



# NanoEX™ Automated Bio-nanoparticle Isolation System User Manual

Doc Num: MAN-NE1000 Rev C



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## Chapter 1 – Product Information

### Safety



Before using this product, read and understand the following information regarding safety when using the unit.

The following symbols marked on the equipment mean:



**Caution:** Read these operating instructions fully before use and pay particular attention to sections containing this symbol.



**Caution:** Risk of electric shock. Before attempting any service to this unit remove power cord from the rear of the unit.

Always observe the following safety precautions:

- Read this entire manual before using the device.
- Use only approved accessories. Do not modify system or components. Any alterations or modifications may be dangerous and will void the warranty.
- Do not position the equipment so that it is difficult to operate the disconnecting device.
- After transport or storage in humid conditions, dry out the unit for 24 hours before connecting it to the power supply.
- Connect only to a power supply that provides a safety ground terminal.
- Ensure that the power supply cord plug is easily accessible during use.

## Background

The NanoEX™ Extracellular Vesicle (EV) and Bio-nanoparticle Isolation System is a next-generation fully automated platform for high efficiency isolation of EV and Bio-nanoparticles, such as exosomes, viruses, and liposomes, etc. The system is designed to work with the VanoFlow™ Filtration Cassettes, which are based on a patented Asymmetric Nanopore Membrane (ANM) technology that allows highly efficient recovery and enrichment of high-quality nanoparticles while effectively removing contaminants.

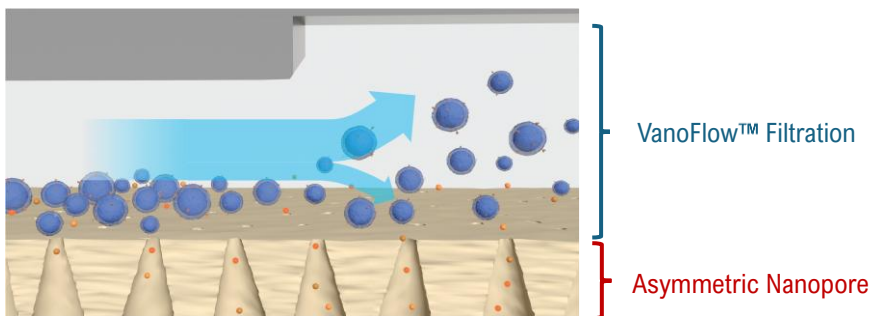
## Intended Use

The NanoEX™ Extracellular Vesicle (EV) and Bio-nanoparticle Isolation System is intended for laboratory use by trained personnel. The instrument is intended for automated isolation of EV or other bio-nanoparticles using the VanoFlow™ EV isolation cassettes.

## Technology Principles

The Asymmetric Nanopore Membranes (ANM) are nanopore membranes with asymmetric pore geometry. The openings at the filtration interface have highly consistent pore sizes (CV<10%), while the trans-membrane channels gradually expand to >20 times larger openings at the opposite side. The VanoFlow™ filtration cassettes feature vortex-enhanced tangential flow filtration. These designs:

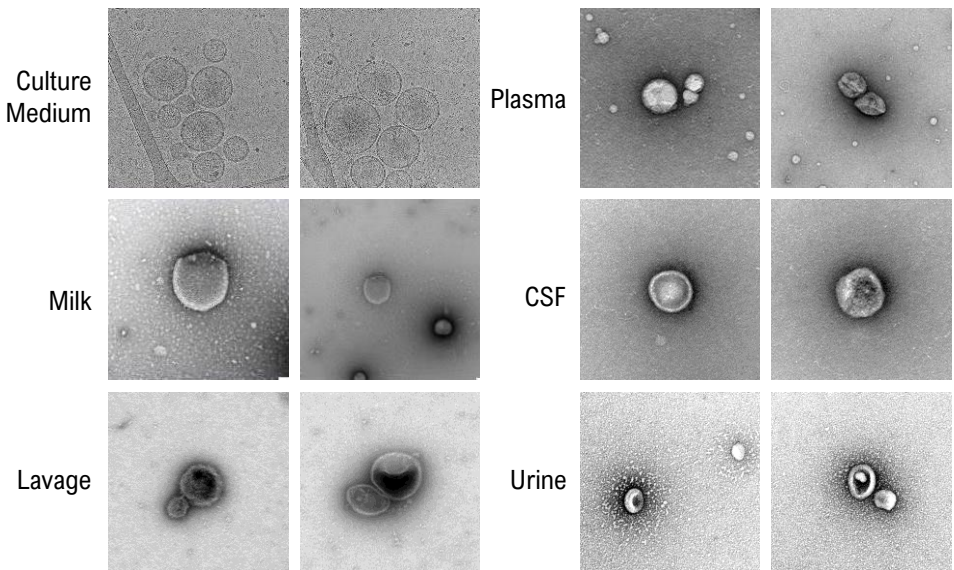
- Allow filtration with substantially low shear-force and trans-membrane pressure
- Effectively prevent nanoparticle loss from trapping, damaging, or fusion
- Effectively prevent pore clogging from protein aggregation and fouling
- Enable highly efficient target particle retention and contaminant removal



NanoEX™ delivers unparalleled purity and quality of isolated bio-nanoparticles with easy-to-use fully-automated processing, therefore provides a perfect solution for vast majority of research applications. The table below shows a technical performance comparison of various technologies.

Method	Yield	Purity	Scalability	Automated
Ultracentrifugation (UC)	++	++	++	No
Polymer Precipitation	++++	+	++	No
Immunoaffinity	+	++++	+	No
Microfluidics	+	+++	+	No
Ultrafiltration	+++	+	++	No
Size Exclusion Chromatography (SEC)	+++	+++	+	Yes
Tangential Flow Filtration (TFF)	++++	++	++++	No
<b>NanoEX</b>	<b>++++</b>	<b>++++</b>	<b>+++</b>	<b>Yes</b>

### Electron Microscope Images of NanoEX isolated Extracellular Vesicles





## Product Specification

Name	Spec
Dimension (main system)	22"W x 10.5"D x 14.5"H
Power input	100-240V AC, 50/60Hz

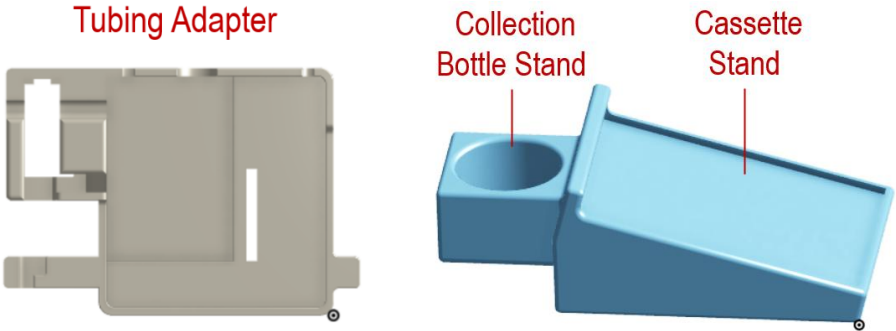
## Materials Provided

Name	Qty
NanoEX™ main system	1
Power cable	1
Power adaptor	1
Serial port line	1
USB drive (For software and protocol update)	1
Removable sample and wash column adapters	2
Waste bottle and tubing	1
Waste bottle base	1
Accessory kit	1

# NanoEX Accessory Kit

- The NanoEX Accessory Kit (Cat # NE1000ACC) is required for the following VanoFlow Cassettes:
  - VanoFlow-EXO-10
  - VanoFlow-EXO-20
  - VanoFlow-EXO-40
  - VanoFlow-EXO-60

Name	Qty
Tubing adapter	1
Cassette stand	1
Cleaning supply set	1
4L waste container	1



## Chapter 2 – Installation

### Main System Installation

#### Unpacking

Remove packing materials carefully and retain for future shipment or storage of the unit. Inspect all materials for damage.

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**IMPORTANT!** Report all shipping damage to the carrier immediately. Shipping damage is covered by the carrier, and repair/replacement for shipping damage must be coordinated through the carrier.

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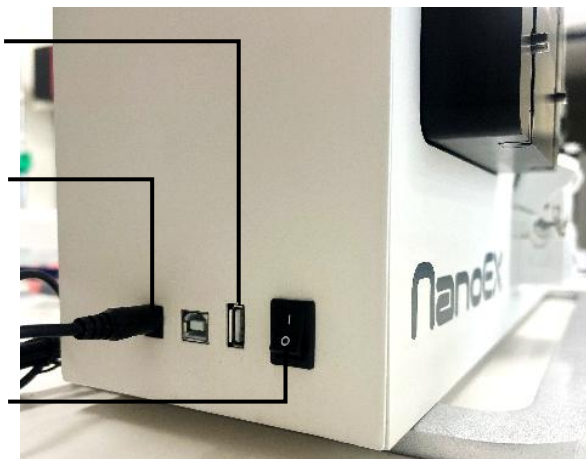
#### Instrument Installation

- Connect the **Power cable** to the **Power Adaptor**, and then connect the **Power Adaptor** to the **Main System**.
- Connect the power cable to a power socket then power on the system (**Power Switch** is located at the lower left-side panel).
- The USB port is used for software and processing protocol update, as well as run log export.

USB port for data  
input/output

Power connector

Power switch



## Collection Tube Holder Adjustment

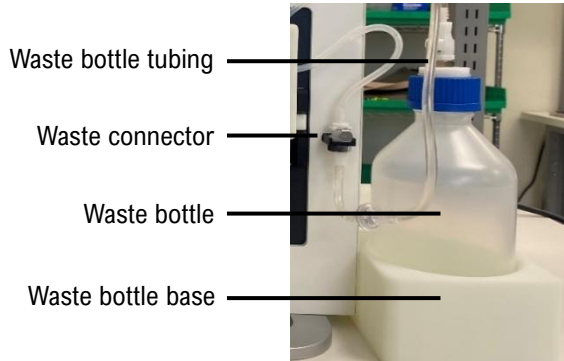
The spring-operated collection tube holder was designed to hold commonly used 15ml conical tubes. The gap can be adjusted with the provided hex-key to widen (counterclockwise) or narrow (clockwise). Adjust both screws to ensure even pinch force.



## Waste System Installation

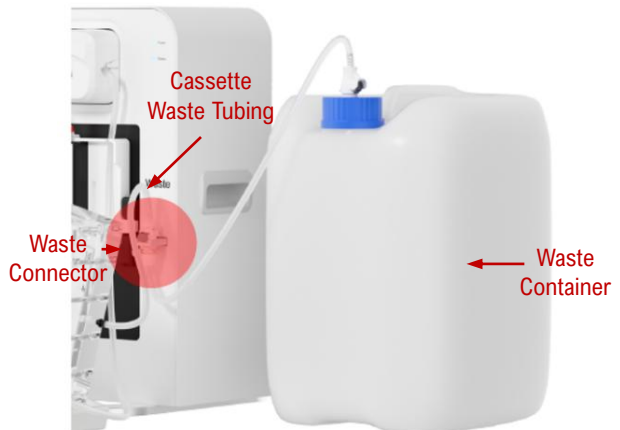
### Regular Volume Processing (300mL or Less)

- Place the **Waste Bottle** on the **Waste Bottle Base** and place on the right side of the main system. Securely tighten the bottle cap.
- Connect the **Waste Bottle Tubing** to the bottom of the **Waste Connector** on the main system.



### Large Volume Processing (Larger than 300mL)

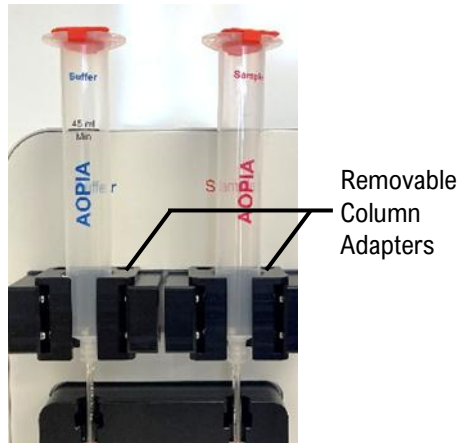
- Use **4L Waste Container**. Insert the **Cassette Waste Tubing** end into the **Waste Connector**.
- Place the **Waste Container** at the same level as the instrument.



## Sample and Buffer Container Installation

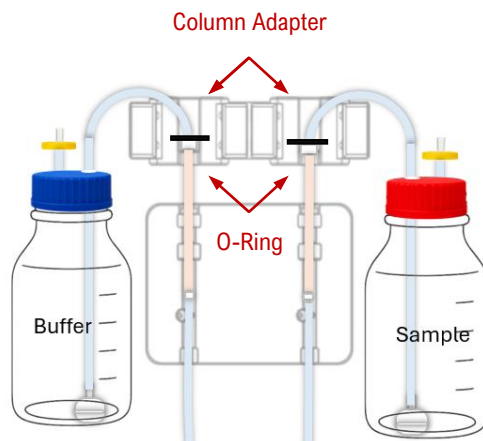
### Using Columns

- For cassettes using **Sample and Buffer Columns**, the columns can be directly installed onto **Removable Column Adapters**.



### Using Bottles

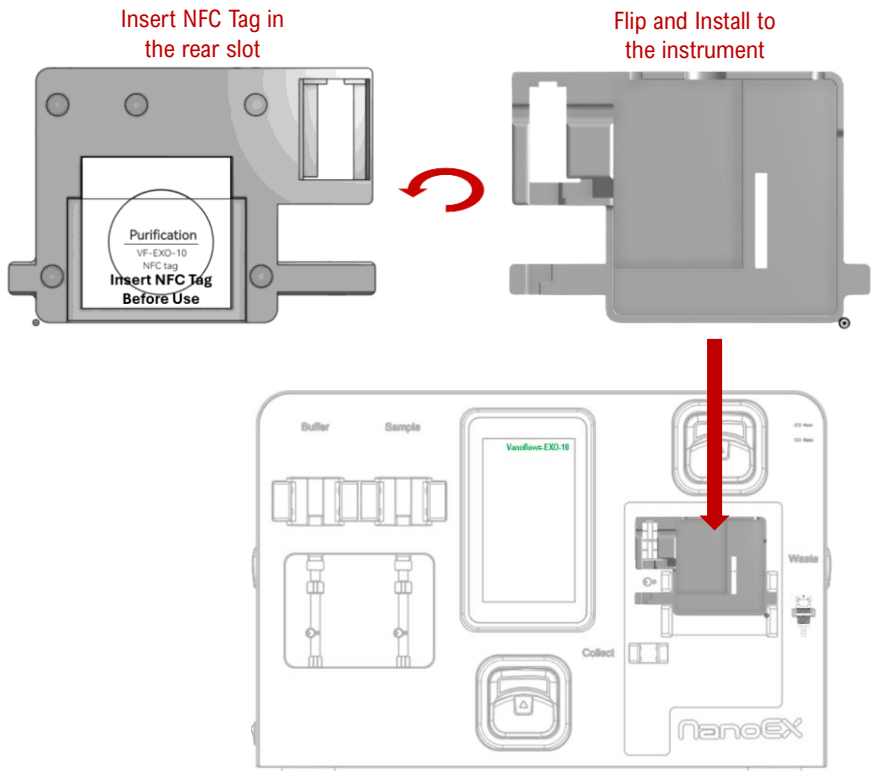
- For cassettes using **Sample and Buffer Bottles**, ensure the **black O-Ring** is installed onto **Removable Column Adapters**.



## Using NanoEX Accessory Kit

### Tubing Adapter

- The **Tubing Adapter** is required for installing **NFC Tags** and **Cassette Tubing** except for pre-integrated cassettes, such as VanoFlow-EXO-01.
- To install **NFC Tags**, place the NFC tag with the liner (back paper) into the rear slot of the **Tubing Adapter**.
- Flip and install the **Tubing Adapter** onto the NanoEX instrument as shown below.

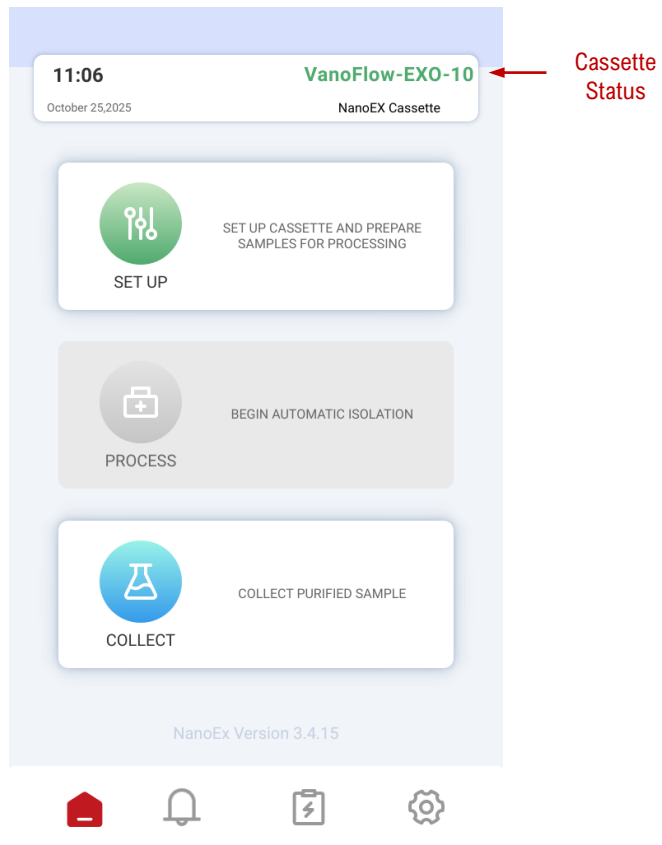




# Chapter 3 – Operation

## User Interface

### Main Setup Screen







- The **Main Setup Screen** is the portal to different processing protocols. Only activated buttons (color) can be clicked.
- The **Cassette Status** field will update automatically when an **NFC Tag** is detected.

## Cassette Status:

Status	Indication
VanoFlow-EXO-01	Cassette is detected and recognized
Not Detected	No Cassette is detected
Used	Cassette has been used
Unknown	Cassette is detected but not recognized. Software update may be needed

## Bottom Menu:

	<b>Home</b> - Return to home page
	<b>Alert</b> - Display warning and alert messages in the current run
	<b>Log</b> - Detailed run events for the last 30 experiments
	<b>Setting</b> - Additional functions

## Processing Mode Selection Screen

Select Processing Mode

Standard Purification Mode

- (Recommended) Optimized for high-purity processing.
- Suitable for most samples, including plasma, serum, and conditioned medium with/without exosome-depleted FBS.

Accelerated Purification Mode

- Processes samples at a faster speed with reduced purification efficiency.
- Suitable only for samples with minimal impurities.

Cleaning Mode

- Cleaning the Vanoflow® Reusable Cassette at a higher flow rate (not suitable for purification).
- The Vanoflow® Reusable Cassette can be used several times if proper cleaning and storage procedures are followed.

Select

### ■ Standard Mode

For processing samples containing significant amount of protein, such as plasma or culture medium containing > 5% serum. This mode ensures high purity bio-nanoparticles with low protein contamination.

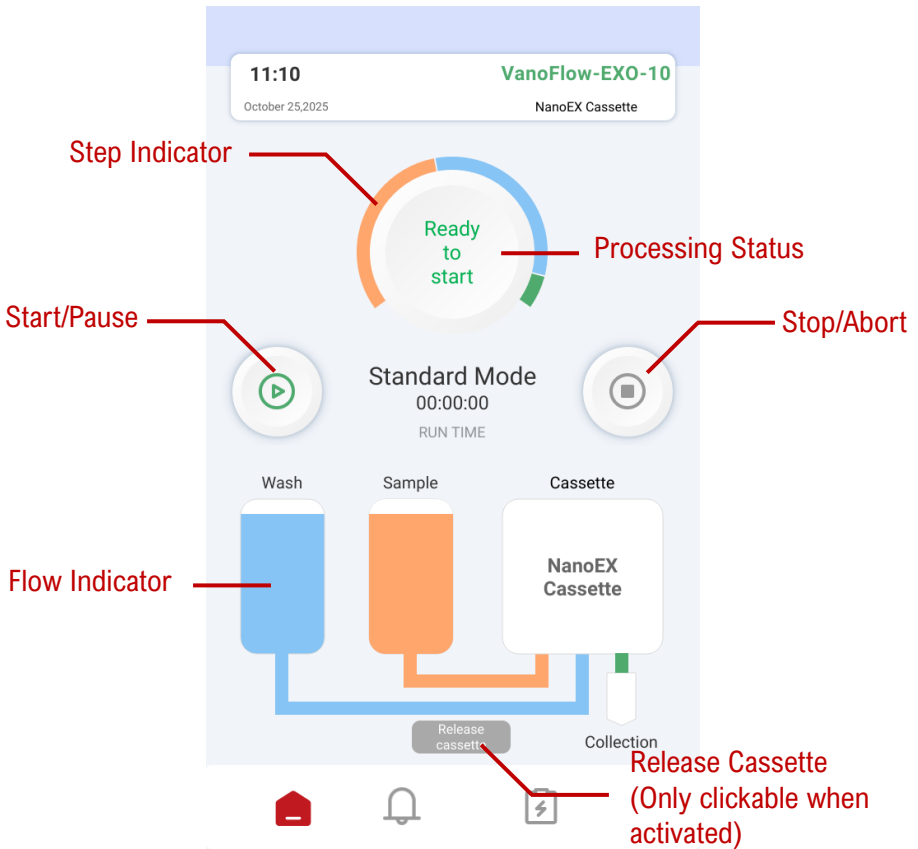
### ■ Accelerated Mode

For processing samples containing low amount of protein, such as serum-free cell culture medium or urine. This mode shortens processing time by 50% while ensuring high purity bio-nanoparticles.

### ■ Cleaning Mode

For cleaning re-used cassettes.

## Main Processing Screen



### Note:

- If processing is manually aborted. The Release Cassette button will be activated. See **Special Operation**.

## Processing and Cleaning

Follow the **VanoFlow Cassette Instruction Manual** to install cassettes and perform processing and cleaning protocols. The instruction manual can be downloaded from: <https://aopiabio.com/documents>

## Aborting a run

The processing protocol can be aborted at any time by pressing the **Stop** button on the main processing interface.

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**IMPORTANT!**

- *Once the run is aborted, the isolated nanoparticles can no longer be retrieved. Therefore, it is strongly recommended that the **Pause** function be used if a temporary stop is needed.*
  - *Only use the **Stop** function if catastrophic errors, such as leaking, occurs.*
- 

After aborting the run, empty the sample and buffer columns and then press the **Release Cassette** button before removing cassette from the instrument.

## Waste System Cleaning

- Empty waste container and rinse with dH<sub>2</sub>O.
- If not processing another sample immediately, clean the waste tubing using the syringe provided in the **NanoEX Accessory Kit**:
  - Flush the waste tubing with **dH<sub>2</sub>O**.
  - Flush the waste tubing with **70% Isopropyl alcohol**.
  - Draw air into the syringe and push air through the waste tubing.

### Draw Cleaning Solution



### Flush Waste Tubing



## Chapter 4 – Additional Information

### Sample Preparation Recommendations

This guide provides general recommendations for common sample types to ensure optimal performance. Additional optimization might be needed depending on the input materials and the target nanoparticles.

#### Step 1: Sample conditioning

The table below lists the recommended sample conditioning protocols and NanoEX Processing Mode. Refer to **NanoEX Operation Quick Guide** for details on NanoEX Processing Modes.

Sample	Sample Conditioning
Culture medium	<ul style="list-style-type: none"> <li>Centrifuge at 500xg for 10min and take supernatant.</li> </ul>
Plasma/Serum	<ul style="list-style-type: none"> <li>Centrifuge at 10,000xg for 10min at 4°C and take supernatant.</li> <li>Dilute 40 times with sterile 1XPBS (no Ca<sup>2+</sup> or Mg<sup>2+</sup>).</li> </ul>
Other samples with ≤1mg/ml protein concentration	<ul style="list-style-type: none"> <li>Centrifuge at 500xg for 10min and take supernatant.</li> <li>Small volume samples can be diluted with PBS to meet the minimal volume requirement.</li> </ul>
Other samples with >1mg/ml protein concentration	<ul style="list-style-type: none"> <li>Centrifuge at 500xg for 10min and take supernatant.</li> <li>Reducing protein concentration to ≤1mg/ml by dilution is highly recommended for best quality.</li> </ul>

#### Step 2: Pre-filtration

It is highly recommended that the sample be pre-filtered to remove large particles and debris to prevent membrane clogging and improve purity. Filter through 0.22µm PES filter (for nanoparticles <200nm) or appropriate filters for the target nanoparticles. Non-PES filters may result in higher bio-nanoparticle loss.

## Post-processing of Purified Nanoparticles

If desired, the purified nanoparticles can be further processed for various applications or purposes. The table below provides recommendations to commonly employed protocols.

Purpose	Recommendation
Sterilization	<ul style="list-style-type: none"> <li>▪ Filter through 0.22µm or 0.45 µm PES filter. Non-PES filters may result in higher nanoparticle loss.</li> </ul>
Further particle concentration	<ul style="list-style-type: none"> <li>▪ For 30-200nm particles, use 100kD MWCO PES concentrating column and centrifuge at 500xg until desired volume is reached.</li> </ul>

## Chapter 5 - Maintenance

### Routine Maintenance

The NanoEX instrument requires minimal maintenance because there is no direct contact of sample or buffer with the instrument except for the waste tubing. However, routine cleaning after each processing cycle should be performed:

- Empty and clean waste bottles every time after processing.
- Rinse waste tubing as recommended in **Operation -> Waste System Cleaning**
- Wipe off any spills on the instrument using lint-free wipe with 70% isopropyl alcohol.
- Turn off instrument if no immediate use is expected.

### Software Update

There are 2 types of software updates:

- System software update – for bug fix and new functions
- Processing profile update – for new cassettes and processing protocols
- The latest **Software** and **Processing Profiles** can be downloaded from: <https://aopiabio.com/software>
- Transfer the software or processing profile files to the **USB Drive** provided with the instrument.
- Connect the USB drive to the instrument, then go to **Setting -> Software Update** and follow the screen instruction to update.

## Replacing waste tubing

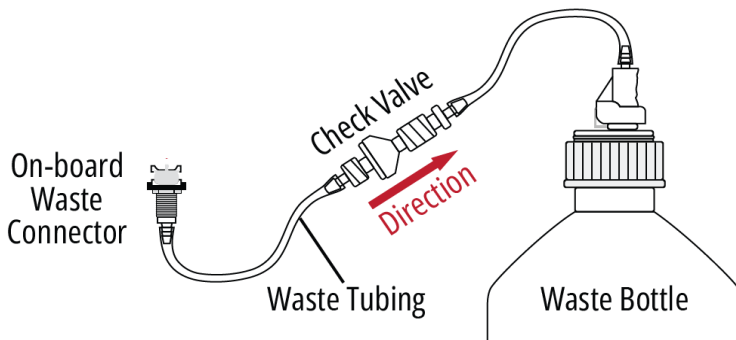
A set of replacement waste tubing is supplied with the instrument in case the **check valve** is clogged. The **check valve** is a filter-like unit between the tubing connected to the instrument and the waste bottle and functions to prevent back flow of waste liquid into the cassette.

To replace the waste tubing, first disconnect and discard the old tubing (including the check valve), then connect the replacement tubing.

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### **IMPORTANT!**

- Ensure that the **check valve** is installed in the correct direction (see figure below).
- 





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