Brief Housekeeping Items

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Thank you!

A Leader in Allogeneic, Off-the-Shelf
Virus-Specific T-Cell Immunotherapies

AT-Closed Vial Process Update

Cell Therapy Handling and IP Training

31-JAN-2022

IP Process Update Timelines
Corning (Screw-Top) Cryovial vs. AT-Closed Vial

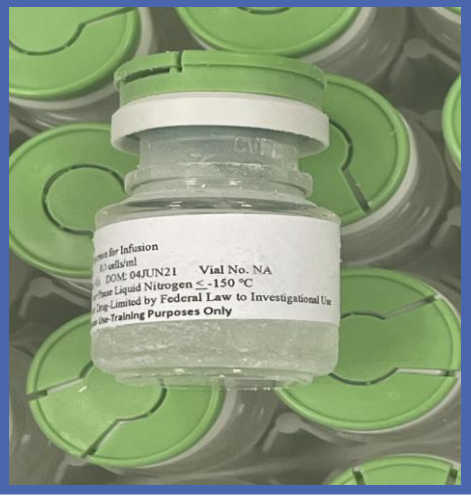
- Currently IP is supplied in Corning (screw-top) cryovials for **P-105-202.**
- **P-105-202** will initiate AT-Closed vials at the start of the randomized portion of the study ~March 2022.

Logistical Caveats

- Patients who screen/randomize **prior** to the switch date will continue to receive IP in corning screw-top cryovials for all doses.
- Patients who screen/randomize **after** the switch date will receive only AT-Closed vials for all doses.

Corning (Screw-Top) Cryovials vs. AT-Closed Vials Key Differences

AT-Closed Vial (BSC optional)



- **Dimensions:** 40.3 mm tall and 25 mm in diameter
- **Cryobox:** 133 x 133 x 57 mm (holds 25 vials)
- No need for Biological Safety Cabinet, can be aspirated at bedside.
- Must use AT-Adapt needleless connection device to draw IP into dosing syringe
- If aspirated at bedside must draw contents of each cryovial into a separate dosing syringe.

Corning (screw-top) Vials (BSC Required)

- Dimensions: 2.76 inches tall and 0.5 inches in diameter
- Cryobox: 133 x 133 x 81 mm (holds 81 vials)
- Product must be aspirated with AlloVir provided 16-gauge blunt needle
- IP **must** be aspirated into dosing syringe under ISO-5 conditions (i.e., BSC), which limits thaw location and adds transport time.
- Since IP aspirated under BSC all IP can be consolidated into 1 dosing syringe.

Labeling and Packaging – AT-Closed Vials

- ALVR105 is a multivirus-specific T-cell product targeting BKV, EBV, CMV, HHV-6, adenovirus, and JCV
- ALVR105 will be supplied in 6.0 mL cryovials at a concentration of 1×10^7 cells/mL in a volume of approximately 2.5 mL
- ALVR105 will be frozen in a cryopreservation medium
- Cryopreservation media (without cells) will serve as the placebo and will be identical in volume and appearance when administered
- Excursions are any temperature warmer than -150°C
- **There is no change to the formulation, fill volume, concentration, storage requirements; however, the vials will look different.**

IP Dosing Day

Administration Equipment (new equipment noted in bold)

Provided by CRO/AlloVir

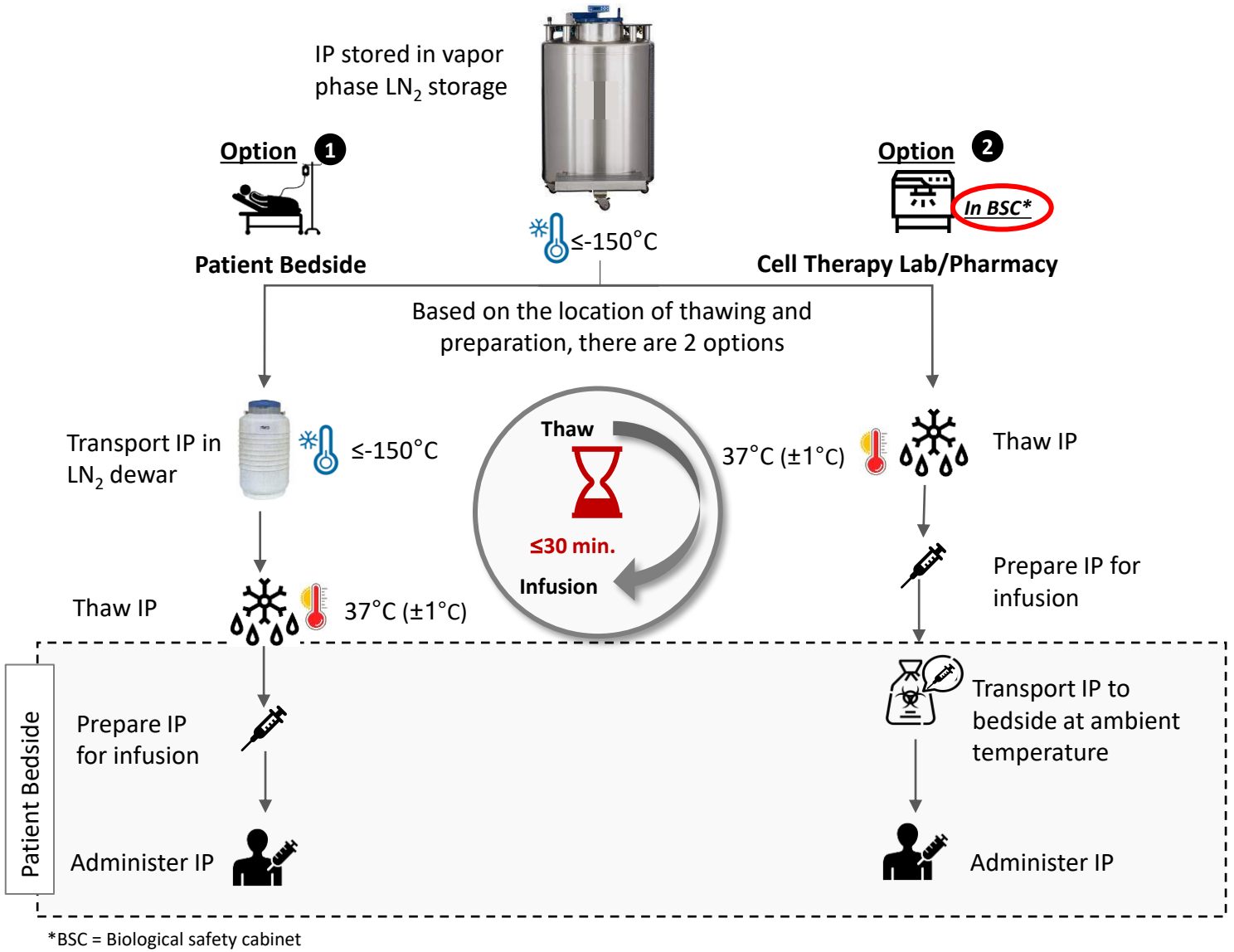
1. Hemo-Nate® Filter
2. **AT-Adapt needleless connection device (for use with AT-Closed Vials)**
3. 3-way stopcock
4. 5 mL Luer lock syringes
5. Syringe caps
6. Pre-Printed Syringe labels (P-105-202)
7. 16-gauge blunt needle (for use with Corning, Screw-Top Cryovials)

****Site must use ancillary supplies provided for the study****

Provided by Site

1. Liquid Nitrogen Freezer
2. Dry Block Heater or Water Bath
3. Bag of sterile normal saline (NS) (e.g., 50 or 100 mL, but any volume is acceptable) for priming of IV line and flushing of line and syringe
4. 5 or 10 mL sterile normal saline flush for priming the Hemo-Nate® filter
5. Infusion tubing for IV injection
6. **Dry Shipper/LN2 Dewar (for Frozen Transport of IP to bedside if applicable)**

Storage, Preparation, and Infusion Flowchart

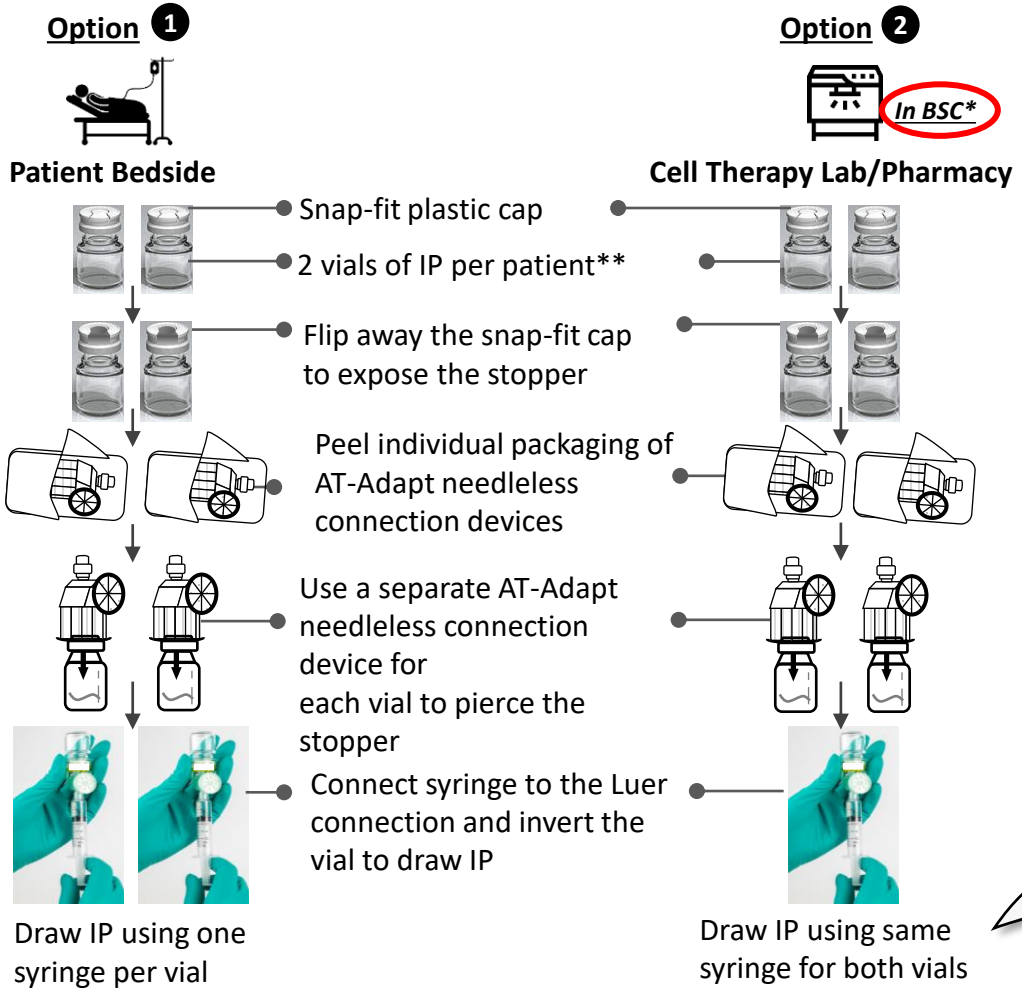


*BSC = Biological safety cabinet

AT Adapt and AT-ClosedVial Demonstration

Link to video: AT-Adapt, needle-less collection device for AT-Closed Vial

Loading of IP in Syringe for Infusion (AT-Closed Vials)



It is necessary to use separate syringes to draw IP from vial at bedside **to maintain aseptic conditions.** However, a single syringe can be used to draw IP when using a biological safety cabinet.

*BSC = Biological safety cabinet

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"AT-Closed Vial" Infusion and Flush Dynamic Review and Updates

#	Process Step
1	**Administer IP as a slow IV push**. The total **time** for the IV push **should be approximately 5 minutes** even if multiple syringes of IP are given. **IV extension tubing should be avoided whenever possible**. **If** extension tubing is **necessary** for use with a peripheral IV, **increase the flush volume as needed to ensure that the entire dose of IP is administered**

2	Following the IP infusion with each syringe, turn the 3-way stopcock and aspirate 5 mL of normal saline from the IV bag into the syringe used to administer the IP and flush it into the patient as a slow IV push
	• **If only one syringe is used** for the IP infusion:
	  • Perform this procedure twice
	• **If two syringes are used** for the IP infusion:
	  • Flush with 5 mL of saline once after IP is administered from the first syringe and twice after it is administered from the second syringe

3	• **The Hemo-Nate filter and the syringe used to administer IP must remain attached during the saline flushes**

Patient Weight	Dose (cells)	Volume Drawn into Syringe(s)	IP Vials Required	Suggested Syringe Size (# of syringes)	
				Bedside	Cell therapy Lab
<40 kg	2×10^7	2 mL	1	5 mL (1)	5 mL (1)
≥40 kg	4×10^7	4 mL	2	5 mL (2)	5 mL (1)

Legend: **Critical step**

"AT-Closed Vial" Equipment Check

- Dry Block Heater Inserts
- LN2 Freezer Metal Rack to accommodate the new Cryobox
- Dry Shipper/LN2 Dewar (for transport of frozen IP to bedside at ≤-150°C).
- Dry Shipper Insert/rack and box (for transport of AT vials to bedside in an upright position)

Critical Note: Please reach out to your CRA/Logistics Coordinator ASAP, should you require any of the equipment listed above.

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Thank you!

AlloVir Memo March 17th 2022

MEMORANDUM

Date:	17-MAR-2022
To:	Investigative Sites
From:	AlloVir
Subject:	Using AT-Adapt for IP (Investigational Product) Withdrawal

This memo is to document AT-Adapt connection to AT-Vial for all AlloVir clinical trials.

To ensure proper connection and product withdrawal:

1. While piercing the vial with AT Adapt, keep the vial upright on a flat surface
2. Enter vials with AT-Adapt needle 90 degrees perpendicular to the septum
3. Do not put pressure (air) in the vial with the syringe

Enclosed is the AT-Adapt guide for product withdrawal. The new instructions will be added to the cell therapy manual on the next warranted versioning of the manual.

2925 Richmond Ave | Suite 1274 | Houston, Texas 77098 | 936.662.3626
www.allovir.com

Aseptic Technologies

Using AT-Adapt™ for product withdrawal

ASEPTIC TECHNOLOGIES

An affiliate of SKAN Group

Values

The constant improvement of cGMP guidelines, in order to avoid any possible contamination of the aseptic process, does not necessarily imply an escalation in the complexity of the equipment for aseptic production and packaging.

We develop, manufacture and market equipment and devices that guarantee optimal sterility assurance level and complies with latest regulatory requirements, while simplifying the validation and operation processes.

AT-Adapt™

Overview

The AT-Adapt™ is a stand-alone, single-use, disposable device which permits access to an AT-Closed Vial® (2, 6, 10, 20 and 50mL format) without the use of a needle.

The device is intended for use by healthcare professionals in a wide variety of healthcare environments, including hospitals, healthcare facilities and pharmacies.

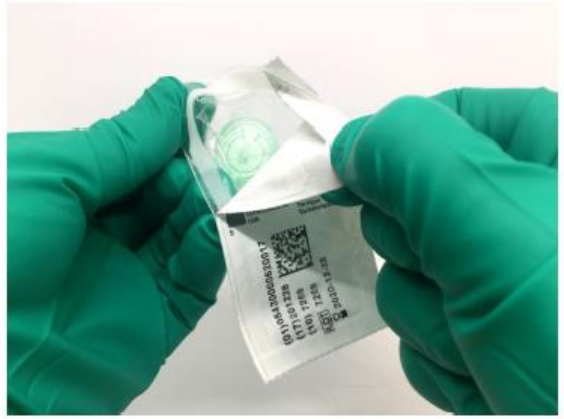
AT-Adapt™

Material

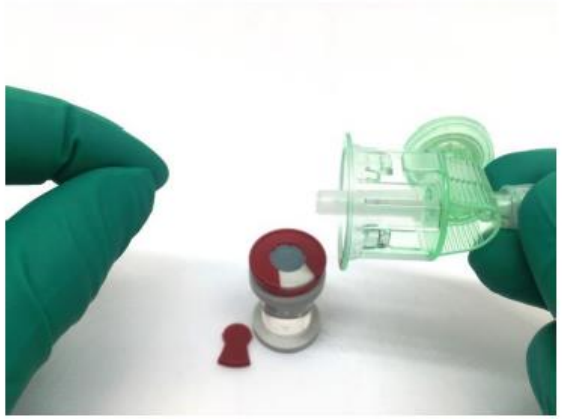
A processed (filled and capped) AT-Closed Vial®;
An AT-Adapt™;
A syringe with luer connection.

AT-Adapt™

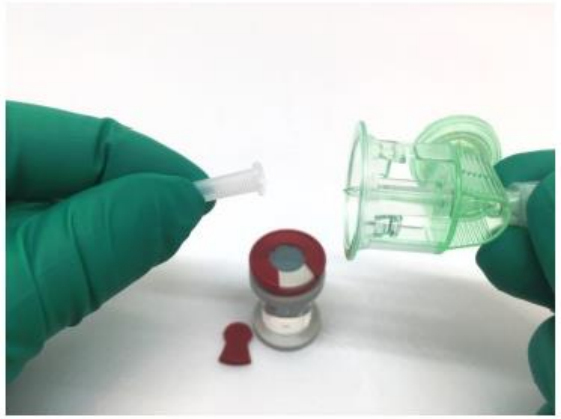
Process



The individual packaging of the AT-Adapt™ is peeled



The flip-off cap protecting the AT-Closed Vial® stopper is removed



The protection of the spike of the AT-Adapt™ is removed

AT-Adapt™

Process

Attaching the AT-Adapt™ to the AT-Closed Vial® is a 3 step process:

Step 1: **ATTACH** the AT-Adapt™ to the AT-Closed Vial®.

Do not press too firmly to avoid tabs of the AT-Adapt™ to be locked on the top ring of the AT-Closed Vial®.

Step 2: **SPIKE** the AT-Closed Vial® by moving the AT-Adapt™ in a downward motion into the vial. Spike should be perpendicular to stopper. Do not insert at an angle.

Step 3: Holding the AT-Closed Vial®, **the AT-Adapt™ shall be lifted up until the lower tab touches the cap (see yellow circle). This ensures an optimal needle positioning for maximal product withdrawal.**

The cap protecting the luer connection can be removed.

AT-Adapt™

Process

A syringe is connected and the product is withdrawn from the AT-Closed Vial® , upside down.

Do not put pressure (air) in the vial with the syringe (prior retrieving)

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