Signature:	Date:
Person performing second check (Please print):	Title:
Signature:	Date:

APPENDIX 9. PARTICIPANT HYGIENE INSTRUCTIONS

Clinical Study Participation Information
Hygiene Guidelines
Study ID: FPI-2068-101

Hygiene Guidelines and Instructions for patients after FPI-2068 treatment

You received a radioactive medicine as part of the clinical study, FPI-2068-101. There are no restrictions to contact with other people after FPI-2068 administrations, however, due to the radioactive nature of the therapy that you were administered, others around you may be exposed to low levels of radiation. Most of the radioactive medicine will exit your body through your urine and feces.

Follow these guidelines for two (2) weeks after each treatment of FPI-2068

Bathroom Use:

- Males should urinate in the sitting position.
- After using the toilet, close the lid and flush the toilet twice.
- Wipe with bath tissue (toilet paper) and flush the tissue down the toilet.
- Wash your hands thoroughly with soap after using the bathroom.
- When bathing, do not share a towel with other members of the household. Wash your towel and other laundry separately from other household members.
- If you have two bathrooms, you should have sole use of one of the bathrooms.

Contact with Body Fluids/Waste (urine, feces, blood, saliva, semen, or vomit):

- Clean any spills, vomit, or any other body fluid right away.
- Use disposable gloves when cleaning up spills and dispose of them in the garbage.
- Soak up any spillage with absorbent papers and flush down the toilet if able. If they cannot be flushed, place waste in a separate garbage bag and keep for four (4) weeks before discarding.
- Wash hands thoroughly with soap after cleaning up spills of body fluids/waste.
- Use disposable underwear or adult diapers if you have diarrhea or urinary incontinence (leaking urine).
- You must use a condom to prevent contact with semen when having sex.
- If you are a man able to produce children, you and your partner must use a highly effective form of contraception or abstain from intercourse for 6 months after your last dose of study drug. Some highly effective forms of contraception include hormonal contraceptives, intrauterine devices, vasectomy, and tubal ligation.

If your clothes/towels/personal items become stained with body fluids/waste:

- Wear disposable gloves when handling clothes/towels/personal items stained with body fluids/waste and dispose. Place waste (including gloves) in a separate garbage bag and keep for four (4) weeks before discarding.
- Wash all stained clothes/towels/personal items separately from other clothes and add an additional rinse cycle.

Before and after administration of the FPI-2068 study drug and imaging scans please increase your fluid intake and void frequently.

Medical / Dental Staff Notification

- If you are required to visit a medical / dental facility after an administration of FPI-2068, inform the medical / dental personnel about your participation in the clinical study by providing them with a copy of this card.