National Research Council Canada

CLINICAL TRIAL MATERIAL FACILITY AT NRC'S ROYALMOUNT FACILITY

FEASIBILITY STUDY

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II. ACKNOWLEDGEMENTS

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III. ABBREVIATIONS AND ACRONYMS

Acronym	Description
°C	°Celsius
A	Amperes
AHU	Air Handling Unit
ASME BPE	American Society of Mechanical Engineers - BioProcessing Equipment
atm	Atmosphere
BMS	Building Management System
BSC	Biosafety Cabinet
BSL2	Biosafety Level 2
BU	Black Utilities
CDC	Center for Disease Control and Prevention
CFR	Code of Federal Regulations
CIP	Cleaning In Place
GMP	Good Manufacturing Practices
CHW	Chilled Water
CL2	Containment Level 2
CO_2	Carbon dioxide
CTMF	Clinical Trial Material Facility
CU	Clean Utilities
CW	Cold Water
dP	Differential Pressure
DP	Distribution Panel
DQ	Design Qualification
DSP	Downstream Process
EMS	Environmental Monitoring System
EVE	Events
FAT	Factory Acceptance Tests
FDA	Food and Drug Administration
FP	Final Product
FS	Functional Specification
FSS	Fire Safety System
g	Gram
GMP	Good Manufacturing Practices
H_2O_2	Hydrogen Peroxide
HMI	Human Machine Interface
HPL	High Pressure Laminate
HVAC	Heating, Ventilation and Air Conditioning (Air Handling)
HW	Hot Water
Hz	Hertz
ICH	International Conference on Harmonization
IFT	Integrity Filter Test

IP/IK	Protection ratings
IQ	Installation Qualification
ISO	International Organization for Standardization
ISPE	International Society for Pharmaceutical Engineering
IT	Information Technology
kVA	Kilovolt Ampere
kW	Kilowatt
LED	Light Emitting Diode
m^3/h	Cubic meters per hour
mA	Milliamperes
MAL	Material Airlock
mg/m^3	Milligrams per cubic meter
mL	Milliliter
NC	Not Classified
NCE	Non-Contaminated Effluent
ODBC	Open Database Connectivity
OPC	OLE for Process Control
OQ	Operational Qualification
P	Pressure
P&ID/PID	Process & Instrumentation Diagram
Pa	Pascal
PAL	Personnel Airlock
PC	Personal Computer
PDF	Portable Document Format
POU	Point of Use
PPM	Parts Per Million
PQ	Performance Qualification
PT	Pass-through
PW	Purified Water
R&D	Research and Development
RH	Relative Humidity
SAT	Site Acceptance Test
SELU	Self-contained Emergency Lighting Unit
SIP	Sterilization In Place
SQL	Structured Query Language
SW	Softened Water
TFF	Tangential Flow Filtration
TOC	Total Organic Carbon
TT	Grounded neutral system
UPS	Uninterrupted Power Supply
USP	Upstream Process
USP	United States Pharmacopeia
UV	Ultra-Violet
V	Volt

V/V	Volume/Volume
VDC	Voltage Direct Current
WFI	Water for Injection
WHO	World Health Organization

1 EXECUTIVE SUMMARY

Project budget: 28.9 M$ (including contingency)

Project duration: 15 months

Project total surface: 14 560 ft^2 (1 350 m^2)

The consulting firm have been mandated to conduct a feasibility study to create a Clinical Trial Manufacturing Facility (CTMF) within the existing buildings available at the at the Human Health Therapeutics Research Centre (HHT) of the National Research Center's Royalmount facility. The production line will be for the manufacturing of vaccines or therapeutics for humans.

The original intent of the project is to allocate space in the L4 building ground floor and some areas on the second floor of that same building to host the activities. This implies relocating occupying tenants of the L4 building and relocation existing R&D activities to other areas. Relocating tenants is not part of the present feasibility study nor the mandate of the consulting firm.

In addition to the installing the facility and equipment for a clinical trial manufacturing facility a QC laboratory as well as a storage space, HVAC, and utility requirements for those activities will be added.

The CTMF will be able to handle activities from subculture of various viral vectors and monoclonal antibodies to the filling in bulk disposable bags of maximum 20L and all required activities in between.

The CTMF will be able to produce 20 lots/year for the 500 L bioreactor. The products intended to be produced in the facility are not known at the time of the feasibility study and therefore flexibility in the design is a key element.

The volume and number of lots indicated above are possible only when CTMF is used to produce the same product as in case of an "emergency". In normal times, CTMF may be able to onboard 3-4 different products in a year for clinical trial material. This would be keeping in consideration the downtime needed for product change, process optimization, etc,

The facility will be designed to meet GMP requirements.

The facility will include equipment and infrastructures necessary for viral seed stock preparation, subculture, cell culture and viral production, purification and bulk fill.

The new GMP manufacturing rooms and airlocks (personnel and material) will be built in an existing building (known as L4) as well as an extension to the existing NRC's premises located in Montreal, Quebec and will consist of GMP classified grade C and D areas (including new dedicated HVAC systems). The manufacturing surface area will be approximately 8570 ft^2. The facility will also include one 2530 ft^2 warehouse on the ground floor as well as a 2860 ft^2 mechanical room and a 1040 ft^2 QC laboratory on the second floor in an existing laboratory room.

The budget of the new facility is CAD$ 28.9 million (excluding taxes and including contingency).

The project will include the move of existing activities such as the fermentation lab, the fill and finish room or existing tenants present in the area. The move and scheduling of the move are the focus of

another project held independently and the present study assumes that all these operations can take place as soon as the CTMF project construction needs to happen. Nevertheless, some time in the schedule has been allocated to relocate tenants. Hence, the overall schedule of this project, including engineering, facility construction, equipment procurement, relocation and validation will be completed end of February 2022. To meet this date, it is necessary to have the Quality System ready at the same time. Finally, the dates presented in the schedule account for tasks taking place in parallel as much as possible.

Note: *Avenues for overall budget reduction identified by the team during the preparation of this study are:*

1) Use of WFI water only and removal of PW water

2) Re-use of existing mechanical and drainage systems. This could not be considered during this feasibility due to time constraints

2 PROCESS

2.1 GENERAL

The facility is designed for production based on cell culture, purification, and bulk filling of biologics such as vaccine, viral vector and/or monoclonal antibodies.

All production will use the same kind of unit operation: cell amplification, production, clarification using depth filtration, purification chromatography, polishing chromatography, ultrafiltration. Some operation will be specific to monoclonal antibody due to the virus safety assessment: chemical inactivation and nanofiltration.

As worst case, the design is based on typical production for monoclonal antibody with volume of 500L bioreactor at 4g/L titer.

The facility is a fully integrated, with two main manufacturing sectors:

- The Production Area, where Upstream Process cell culture, Downstream Process purification and bulk fill take place
- Both are supported by solution and material preparation rooms

Areas where the virus is present, such as production rooms where the virus is cultivated, purified or where filling activities take place are classified as biosafety containment level 2 (CL2). The rooms classified as CL2 were designed accordingly.

2.2 PRODUCT DESCRIPTION

At the time of the study, NRC has not defined a specific product for the CTMF. The CTMF is designed to be able to produce viral vectors from animal cells and monoclonal anti-bodies. Indeed, it is not designed to produce both type of product concurrently but successively.

2.3 PRODUCTION OBJECTIVES

The products are intended for the Canadian market, regulated by Health Canada under the authority of the Food and Drugs Act. The facility will require being compliant with current Good Manufacturing Practices.

The facility should be operational in end of February 2022. The facility will optimize and produce GMP batches of various vaccines and biologics primarily for clinical use. Under this scenario, the facility could onboard 3-4 products per year. Furthermore, in the case of an emergency, the facility could be repurposed to produce 20 batches of the same product.

2.5 PLANT CAPACITY

The new facility has been designed for the manufacturing 20 batches per year based on one 500L bioreactor train.

Available weeks[1]	48	/ year
Work hours per day:	16	Hour / day
Workdays per week	7	Days / week
Cell culture volumes:	500	L
Final product volumes [3]	12-20	L
Number of lots per year [3]	20	Lots / year
Mean number of batches per month [3]	1.67	/ month

[1] Working Cell Bank (WCB) preparation included in overall production time.

[2] This production capacity excludes samples required for in process control, quality control or other purposes

[3] Production chronograms based on mAb mass balance and must be confirmed by NRC for detail design (referred to Appendix E)

2.6 ASSUMPTIONS

- Production times used to evaluate plant capacity (ref. to NRC-14-NDC-01-00 and NRC-14-NDC-03-00)
  - 2h for one preparation then 5 preparation per shift
  - 20 days of Subculture
  - Preparation could be in parallel of production (dedicated team)
  - Days of batch preparation (room cleaning, raw material Supply)
  - 1 day room clearance after batch
  - No Support operation during weekend
  - Production 7j/7
  - Similar preparation schedule per week
  - 15 days of mAb production
- If required, preparation of MVSS are included in overall production time
- Water For injection capacity estimation (ref. to NRC-14-NDC-05-00)
  - Water for injection requirement-based NRC-14-NDC-03 (Mass Balance mAb)
  - Clarification skid 109LMH
  - 15L/min 50L mixer
  - 35L/min large mixer
  - 11,4 L/min sink based on Code de Plomberie du QC (Évier de service = 0,19 L/s)
  - Affinity chromatography skid: 45cm diam column - 200cm/h flowrate
  - Cation exchange chromatography skid: 35,9diam column - 200cm/h flowrate
  - Anion exchange chromatography skid: 5L membrane - 1MV/min flowrate

- Nanofiltration skid: 1sqm membrane - 90LMH flowrate
- UDF/DF skid: 9sqm filtration - 240LMH
- Maximum working volume for Mixer system could be 105% of working volume specification
- Mixer 50L includes 10L adaptor as minimal working volume
- Media/Buffer preparation follows Campaign mode _ one preparation at the same time

- Water For injection capacity estimation (ref. to NRC-14-NDC-08-00):
  - Main user is the WFI generator system
  - Storage tank and purified water generator is included as worst-case scenario

- Equipment temperature requirements (ref. to NRC-14-NDC-04-00):
  - 1,1 kg of purified water is required to generate 1,00 kg of pure steam
  - Medium cooling from 37 to 30°C in 20 minutes for the bioreactor 50L
  - Medium cooling from 37 to 30°C in 75 minutes for the bioreactor 500L
  - Medium cooling from 37 to 6°C in 60 minutes for the bioreactor 500L
  - Medium heating from 20 to 37°C in 15 min for the bioreactor 50L
  - Medium heating from 20 to 37°C in 45 min for the bioreactor 500L
  - Medium heating from 6 to 20°C in 60 min for the storage tank 500L

- QC laboratories
  - Microbiology tests will only concern environmental testing and bacterial endotoxin testing.
  - In the CL2 biochemistry laboratory, only in process testing will be performed.
  - Equipment for samples which storage conditions must be -80 °C, -20°C, 4°C and 25°C are included in the QC laboratory.
  - Each storage unit has a back-up except for the 25°C incubator. These back-up units will also host long term storage samples to limit the number of opening of the storage unit.

- Storage and warehouse
  - Storage duration:
    - Raw material: 1 month
    - Consumables (filters, bags, tubing, gloves, hats, suits): 1 month
  - Minimum of one palet per item
  - Warehouse required surface area calculated for 2-high racking pallets
  - 882 lbs (400 kg) maximum allowable per pallet space
  - If many formulas require the same raw material, they will be packed on the same pallet if space is sufficient
  - Storage with pallets or cart (2 carts in 1 pallet space)
  - Three (3) pallet spaces for QC lab

Note: *for calculations reason the maximum allowable per pallet space weight is 400 Kg but the racking should be designed to be able hold 1500 Kg per pallet space.*

- Waste / decontamination
  - All process solution in contact with product will be decontaminated in kill tank
  - Solution using for step preparation are not considering as biological contaminated liquid waste

  - Sizing of the thermal decontamination system is based on mAb production at the scale of 500l and titer of 4g/L
  - Contaminated wastes Upstream/Downstream1/Downstream2/Bulk filling/QC lab
  - Wastewater to be treated in specific way
  - All solid waste volume is estimated or based on technical specification from random suppliers
  - Waste from toilet, janitor and office are not included
  - Volume of disposable bags corresponding to 0.75 x bag volume

- Chromatography columns are prepacked and ready to use only.

- Fill and finish activity is out of scope

- Secondary packaging activity is out of scope.

- Offices, archive room, rest rooms (cafeteria), meeting rooms are out of scope.

2.7 MANUFACTURING PROCESS

The typical manufacturing operation available in the CTMF consists of the following main procedures:

- Upstream process (USP)
  - Cell thawing and sub-culture
  - Virus stock preparation
  - Cell culture and infection
  - Media cooling and storage in jacketed tank

- Downstream process (DSP)
  - Cell lysis and nucleic acid digestion (viral vector production)
  - Clarification by depth filtration
  - Virus chemical inactivation (mAb production)
  - Affinity chromatography (AFF)
  - Anion Exchange Chromatography (AEX)
  - Cation Exchange Chromatography (CEX)
  - Multi-Mode Chromatography (MMC)
  - Virus removal by nanofiltration
  - Ultrafiltration/Diafiltration (UF/DF)
  - Drug substance formulation and bulk filling

Note: *The CTMF must have the possibility to get clarification using centrifuge as an option. The technical requirement must be studied in the detail design. The feasibility only includes the footprint for this kind of equipment.*

One production line: one 500 L single use bioreactor with three (3) dedicated rooms for purification.

Additional supporting procedures include:

- Raw material weighing and dispensing
- Media preparation
- Buffer preparation
- Component / equipment washing, preparation and sterilization
- Cryostorage

Most manufacturing steps are performed in classified clean rooms (Grade C and D).

The CTMF must have the capabilities to handle different kind of biological production such as viral vector or monoclonal antibodies. This study has been based on one typical mAb process. All details about those assumptions are available in the appendix E and J as the following information:

- Mass balance
- Production schedule

The following figures show the two main process to be handle in the CTMF.Figure 1: Monoclonal

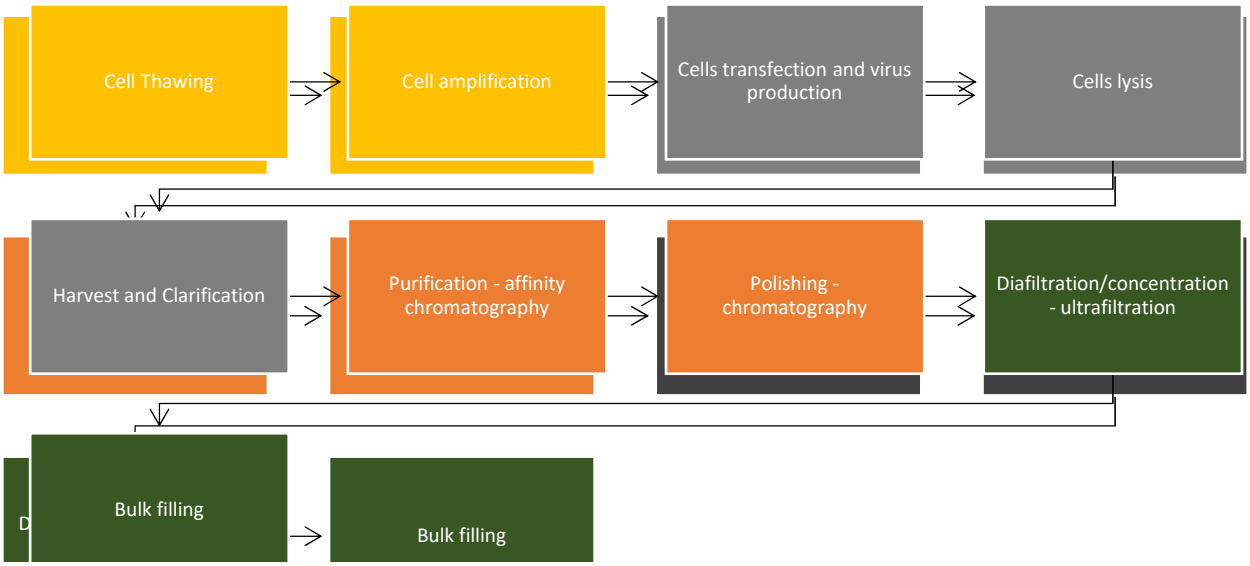


Figure 2: Viral Vector processing based on Client 62 (yellow: subculture; light grey: upstream; orange; downstream no.1; green: downstream no.2 or bulk filling)

Antibodies Typical Processing (Yellow: Subculture; Light Grey: Upstream; Orange: Downstream no.1; Dark Grey: Downstream no.2; Green: Bulk filling)

2.7.1 Upstream process (USP)

Cell thawing and sub-culture

Cell line such as CHO or HEK 293 (depending on the process) from the GMP Master/Working Cell Bank are shipped to NRC and stored in a liquid nitrogen cryogenic tank. Frozen cells are thawed and then sub-cultured in shake flasks for several passages to maintain de cells in exponential growth phase and to amplify the culture volume. Thawing and subculture is performed in the Subculture Room, a dedicated Grade C, CL2 room. Cell culture is conducted in incubators.

Note: *NRC will confirm the production schedule depending on the process to be done the CTMF.*

Virus stock preparation (in case of Viral Vector production)

A viral stock received from an external facility is used to build up the production viral stock to be used for infection of culture in the production 500 L bioreactor. The virus stock preparation is performed in the Master Viral Seed Stock Room (MVSS), a dedicated Grade C, CL2 room. Cell line HEK-293 is cultured in the 50-liter bioreactor and then infected with the virus stock prepared in the MVSS Room.

The viral stock produced in the 50-liter bioreactor is harvested in single-use bags and kept frozen at -80 °C until needed for viral propagation in the 500 L bioreactor.

Note: *NRC will confirm the MVSS required volume depending on the process to be done the CTMF.*

Cell culture

Sub-cultured cells are transferred from the Subculture Room to a seed bioreactor (50 L bioreactor for final expansion where they are cultivated at 37°C for a couple of days until the desired cell density. Cells are diluted with fresh medium up to the final volume and allowed to grow for additional days to reach target cell density before being transferred to the 500 L production scale bioreactor.

Dissolved oxygen is controlled during cell culture using sparging of clean oxygen. The pH value is controlled using CO_2 sparging and alkaline solution addition. The bioreactor itself is a closed system designed for cell culture in aseptic conditions. Connections between the bioreactor and medium bags/inoculum are performed aseptically by using a thermal tube welder and using sealable/weldable tubing designed for aseptic welding (or aseptic connector as Lynx® or Steamthru® technology).

Cell infection is performed in the Upstream Processing rooms (USP), dedicated grade C, CL2 rooms.

Cell infection (in case of Viral Vector production)

Cells grow in the production bioreactor until the target cell density is reached, then are diluted with fresh medium, and infected with thawed viral stock (MVSS). The volume of viral stock to use for infection will depend on the titer of the MVSS and the cell density and culture volume of the bioreactor.

Cell culture is stopped approximately two days after infection with the MVSS. Cell infection is performed in the Upstream Processing rooms (USP), dedicated grade C, CL2 rooms.

Note: *NRC will confirm the production schedule depending on the process to be done the CTMF.*

Biologics Production (in case of mAb production)

Cells grow in the production bioreactor until the target cell density is reached, then are diluted with specific medium to change their metabolism. This action will get them producing the target monoclonal antibody. During this phase of production, feeding addition should be controlled following in process control result such as glucose and lactate concentration in the media.

Biologics production is performed in the Upstream Processing rooms (USP), dedicated grade C, CL2 rooms.

2.7.2 Downstream process (DSP)

Cell lysis and nucleic acid digestion (in case of Viral Vector production)

Two days after infection with the MVSS in the bioreactor, lysis of the cells is conducted by the addition of detergent-based lysis buffer into the bioreactor to release the Ad5-nCoV (viral vaccine candidate). Along with lysis buffer, benzonase (nuclease) will be added into the bioreactor to digest the released nucleic acids.

This step is performed in the Upstream Processing rooms (USP), dedicated grade C, CL2 rooms.

Clarification

The lysed cell culture is harvested from the bioreactor clarified using depth filtration to remove cell debris after cell lysis. The clarified broth is harvested into a tank that will be used to feed the clarified culture to the next process step, also taking place in a USP Grade C CL2 room.

This step is performed in the Upstream Processing rooms (USP), dedicated grade C, CL2 rooms.

Chromatography

The purification process and operating conditions are designed to effectively reduce the residual host cell and residual host cell DNA content.

Depending on the process and the contamination risk assessment, the purification steps are performed in the Downstream processing no.1 or no.2 room, a dedicated grade C, CL2 rooms.

In case of viral vector, two chromatographic steps are performed in Downstream processing no.1 room: an anion exchange chromatography followed by a multimode chromatography (polishing). The eluate of the affinity chromatography is collected in a tank which is moved to the second Downstream Process Room.

In case of Monoclonal Antibodies production, one main purification step is performed in the Downstream processing no.1 as the affinity chromatography. The eluate will be transferred to a mixer for viral inactivation step (ref. below). The two next chromatography such as Anion Exchange and Cation Exchange will be part of the polishing steps. They will be performed in the second Downstream processing room, a dedicated grade C, CL2 room.

Note: *It might be possible to transfer the bulk directly to the next DSP room through a port in the wall (or pass-through for small volume) if the DSP rooms are adjacent. Transfer strategy between these two rooms will be determined in the detailed design based on the new layout possibility.*

Virus inactivation and removal (in case of mAb production)

Protein products based on cells culture could represent a risk of viral contamination especially if the production uses cell lines from human or animal origin (more details are available in the chapter 2.9.5). Then the CTMF will include the capacity for chemical inactivation and nanofiltration.

Inactivation will be based on acid addition in the mixer using calibrated peristaltic pump or floor scale. The pH will be maintained during validated time to enable all potential virus to be inactivated (be in contact with acidic solution). Then the product must be transferred to another mixer bag through dept filter to avoid any risk of none inactivated product drop. Finally, the pH will be neutralized using basic solution. Osmolarity could be adjusted as well to prepare the intermediate to be transferred to the polish chromatography.

After polishing, the product will be purified from inactivated virus using nanofiltration skid. This skid includes peristaltic pump, pressor sensors, and depth filtration membrane.

Those operations will be performed in different Downstream processing room, a dedicated grade C, CL2 room.

UF/DF

Depending on the process the final diafiltration takes place either in the Downstream processing no.1 or no.2 room (ref. to chapter 2.9.5). This final step will be part of the final formulation step (boundary between drug substance and drug product). Indeed, the drug substance formulation buffer will have the same composition as the final drug product formulation buffer (excipients and stabilizer).

Drug Substance Formulation and Bulk Filling (in case of Viral Vector production)

This UF/DF is followed by a concentration adjustment step to adjust the concentration of the drug substance in the same processing room.

Each batch of drug substance will be filtered through a 0.22 µm sterile filter and then stored temporarily in bulk bags until further processing and drug product formulation. The drug substance is kept between 2 and 8 °C. The samples of the drug substance will be taken for quality control testing.

Note: *The drug substance could be used for drug product formulation and filling at risk (without waiting for the release of test results). In this case the product will not be cooled down between the two activities. This strategy must be confirmed in the detailed design by the NRC. In case of cooling the product is required, the NRC must transfer the product in the cold room available in the Warehouse area.*

2.7.3 Storage

The CTMF will include one (1) Warehouse including various activity such as raw material receiving, room temperature storage (racking), cold room, solvent storage into safety cabinet, drug substance storage and shipping.

This storage area will be designed according to the following assumptions (refer to warehouse capacity estimate in Appendix J):

- 1.5 months of storage of raw materials
- 1.5 months of storage of consumables

The CTMF will need to store various type of raw material as the following:

- Chemical powder
- Media tank
- Concentrated buffer tank
- Solvent
- Ready to use chromatography column
- Various disposables as tubing, filter cartridge, connectors, bags etc.
- Gowning items as suits, gloves, shoes cover, etc

The bulk tanks are transferred to the cold room storage area in the warehouse to be quarantined before expedition.

Note: *This cold room will be shared with raw materials. Then NRC will have to set-up segregation strategy to avoid any risk of mix-up.*

for a month of storage, pallet spaces must total 51.5 pallet spaces. The space available in the facility only permits to have 48 pallet space as shown on the layout in Appendix B.

For various reasons, the process would benefit to be able to stock goods for 1.5 months which would lead to 77 pallet spaces required. One possibility to increase storage capability in the warehouse that could be studied during detailed design phase would be to consider high density storage.

2.7.4 Weighing and Dispensing

The new GMP facility includes one weighing and one sampling room. These rooms will be classified as Grade C. Weighing of raw materials and sampling will be conducted within a weighing booth.

2.7.5 Preparation of Solutions

The media and buffer preparation area are located in a Grade C clean room outside the CL2 area.

This preparation area will oversee the preparation of process solutions such as the media for seed culture and production culture. The buffers and solutions used for the purification of the products in the DSP rooms will also be prepared in the preparation room. Some of the solutions will be however bought ready-to-use. To solubilize powders and mix liquids to obtain homogeneous solutions, this area includes mixers.

All the raw materials will originally come from the GMP warehouse, but some materials will be weighed and dispensed in the Weighing Room located next to the Preparation Room.

Prepared solutions will be transferred to production room using mobile tanks or bags (on cart) going though dynamic pass-through.

2.7.6 Cleaning, Preparation and Sterilization of Equipment and Components

The new CTMF facility cleaning room will be equipped for manual cleaning and cleaning via a parts washer. A pass-through will be installed for dirty equipment transfer to reduce the risk of cross-contamination.

After washing, glassware, components, small equipment, tooling, and individual connections for the bioreactor can be assembled and/or be placed in a single-door autoclave for sterilization. They will be sterilized in an autoclave using clean steam.

Note: *If reusable parts have been in contact with biohazard solution classified CL-2 such as cells or viruses; they must be decontaminated prior to be transferred to the cleaning area. The CTMF will enable two possible ways: going through the decontamination area (autoclave) or chemical decontamination in the production room. NRC must confirm the strategy being aware that using open water system for decontamination in the processing room is not recommended by guidelines.*

2.8 QUALITY CONTROL

The CTMF project will include quality control area for in process control and microbiological environmental control.

This biochemical laboratory will enable to provide quick result to enable the manufacturing area releasing intermediate product all along the production. This laboratory will take place in the second level of the L4 building. It will be classified as CL-2 in the biosafety containment level

Biological product will be tested according the following analyses:

In-House Analysis	Method
Residual Host DNA	RT-PCR (Reverse Transcriptase Polymerase Chain Reaction)
Sterility	PCR, Microbiology culture
Purity	HPLC (High-performance liquid chromatography)
Cell identity	Western blot
Potency	Microscopy, cell culture

All activities involving the open manipulation of biological material is performed in a Biosafety cabinet located inside the QC CL-2 (referred to chapter 5. for detail on biocontainment design requirements). CL-2 sample is manipulated under biosafety cabinet type II following CL-2 recommendations.

Some activities as microbiology will be performed in dedicated laboratories to avoid any risk of contamination with or by others analysis manipulation. This laboratory will be available for environmental control incubation at required temperature (various chambers).

Both laboratories will share on cleaning and material preparation room. This room will include glass washer and autoclave.

This area will have restricted access due to the GMP requirements. Indeed, badge accesses and airlocks will ensure the proper control and gowning of the authorized personnel (referred to chapter 2.9. Operational strategies).

2.9 OPERATIONAL STRATEGIES

The new CTMF facility will be equipped with airlocks to separate the flow of people and materials, and for transfer of people and materials from one room classification to another in order to reduce the risk of cross-contamination.

A goods lift will also be installed in the warehouse in order to bring samples to the QC lab on the second floor.

2.9.1 Material reception and flow to clean rooms

All materials (raw materials, tools, consumables, pre-sterile components, primary packaging components) used must enter through the loading dock of the warehouse and be stored temporarily.

The raw materials will be quarantined until their release following lab analysis. Released raw materials and other components will be packaged and sent to the appropriate locations:

- Any equipment entering the clean rooms shall go through a Material Airlock (MAL).
- Raw materials will be transferred to the weighing and preparation rooms for weighing, dispensing and preparation of medium, buffers and solutions.
- Pre-sterilized filters and tubing will be brought to the equipment in plastic bags. They will be transported within the clean room on a transfer cart.

2.9.2 Finished products transfer to warehouse

- Once filled the 20L bags will be transferred to a cold room for storage, in quarantine, waiting for QC release.
- Loaded pallets of finished products will be, then, loaded onto a truck from the shipping dock.

2.9.3 Personnel flow to clean rooms

- Personnel entering the Grade D area of the new CTMF facility goes through a set of Personnel Airlocks (PAL) for gowning/de-gowning.
- Personnel entering the grade C area goes through a set of two Personnel Airlocks (PAL) for gowning/de-gowning.

2.9.4 Dirty equipment parts and waste

- None contaminated solid waste from the clean rooms will be collected in a mobile garbage bin, wrapped in a bag, and transferred to the warehouse waste room via the dedicated unidirectional dynamic pass-box.

- Contaminated solid waste from the clean rooms will be collected in a mobile garbage bin, wrapped in a bag, and transferred to the decontamination autoclave in the warehouse waste room via the dedicated unidirectional dynamic pass-box.
- Small parts requiring cleaning will be transferred to the facility cleaning room equipped for manual cleaning or cleaning via a parts washer. If required, they are decontaminated in the decontamination autoclave prior to transfer to cleaning are.
- After washing, components needing to be steam sterilized will be wrapped in a bag for autoclave under laminar flow system, placed in an autoclave for sterilization and then transferred with a cart in the manufacturing rooms. They could also be stored in dedicated sterile storage room directly linked to the outlet door of the autoclave.

2.9.5 Purification segregation strategy

Proteins product based on cells culture could represent a risk of viral contamination especially if the production uses cell lines of human or animal origin.

As mentioned in Guidance for Industry Q5A (Services, Administration, (CDER), & (CBER), 1998) "the risk of viral contamination is a feature common to all biotechnology products derived from cells line. Such a contamination could have serious clinical consequences and can arise from the contamination of the source cell lines themselves (cell substrates) or from adventitious introduction of virus during production" (viral vector production).

There are few solutions to prevent virus contamination. Basically, all product will be tested all along the production to highlight any virus contamination. Cells lines and other raw material such as media must be chemically wellknown and validated. In process and design side, some specific steps must take part of the production steps. There include virus inactivation (detergent or acid/base solution) and virus clearance using nanofiltration system.

Because of adventitious virus contamination could be introduced during production, the design of the facility must include risk assessment and production room segregation.

The following scheme shows the different steps of mAb production with highlights on virus removal.

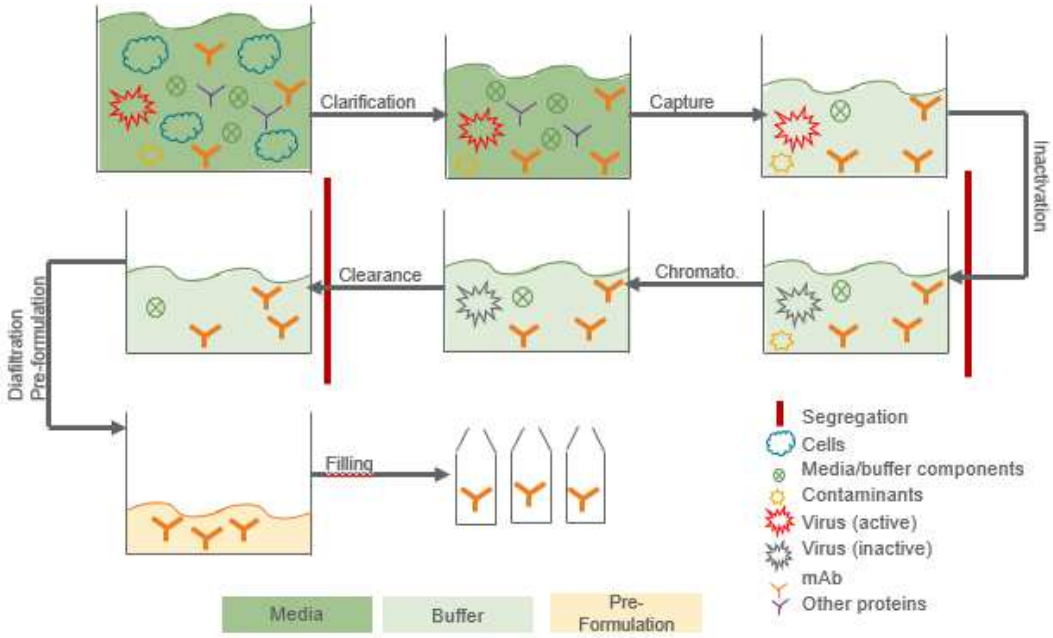


Figure 3: *Purification of Biologics*

As mentioned above, the regulations try to lead the GMP facility in this way (referred to quotation below):

[GUI-0027 - 4.0 Interpretation of Regulations - Premises C.02.004]

"6 - Facilities are designed to prevent cross-contamination during movement of personnel and materials between different areas.

6.1 Where required, facilities are designed to permit effective segregation between processes, materials and personnel involved at different stages of production (for example, pre- and post-viral inactivation/reduction, and detoxification)."

Then it is necessary to get at least two (2) production rooms to get segregation between pre- and post-virus rooms in case of protein production based on cell culture such as monoclonal antibodies. For safety, the CTMF will get 3 purifications rooms to avoid any risk of contamination because of the clinical material production process is not fully controlled at this stage. Depending on the process to handle, NRC must go through complete risk assessment to evaluate the required purification segregation.

2.10 MAJOR PROCESS EQUIPMENT DESCRIPTION

2.10.1 General Equipment Design Considerations

As per regulation section C.02.005, the equipment with which a lot or batch of a drug is fabricated, packaged/labelled, or tested shall be designed, constructed, maintained, operated, and arranged in a manner that

- Permits the effective cleaning of its surfaces.
- Prevents the contamination of the drug and the addition of extraneous material to the drug; and
- Permits it to function in accordance with its intended use.

To respect the regulation requirement, a non-exhaustive list of design criteria is presented below:

Materials

- Use of 316L stainless steel for process contact surfaces
- Use of 304 stainless steel for other parts
- Elastomers conform to USP class VI

Surface Finish

- Surface finish of at least Ra 0.5 µm / 20 µinch
- External finishes (including welds) smooth to facilitate cleaning
- All stainless steel, including welds passivated

Cleanability (sanitary design)

- No dead legs in process piping and nozzles
- Vessels fully drainable
- Sloping of lines to ensure proper drainage
- Full coverage of spray ball (confirmed by test report)
- When possible, single use equipment will be preferred to diminish the cleanability requirement of the process contact part.

Documentation

- Material certificates for parts in contact with process
- Surface finish certificates for parts in contact with process

- Weld certificates
- Passivation certificate of stainless-steel parts in contact with the process

Those design requirements will be verified during Installation qualification (IQ) when applicable for all equipment where qualification process will be performed. Refer to section 8 of this report for complete validation strategy.

2.10.2 Equipment for Solution Preparation

Weigh booth:

This system will enable to split powder raw material in correct quantities before solution preparation. It also protects the operator from inhaling chemical powders.

Specifications:

- One (1) cabinet large enough for a scale
- Air extraction

Mixer

This system will enable to solubilize powders in purified water (or water for injection) for the preparation of solutions, medium and buffers.

Specifications:

- Vessel with adequate volume: from 50 to 500 L
- Single-use bag with addition port
- Magnetic agitator with motor drive
- Process monitoring sensors such as pH, temperature, and conductivity

2.10.3 Cell Culture Equipment

Dry bath

This equipment will enable the thawing of biological material in a predefined time and temperature without affecting the quality of the product (e.g. formation of crystals which can destroy the cell membranes).

Specifications:

- Temperature adjustable up to 42°C
- Capacity from1 mL vials (cryopreservation type) to 100mL bags
- No opened water system
- Includes temperature sensors and temperature control

Agitated CO_2 incubator

This equipment will enable the set up and maintaining of optimum environmental conditions for cell culture in shake flasks (suspension culture).

Specifications:

- Humidity control
- 37°C temperature control
- CO_2 level control (5%)
- Capacity of at least eight (8) x 2L shake flasks (to be confirmed)
- Transmission of data to a centralized monitoring system

Type II biosafety cabinet (BSC)

The future process described by NRC being at laboratory scale, the process contains several open steps (e.g. change of media and passage of the cells). To prevent contamination of the cultures, the panel will provide Grade A environmental conditions in terms of numbers of particles in the air.

Specifications:

- Work area with a width of 4 or 6 feet (depending on the rooms)
- Pharmaceutical Grade A environment
- Includes HEPA filters on air inlet and outlet

Bioreactor single-use

This system will enable cells expansion by maintaining optimum environmental conditions for cell growth or viral production.

Specifications:

- One (1) vessel of 50 or 500 total working volume
- One (1) bag holder with ergonomic installation operation
- One (1) temperature control unit with electrical heating (up to 37°C) and chilled water-cooling system (minimum room temperature)
- One (1) port for medium inlet (day 0 and dilution)
- One (1) port for inoculation
- One (1) port for pH regulation solution NaOH, $NaHCO_3$
- One (1) port for Glutamine solution addition (only for 2000 L)
- One (1) port for viral seed infection (as option for viral vector production)
- One (1) bottom valve for harvest
- Six (6) pumps for addition
- One (1) gas inlet filter line
- One (1) gas outlet filter line to vent
- Four (4) loadcells
- One (1) magnetic agitation system
- Process monitoring sensors such as pH, temperature, dissolved oxygen, pressure

CFR 21part 11 data acquisition and automation control

Storage Tank:

This system will enable either the storage of medium or the collection and storage of the harvested clarified product solution from bioreactors.

Specifications:

- One (1) vessel of 500L
- Jacket connected to temperature control unit (TCU) with cooling-water and electrical heating system (range from 4°C to room temperature)
- Load cells to measure the product weight
- One (1) floor scale with digital screen for double check

2.10.4 Purification Equipment

Chromatography system

This system will enable the elimination of impurities present in the suspension.

Specifications:

- Standalone model

- Large scale
- Compatibility with anionic resin columns
- Compatibility with affinity membrane columns
- Compatibility with chemical sterilization treatments such as NaOH
- Process monitoring sensors such as pressure, conductivity, and pH sensors
- Pump(s)
- CFR 21part 11 data acquisition and automation control

Tangential filtration

This system will enable the elimination of impurities and replace the suspension medium by a formulation buffer before the final filtration.

Specifications:

- One (1) Benchtop pilot scale model
- One (1) Large scale
- Filtration area: up to 9 m^2 (large scale to be confirmed)
- Mode: Diafiltration/concentration (recirculation)
- Compatibility with chemical sterilization treatments such as NaOH
- Process monitoring sensors such as pressure and conductivity sensors
- Pump(s)
- CFR 21part 11 data acquisition and automation control

Formulation mixer

This system will maintain the proper conditions (temperature, agitation) for product pooling, excipient addition and pH adjustment before filling.

Specifications:

- Vessel with adequate working volume: from 10 to 50L
- Single-use bag with addition port
- Minimum holding volume
- Magnetic agitator with motor drive
- Process monitoring sensors such as pH, temperature, and conductivity

2.10.5 Cleaning, Preparation and Sterilization Equipment

Parts washer

Dirty parts will be cleaned by the parts washer located in the cleaning room. This washer will allow the cleaning of dispensing and manufacturing components such as glassware, utensils, handling tools, etc.

Specifications:

- Type: single-door part washer GMP design pharmaceutical grade
- Model: Steris Reliance 480 PG
- Chamber size: 56" H x 35" W x 29" D

Sterilization autoclave

This system is used to reduce the bioburden present on glassware or on various assemblies made of disposable materials such as the transfer, filtration, or sampling lines.

Specifications:

- Type: double-door autoclave
- Steam: clean steam
- Reduces the bioburden by 6 logs
- Chamber load capacity of 1837L
- Cycles:
  - Gravity/wrapped goods
  - Vacuum/wrapped goods
  - Liquid
  - Leak test

2.10.6 Decontamination equipment

Solid Waste Decontamination Autoclave

This system is for biohazardous decontamination of solid waste such as bioreactor single-use bags.

Specifications:

- Type: single-door pit-mounted autoclave
- Model: Finn-Aqua BPS GMP steam sterilizer
- Chamber load capacity of 900 mm x 1200 mm x 1500 mm
- Steam: plant steam

Biological effluent treatment system

This system is for the thermal decontamination of all biological effluents.

Specifications:

- Type: Thermal decontamination system
- Model: Actini Ultimate 1000
- Nominal flow rate: 500 liters per hour
- Select agent: BSL2
- Lethality rate: F0 = 25
- Cycle:
  - 135ºC for 60 seconds
- 8000 liters stainless steel effluent collection tank

The biological effluent treatment system must be equipment with easily accessible sampling ports

2.10.7 Miscellaneous Equipment

Many other equipment will be installed in the new CTMF such as fridges and freezers, cold rooms, carts and pass-throughs, Biosafety Cabinets, QC Laboratory equipment, etc. Refer to Appendix E for the complete equipment list.

3 REGULATORY FRAMEWORK AND BEST PRACTICES GUIDELINES

3.1 INTRODUCTION

The Human Health Therapeutics Research Centre (HHT) of the National Research Council (NRC) was mandated to establish a Clinical Trial Material Facility at the Royalmount facility GMP compliant to enable the production of vaccines and/or therapeutics for clinical trials in Canada.

3.2 ASSUMPTIONS

The products to be produced at the CTMF are produced for the Canadian market only.

3.3 APPLICABLE REGULATIONS, STANDARDS AND BEST PRACTICES

3.3.1 Applicable Canadian regulations

- Food and Drug Regulation, Division part A, Part C (Division 1,2,4 and 5)
- Health Canada – Good Manufacturing Practices guide for drug products, 2018, GUI-0001
- Annex 1 to the Good Manufacturing Practices Guide – Manufacture of sterile drugs (GUI-0119)
- Annex 2 to the Current Edition of the Good Manufacturing Practices Guidelines Schedule D Drugs (Biological Drugs) (GUI-0027)
- Health Products and Food Branch Inspectorate, Guidance Document, Annex 13 to the Current Edition of the Good Manufacturing Practices Guidelines, Drugs Used In Clinical Trials, 2009, GUI-0036
- Guidelines for Temperature Control of Drug Products during Storage and Transportation, 2011, GUI-0069
- PIC/S Good Practices for Data Management and Integrity in Regulated GMP/GDP environments,2016 (Referred by Health Canada GUI-0001)

3.3.2 Applicable standards

- United States Pharmacopeia (USP)
- ISO 14644 Cleanrooms and associated controlled environments

3.3.3 Applicable best practices

- PDA Technical Monographs
- ISPE Baseline – Volume 5: Commissioning and Qualification, Second Edition, 2019
- ISPE Baseline – Volume 6: Biomanufacturing
- ICH Q9: Quality Risk Management
- ISPE GAMP 5 Guide: Compliant GxP Computerized Systems and ISPE GAMP series of Good Practice Guides
- ISPE Applicable Technical Guidelines

3.3.4 Public Health Agency of Canada (PHAC) – Biosafety and Biosecurity

- Canadian Biosafety Standards (CBS)

4 LAYOUT AND ARCHITECTURE

4.1 GENERAL

The new CTMF facility will be built as a 15 740 ft2 in the existing building and with an extension to the existing L4 building of the National Research Center in Montreal, Quebec. The CTMF facility will consist of two levels. The manufacturing area, warehouse, clean utilities, mechanical room will be on the ground floor, while the QC laboratory will be located on the first floor in an existing lab.

4.2 SCOPE OF WORK

The CTMF manufacturing rooms and airlocks (personnel and material) will be built within the existing NRC's premises located in Montreal, Quebec and will consist of GMP classified Grade C and D areas (including new dedicated HVAC systems). The production area (8570 ft^2) due to the nature of the products intended to be produced in the CTMF will be classified as a Containment Level 2, refer to section 5 for biocontainment.

The manufacturing surface area will be approximately 8 570 ft^2. The facility will also include one Controlled Not Classified 2 530 ft^2 warehouse and a 2 860 ft^2 mechanical room on the ground floor as well as a 1 040 ft^2 QC laboratory on the second floor. Controlled access will be installed to separate the GMP activities from the existing activities in the rest of the L4 building. This control will be installed in each GMP entrance. Indeed, people working in the warehouse will shared corridor with others worker before accessing to the dedicated GMP entrance.

This dedicated corridor leads to the mechanical room and the warehouse. Lockers will allow personnel to gown appropriately before entering further gowning airlocks to access production or support areas.

The construction of the new CTMF cleanrooms area will use prefabricated modular clean room panels and flooring is pharmaceutical-grade vinyl.

The proposed layout was developed considering the process assumptions (referred to 2.6). The new CTMF will be equipped with airlocks in order to separate the flow of people and materials, and for transfer of people and materials from one room classification to another in order to reduce the risk of cross-contamination.

Room pressurization is required to ensure air flows from rooms of higher to lower classifications. Pressure monitoring is installed to continuously measure the pressure differential between rooms of different classifications. This monitoring is installed across airlocks and other openings in the clean room enclosure (i.e.: pass-through).

All power and control panels, including variable speed drives will be located, whenever possible, in the mechanical area for cleanability purpose.

A new mechanical room in the extension will serve the CTMF and will house new HVAC dedicated systems, bag-in/bag/out HEPA filter and electrical panels. A smaller mechanical room (effluent room) in the extension will house the biological treatment and neutralization systems. This last room will be considered Containment Level 2 as well. The extension will also host an IT room and an electrical room.

A preliminary layout is presented in Appendix B.

4.3 ASSUMPTIONS

The following hypotheses were used as a basis of design:

- No structure study has been done prior to this study. All revamping has been considered feasible excepted for the structural column that has been kept as constraint for the layout design.
  Note: *Architectural study must be made prior or during the detailed design to confirm this hypothesis. As well as the slab load has to be confirmed.*

- Operators will use the existing cafeteria facility located in another wing of the Royalmount facility

- Archives could be kept in a closed office on the second floor (with restricted access) or be outsourced

- Locker rooms and offices will be designed according to (refer to Human Resources estimate in Appendix J):
  - No overlap between shifts except for DSP
  - min two (2) people per activity in production (double check requirement)
  - closed office for the facility manager
  - one shared office to support the facility day to day (mgt Project)
  - HHT has as policy to give a closed office to team leads (TL) // possibility to share (2 in office)
  - larger QA shared office to deal with the documents
  - one (1) open space with shared desk over shift for operator and production personnel

- Biosafety classification:
  - Viral vectors – Containment level 2 (CL2)
  - Monoclonal anti-bodies – Containment level 2 (CL2)

Note: *Offices space (not shown on the layout) could potentially be placed above the extension or north of the lockers. These options are not considered in the budget of the project but could be feasible.*

Note: *The QC laboratories could be also placed above the extension. This option is not included in the budget of the project but could be feasible.*

4.4 ZONING AND ROOM CLASSIFICATION

The classification strategy must follow the GMP guidelines as much as possible:

- Grade C: Preparation of solution which will be filtered
- Grade D: Handling of material after cleaning or sterilization
- Grade A: Preparation, final filtration, and aseptic filling

  Any operation where the final product is in direct contact with environment air

Then production areas are classified according the following environmental classification:

- Grade C: Background area of sub-culture, downstream processing, bulk filling, sterilization (post-sterilization area), preparation of buffer and media, weighing and dispensing, sampling room, staging rooms (1 & 2) and pass-through.
- Grade D: Cleaning rooms (dirty side) and sterilization (pre-sterilization area).
- Controlled Not Classified: Warehouse, decontamination area, cryostorage.

To transfer from one grade to another grade, airlocks are required. These areas are created within a room by either using a separate Biological Safety Cabinet. In order to segregate downstream processing and bulk filling from other activities in subculture and upstream, these two areas are designed with dedicated airlock for material and personnel.

4.5 PRODUCTION ZONES

Spaces will be distributed as follows on the first floor. Refer to layout for the ground floor and for the 1st floor in Appendix B.

4.5.1 Ground floor

Manufacturing zones

- Material and personnel Airlocks
- Corridors
- Subculture
- Upstream processing
- Downstream processing no.1
- Downstream processing no.2
- Bulk filling
- Staging 1 and 2
- Janitor

Supporting areas

- Cleaning room
- Clean storage
- Sterilization
- Preparation room
- Weighing room

Warehouse

- Sampling room
- Cryostorage
- Warehouse
- Cold room
- Decontamination/Waste room
- Shipping and receiving dock

- Technical area (for TCUs)
- WC
- Janitor

Mechanical room

- Mechanical room
- Clean utilities room
- IT room
- Electrical room
- Effluent treatment room

Other

- Lockers (production)
- Communication room (existing)
- WC

4.5.2 First floor

Quality Control Laboratory

- Personnel Airlocks
- Sample storage
- CL-2 General Laboratory including a preparation area and space for chemical storage
- Cleaning room
- Microbiology room

Offices

- QC laboratory personnel office

4.5.3 Facility Area

The area of the new GMP Manufacturing at NRC's facility project is as follow:

▪ Manufacturing zone and supporting areas	8 570 ft^2
▪ Warehouse (2 storeys)	2 530 ft^2
▪ Services (lockers, etc.)	600 ft^2
▪ Mechanical room (Electrical/IT/clean utilities)	2 860 ft^2
TOTAL GROUND FLOOR:	**14 560 ft^2**
▪ QC Laboratory	1 040 ft^2
▪ Office	140 ft^2
TOTAL FIRST FLOOR:	**1 180 ft^2**

4.6 GENERAL PRODUCTION FLOWS

Refer to section 2.9 for the Operational Strategies and general flows description.

4.7 PROPOSED GOWNING

Gowning wear by personnel in the different rooms of the CTMF facility will differ based on the classification of the room. Gowning will be put on in personnel airlocks before entering a room:

Grade C:	The hair and, where relevant, beard and moustache should be covered. A one-piece jumpsuit, gathered at the wrists and with a high neck, and appropriate shoes or overshoes should be worn. The clothing should shed virtually no fibres or particulate matter.
Grade D:	The hair and, where relevant, beard and moustache should be covered. Protective clothing and appropriate shoes or overshoes should be worn. Appropriate measures should be taken to avoid any contamination from outside the clean area.
Controlled, not classified (CNC):	The person's hair shall be covered. Plant uniform and dedicated shoes or overshoes are worn.

Clothing used in clean areas should be laundered or cleaned in such a way that it does not gather additional particulate contaminants that can later be shed.

To ensure personnel protection, gloves and a face mask will be donned by personnel entering rooms where the virus is handled such as the USP rooms during infection, DSP rooms and the bulk filling room.

For detailed gowning procedure at HHT's GMP facility, refer to SOP GMP.P.007 *GMP Gowning Procedure* and refer to Appendix E for example of gowning requirement for each sector/room grade area of the CTMF facility.

5 BIOCONTAINMENT

5.1 GENERAL

A biocontainment strategy will be put in place and will consist of physical and procedural containment methods to ensure operator safety and containment of biological material within the appropriate area. This will ensure that no biological material can contaminate the public or the environment and that the facility and its activities will comply with applicable regulations and guidelines.

Adequate control of biohazards is required in a biomanufacturing facility, particularly with respect to protection of individuals and the environment. The Canadian Biosafety Standards (CBS) document published by the Public Health Agency of Canada (PHAC) is used in describing safe methods, facilities, and equipment for managing infectious materials in the environment where they are being handled or maintained. Containment controls have been grouped into increasing levels of protection labeled Containment Levels (CL), with CL-1 appropriate for work with agents with the least risk and CL-4 required for work with agents with the greatest risk.

5.2 ASSUMPTIONS

There are two types of biological material considered in this feasibility study:

- Viral vectors
- Monoclonal anti-bodies

The new CTMF at NRC's facility will use different kind of biological organisms such as HEK-293 cells adapted for suspension growth to produce an adenovirus (Ad5-CoV) or CHO cells genetically modified to produce specific monoclonal antibodies.

According to the Health Canada ePATHogen – Risk Group Database the agents are classified as follows and the Centers for Disease Control and Prevention (CDC) guidelines:

- HEK-293 noninfected cells
  - Classified as a Risk Group 1 (RG1). These organisms pose a moderate health hazard. CL-1 containment is required for work with HEK-293 cell lines.
- Adenovirus in suspension
  - Classified as a Risk Group 2 (RG2). These organisms pose a moderate health hazard. CL-2 containment is required for work with Adenovirus type-5 vectors.
- CHO genetically modified cells
  - Classification will depend on the gene modification. NRC choose the assumption to handle maximum Risk Group 2 (RG2). These organisms pose a moderate health hazard. CL-2 containment is required for work GM CHO cells.

5.3 BIOCONTAINMENT STRATEGIES AND CLASSIFICATION

The new CTMF at NRC's facility will be designed according to the following strategies:

- Containment Level 2 (CL2) for rooms where virus will be handled, such as:
  - Subculture room where the viral stock is prepared, or the genetically modified CHO cells will be amplified.
  - USP room where the virus is produced at a larger scale by infecting the HEK-293 cultured cells or the CHOs will produce mAb.

  - DSP rooms where the drug substance is separated, purified, and formulated into a drug product
  - Bulk filling room where the virus preparation is filled into bags

- CL2 rooms will be maintained in negative pressure referred to adjacent room
- Airlocks designed as «bubble» to be maintained in positive pressure with the exception of the DSP2 and Bulk fill room airlocks that will be designed as «sink» to be maintained as negative pressure
- Process equipment and AHU related to risk group agent will be on emergency power in case of power outage.
- Restricted access as per section 5.4 will be applied
- Proper ventilation strategy as per section 5.5 will be applied.
- Proper decontamination strategy as per section 5.6 will be applied.
- Proper gowning strategy as per section 5.7 will be applied.

5.4 RESTRICTED ACCESS

Rooms with containment level 2 containment are separated from public access points by doors and access is limited to authorised personnel. Access is controlled via access cards.

Rooms with containment level 2 containment have entry/exit airlocks with interlocked doors.

5.5 HVAC

The HVAC system design assures the required CL2 conditions. Pressure differentials assure air flows from lower towards areas of higher containment. Pressure differentials are monitored and alarmed. The CL2 areas each have a dedicated air handling system and their return air is HEPA filtered with bag-in/bag-out (BIBO) modules.

Refer to section 6 below for more details on the Air Handling Units for the CL2 areas.

An existing laboratory on the first floor will be fit-up to assure CL2 and GMP requirements are satisfied.
The existing laboratory HVAC distribution system will be modified to suit the new layout.

5.6 DECONTAMINATION

5.6.1 Solids

Two types of solid waste will be decontaminated within the new CTMF.

The first type of solid waste that will be generated by the production will consist of single-use consumables such as single-use bioreactor bags, tubing, and other single-use components. This waste will be decontaminated in a dedicated autoclave located in a Decontamination Room, within the Warehouse. Once this waste has been properly decontaminated, it will be disposed of with other general waste.

The second type of solid waste concerns reusable glassware and components, which will be decontaminated within the production area in a dedicated autoclave located in the Decontamination Room. This waste will be decontaminated in a dedicated autoclave located in a Decontamination Room, within the Warehouse and will mostly come from the Subculture room. Once this equipment is properly decontaminated, it can be washed and sterilized to be used again.

Decontamination will be conducted in validated autoclaves by qualified and trained personnel following applicable SOPs.

5.6.2 Liquids

Biological effluents will be collected in an underground double-containment collection pit and will be periodically pumped to an effluent treatment system for thermal decontamination. Once a certain level is reached in this tank, its contents will be thermally inactivated (135 ºC for 6 minutes) in the decontamination system. Refer to section 2.10.6 for additional information on the biological effluent treatment system.

The system will be composed of one (1) large storage tank of 8,000L to handle 5,400L of biological wastewater as the worst-case day with 10% contingency. This tank will be equipped with one (1) event and one (1) level switch. The system will get the decontamination capacity of 500LPH.

Note: *The detailed design will study the possibility to get 1000LPH system capacity to try reducing the storage tank even if supplier recommends getting 2 worst day effluent volume storage tank.*

The decontamination system will be equipped with:

- One (1) heat exchanger with concentric tubing composed of one (1) energy recovering section, one (1) steam heating section, one (1) holding section to insure the efficient decontamination timing and one (1) cooling section.
- One (1) starting container
- Two (2) chemical solution container (acid/base)
- One (1) filter for solid retention prior to the pump
- One (1) pumping system for acid/base solution
- One (1) pumping system for starting boost
- One (1) pumping system for process flow
- Various instrumentation such as temperature, pressure, flowrate sensors and level switch
- Various valves such as flow control or temperature control valves
- The system must be fully automated

5.6.3 Gas and aerosols

Main operations with biological material take place in closed systems that are equipped with 0.2 µm sterilization-grade filters. Open manipulations are conducted within Biological Safety Cabinets or isolators that protect the product, operators, and the environment.

All processes are done in clean rooms, where HEPA filters are used to remove contamination (referred to chapter **Erreur ! Source du renvoi introuvable.**).

5.7 GOWNING

The CL2 areas will be accessible to authorized personnel already gowned for Grade C activities and will go through personnel airlock where they will put on a one-piece jumpsuit, face mask and gloves. This will ensure the protection of personnel and by removing the one-piece jumpsuit, face mask and gloves when exiting the area, the risk of bringing RG2 material outside the CL2 room is controlled and minimized.

In case of protein product production based on cell culture, the two last purification rooms must be protected from the previous processing room (back contamination; referred to chapter 2.9.5). Then the CTMF will include additional airlock to segregate those rooms as shown on the layout in Appendix

B. Workers will be able to change their gowning, and material to be decontaminated before entering to those rooms.

6 MECHANICAL – BUILDING AND PROCESS

6.1 SCOPE OF WORK

This section describes the mechanical systems necessary to generate and distribute HVAC, energy, and utilities for the process and base building loads. Its purpose is to define the engineering standards considered and incorporate design elements that benefit from the experience gained during similar projects, and especially the adjacent new Biomanufacturing Centre (BMC) project. It describes the minimum requirements to be taken into consideration during the design, selection and fabrication of HVAC equipment and design criteria for building mechanical systems and utilities.

Building mechanical services include:

- Heating, Ventilating and Air-Conditioning (HVAC)
- Domestic hot and cold water (potable)
- Storm water drainage
- Sanitary water drainage
- Chilled Water
- Plant steam
- Humidification steam
- Heat-recovery glycol
- Building automation and controls
- Fire protection.

Process mechanical services include:

- Purified water
- Clean steam
- Process water
- Softened water
- Process drainage (effluent to treatment)
- Clean Compressed Air
- Laboratory gases
- Nitrogen gas
- Process cooling water

6.2 ASSUMPTIONS

Our basis of design study is based on the requirements of standard GMP pharmaceutical manufacturing facilities with biosafety considerations. There will be new mechanical services and systems as well as connections to the existing building services where there is sufficient residual capacity.

Please note that due to time constraints for the preparation of this study, we have assumed that the existing HVAC systems serving the existing L4 ground floor facility will not be reused for the new CTMF facility. Therefore, all new HVAC systems are considered in the design and cost estimates. Nevertheless, existing plumbing and piping systems will be reused where deemed adequate and beneficial to the project.

Chilled water: we assume that the existing NRC chilled water plant is adequate for the requirements of the new facility.

Process cooling water: we assume that the existing NRC process cooling water system (ice bank) is adequate for the requirements of the new facility.

Plant steam: we assume that the existing NRC steam plant is adequate for the requirements of the new facility.

Clean steam: we assume that the existing NRC clean steam generator is adequate for the requirements of the new facility.

Compressed air: we assume that the existing NRC compressed air system is adequate for the requirements of the new facility.

Process drainage neutralization: we assume that the existing NRC process drainage neutralization is adequate for the requirement of the new facility.

Storm water drainage: we assume that the existing NRC storm water drainage system (civil) is adequate for the requirements of the new roof area being added to the building.

Sanitary drainage: we assume that the existing NRC sanitary drainage system is adequate for the requirements of the new facility.

Note: *without an interstitial space for HVAC and piping/plumbing, mechanical services will need to be installed in the ceiling plenum. This will have an impact on the final ceiling heights to allow the installation of all required equipment and systems.*

Also, the new mechanical room dimensions may need to be adjusted to allow for the installation of the HVAC and mechanical systems. This work will be undertaken during the detailed design phase as equipment dimensions are formalized.

6.3 APPLICABLE CODES AND STANDARDS

The following codes, standards and regulations were considered in the conceptual design:

- Canadian National Building Code – 2005 (including Quebec amendments)
- Canadian National Plumbing Code – 2010 (including Quebec amendments)
- Canadian National Fire Code - 2010 (including Quebec amendments)
- CAN/CSA, B149.1-10, Natural Gas and Propane Installation Code
- ANSI/ASHRAE 62.1 – Ventilation for Acceptable Indoor Air Quality
- ANSI/ASHRAE 90.1 – Energy Standard for Buildings Except Low-Rise Residential
- ANSI/SMACNA 001-2008 – Seismic Restraint Manual – Guidelines for Mechanical
- CSA B51-2014 – Boiler, Pressure Vessel and Pressure Piping Code
- CSA B52-2013 – Mechanical refrigeration code
- CSA B64.10-2011/B64.10.1-2011 – Selection and installation of backflow preventers/ Maintenance and field testing of backflow preventer
- CSST – Commission de la Santé et de la Sécurité du Travail
- GMP – Good Manufacturing Practices for Drug Manufacturers and Importers
- Health Canada
- NFPA 10 – Standard for Portable Fire Extinguishers
- NFPA 13 – Standard for the Installation of Sprinkler Systems
- NFPA 30 – Flammable and Combustible Liquids Code
- NQ 5710-500-2000 – Gaz médicaux ininflammables - Réseaux de distribution des établissements fournissant des services de santé - Caractéristiques et méthodes d'essais
- Quebec Construction Code - 2014
- Quebec Regulation respecting energy conservation in new building – 2014
- Quebec Regulation respecting environment quality – 2014
- Quebec Regulation respecting pressure vessels – 2014
- Quebec Regulation respecting stationary Enginemen – 2014 Clean utilities

Note: *a detailed review of codes mentioned above is required to ensure that the presented codes are respected in case of execution of the project and might imply modification to the layout or arrangement of the facility as presently designed.*

6.4 CLEAN UTILITIES

6.4.1 Water for injection

The proposed strategy in terms of water usage at the CTMF is to use Water for injection from the whole production.

Weekly demand created by the CTMF is estimated to be 29.978 L per week including a 15% contingency with a peak demand of 2,103 L in two hours. Uses include equipment cleaning, media preparation, concentration and chromatography or filtration wetting and rinse step, as well as the demand from the new clean steam generator. Refer to the WFI consumption simulation in Appendix J.

The produced water for injection must meet the USP water criteria:

Typical test	Acceptance criteria
Conductivity	Comply to USP<645>
Total Organic Carbon as per USP<643>	≤ 0.5 mg/L
Microbial Content	≤ 10 CFU/mL
Bacterial endotoxins	≤ 0.25 EU/mL

A new distribution loop to feed 13 point of use (POU) in the new GMP facility will be added. The new loop will be sloped to drain and will include the piping, point of use valves and required accessories. All piping will be made of 20 Ra 316L stainless steel orbital welded. Manual stainless steel zero static diaphragm valves will be installed at the points of use.

Note: *The temperature requirement for the distribution loop and point of use must be studied in the detailed design. No cooling system has been considered in this feasibility. As well as the sanitization strategy that could impact the heating and cooling requirements for this facility.*

6.4.2 Purified water

The proposed strategy in terms of water usage at the CTMF is to use purified water for first step of cleaning procedure but the main user will be the water for injection generator.

Weekly demand created by the CTMF is estimated to be 44,484 L per week including a 15% contingency with a peak demand of 3,037 L in two hours. Uses include equipment cleaning, media preparation, concentration and chromatography or filtration wetting and rinse step, as well as the demand from the new clean steam generator. Refer to the PW consumption simulation in Appendix J.

The produced water for injection must meet the USP water criteria:

Typical test	Acceptance criteria
Conductivity	Comply to USP<645> (≤ 1,3 µS/cm at 25°C stage 1)
Total Organic Carbon as per USP<643>	≤ 500 ppb
Microbial Content	≤ 100 CFU/mL

A new distribution loop to feed 5 point of use (POU) in the new GMP facility will be added. The new loop will be sloped to drain and will include the piping, point of use valves and required accessories. All piping will be made of 20 Ra 316L stainless steel orbital welded. Manual stainless steel zero static diaphragm valves will be installed at the points of use. The new QC lab will be connected to the same distribution loop for his 2 point of uses.

Note: *Due to the few point of use requiring Purified Water and the lack of available space in the L4, the detailed design might take in consideration to not include Purified Water storage tank. Indeed, one (1) system might be taken in consideration to supply water for injection to the whole facility.*

6.4.3 Process Clean steam

The CTMF facility is equipped with one 1654 lb/hr (750 kg/hr) clean steam generator PSG 1500 Siltmas with an outlet pressure of 50 psig. The new load to be added to the generator will be two autoclaves for the new GMP facility, for a total peak load of 862 lb/hr if all users are in operation simultaneously. It is considered however that all demands will be distributed in time throughout the day.

Installation of 1 ½'' diameter clean steam distribution piping will be done to supply the points of use in the new CTMF. The piping will be sloped to drain and will include the piping, point of use sanitary ball valves, steam traps and required insulation and accessories. All piping will be made of stainless steel 316L.

Contaminated steam condensate will be drained to effluent neutralization treatment system before the sanitary drain. Refer to the Heating requirement simulation in Appendix J.

6.5 PIPING AND PLUMBING

This section describes the proposed piping/plumbing systems for the project. Systems will be designed in accordance with the latest applicable codes, standards, and can be modified to suit additional requirements of any authorities having jurisdiction (AHJ).

6.5.1 Plant steam and condensate

Plant steam will supply process equipment such as purified water production and autoclaves, biological water treatment (kill tank) and a steam-to-steam generator for humidification purposes. Condensate will be returned to the steam plant where possible.

The existing plant steam design pressure is 7 barg (100 psig). Peak consumption for plant steam in the CTMF is estimated to be 2,270 kg/h (5,000 lbs/hr) or approximately 145 BHP.

Condensate will be recuperated when possible or cooled and sent to sanitary drain when not. Some condensate is considered contaminated (eg. autoclave) and will therefore be cooled and sent to process drain for treatment.

System Description
Steam from the existing steam boilers plant will be used to supply the new facility. The new distribution piping will be connected to the existing main steam header located in the existing boiler room. Steam will be at high pressure (100 psig) to optimize pipe sizing up to L4. Pressure reducing stations will be installed for equipment and systems that require lower steam pressures to operate.

Condensate will be pumped back to the existing condensate receiver in the boiler room.

Condensate from distribution piping will be returned to the atmospheric sloped main condensate return pipe.

Condensate collection is included at vertical pipe rises, drip legs (100 ft maximum intervals on distribution piping, and upstream of control valves. Thermodynamic steam traps will generally be used for drip legs.

Preliminary Piping Specifications
- Plant Steam: Schedule 40 Carbon Steel; Welded and threaded fittings and connections.
- Plant Steam Condensate: Schedule 80 Carbon Steel; Welded and threaded fittings and connections.

Insulation:
- Fibreglass
- Hight temperature PVC jacket for exposed piping.

6.5.2 Humidification steam

Clean steam is required for humidification.

Humidification steam will be generated with a steam-to-steam generator and then supplied to short-absorption distribution manifolds in HVAC air-handling units for humidification.

Steam design pressure for humidification is 1 barg (15 psig). Humidification steam peak load is estimated to be 90 kg/h (200 lbs/hr).

System Description
A dedicated humidification-steam generator will be installed in the new mechanical room and will distribute to steam manifolds in the new air-handling units. The new steam generator will be powered by plant steam (steam-to-steam). A dedicated water softener with filters will be installed for conditioning makeup water.

Preliminary Piping Specification
- Clean Steam: Schedule 40 Stainless Steel 304L; Screwed fittings and connections.
- Clean steam condensate: Schedule 80 Stainless Steel 304L; Screwed fittings and connections.

Insulation

- Fibreglass
- High temperature PVC jacket for exposed piping

6.5.3 HVAC - Chilled water

Performance Requirements

The existing facility chilled water plant will provide chilled water for the new HVAC units. Note that the chilled water supplying the existing HVAC unit will become available for the new AHU units as that system will be decommissioned.

Design chilled water temperatures for cooling coils are 42°F/52°F.

The fluid will be water as all the piping will be installed indoors and mixed air temperatures will be above the freezing point.

Preliminary cooling loads were calculated for HVAC. The estimated total load is approximately 350 kW (100 TR) and is largely to condition outdoor air for ventilation. This is the probable peak load in summer.

System Description

The existing chilled water plant includes three water-cooled chillers installed in the main mechanical rooms We assume that there is adequate capacity to supply the new CTMF facility. Note that the existing make-up air unit serving the ground floor (L4) will be decommissioned for this project and the associated cooling capacity will become available for our new facility HVAC cooling requirements.

The existing chilled water system is designed as a primary-secondary system configuration. A new dedicated secondary pumping system (15 L/s or 240 gpm) will be installed for the CTMF facility. This system will be variable water flow. One new secondary distribution pump with VFD will supply chilled water to the new HVAC air-handling units.

The proposed pump technology is vertical inline self-sensing centrifugal pump with integrated variable frequency drive (VFD). It will be installed in the existing mechanical room if possible.

Preliminary Piping Specifications

- Schedule 10 Stainless Steel; Welded connections.
- Carbon Steel, SCH 40, Threaded and flanged connections (Victaulic could be considered).

Insulation

- Fibreglass with PVC jacket

6.5.4 HVAC - Heat recovery glycol

Performance Requirements

The heat recovery glycol system will exchange sensible heat between process exhaust air and outdoor air for ventilation via a run-around loop.

This system will be designed to also serve as a back-up to the main electric heating coils in the DOAS, in the case of an electric power failure, with a steam to glycol heat-exchanger.

System fluid will be Propylene glycol 40%.

System Description
The glycol run around heat recovery system will have one cooling coil installed in the process/laboratory exhaust air plenum and with a pre-heat coil installed in the dedicated outdoor air supply (DOAS) unit.

The system will have one circulation pump with integrated VFD to provide glycol flow in the system. The loop will include a glycol feed unit and an expansion tank.

The system will be designed with backup heating in case of an electric power failure feeding the main electric heating coils in the DOAS. The glycol pre-heat coil in the DOAS unit will be sized for the total heating load. A steam/glycol shell and tube heat exchanger will be installed on the system for backup heat (steam boilers are on emergency power). The heat exchanger will boost the temperature of the glycol heat recovery loop to assure adequate coil temperatures. This will allow for the heating of the outside air during electrical power failures to assure the ventilation required for building pressurization.

The proposed pump technology is vertical in-line self-sensing centrifugal pumps with integrated variable frequency drives (VFD).

The proposed heat exchanger will be a packaged skid-mounted shell and tube heat exchanger with all required accessories including a pumping trap station for condensate recovery.

Piping specification (Preliminary)
- Schedule 10 Stainless Steel; Welded connections.
- Or Carbon Steel, SCH40, Threaded and flanged connections.

Insulation
- Fibreglass with PVC jacket

6.5.5 Process cooling water

Performance Requirements
Provide process cooling water distribution pump and piping. Process cooling water will provide cooling for some process equipment (Bioreactor, Washer, Autoclave and TCU). Piping will be installed indoors, and supply temperature is above freezing point. Assure longevity of piping and materials within the distribution system.

Initial cooling estimate for the connected process loads is approximately 210 kW (60 TR). This is also the probable peak load.

System Description
Existing centralized ice-bank equipment is installed in the main mechanical room. Process cooling water piping will be installed and will distribute cooling water to the various process equipment.

One new pump will provide cooling water flow to the CTMF process equipment. Proposed pump technology is vertical in-line self-sensing centrifugal pump with integrated variable frequency drive (VFD). Controls will be compatible with the building's control system. Pump is sized for full load and will be installed in the new mechanical room if there is sufficient space.

Outline Piping Specification (Preliminary)
- Carbon Steel, SCH40, Threaded and flanged connections.

Insulation

- Insulation: Fibreglass
- Jacket: PVC for exposed piping.

6.5.6 Domestic (potable) water

The building domestic water system is to supply potable water to all locations where required. The system will also supply domestic fixtures such as water-closets, urinals, mop sinks, showers, lavatories, sinks and wall hydrants.

Supply potable hot and cold water to Emergency Showers and Facewash stations. Emergency fixtures are to be installed on the domestic water system. The emergency shower stations are designed considering tempered water at 28°C (85°F) for a minimum of 15 minutes at a flow rate of 5.6 m^3/h (25 USgpm) at a minimum of 2 barg (30 psig). Tempered water mixing valves are to be installed at each emergency fixture.

System Description

The new cold domestic water distribution system will be connected to the existing system piping in the service shaft at the ceiling slab level.

The domestic hot water system will be connected to the existing water heaters. A domestic hot water return-piping loop and a recirculation pump will keep the water temperature in the return above 55°C (130°F).

All plumbing fixtures will be selected with sustainable design considerations and in accordance with code requirements and accessibility standards. Plumbing fixtures in production areas will be stainless-steel.

A pressure booster pump will be supplied to assure adequate pressure in the domestic water supply to the purified water systems.

Outline Piping Specification

- Above ground:
  - Copper tube, hard drawn, type L, ASTM B88M
  - Stainless steel Grade 304L sch10S ASTM A312
- Buried or embedded:
  - Copper tube, soft annealed, type K with no buried joints.
  - Stainless steel Grade 304L sch10S ASTM A312

Insulation:

- Hot Water and recirculated hot water:
  - Rigid mineral fiber with PVC jacket for exposed piping.
- Cold Water:
  - Rigid mineral fiber with vapour barrier and PVC jacket for exposed piping.

6.5.7 Process Water

Performance Requirements

Process water will be separated from the domestic water by a reduced pressure backflow preventer (RpBFP). Water from this system will be supplied to mechanical equipment (make-up water), and process equipment as required. It should be considered non-potable.

System Description

For the process hot water, a dedicated electric water heater, and a hot water recirculating pump will keep the hot water laboratory return loop at a minimum temperature of 55°C (130°F).

Outline Piping Specifications

- Above ground:
  - Copper tube, hard drawn, type L, ASTM B88M
  - Stainless steel Grade 304L sch10S ASTM A312
- Buried or embedded:
  - Copper tube, soft annealed, type K with no buried joints.
  - Stainless steel Grade 304L sch10S ASTM A312

Insulation

- Hot Water and recirculated hot water:
  - Rigid mineral fiber with PVC jacket for exposed piping.
- Cold Water:
  - Rigid mineral fiber with vapour barrier and PVC jacket for exposed piping.

6.5.8 Compressed Air

ISO standard 8573-1 identifies three primary contaminant types as prevalent in a compressed air system. Solid particulates, water, and oil (in both aerosol and vapour form) are recognized. Each is categorized and assigned a quality class ranging from class 0, the most stringent, to Class 9, the most relaxed. The end-user is responsible for defining the air quality required for their application or process.

Performance Requirements
Air quality grade ISO 8573-1: Class 1.2.1.

- Peak Load: TBD
- Design Pressure: 8 Bar (115 PSIG)

System Description
A compressed air receiver will be added to the system to minimize system pressure losses due to sudden large demands in compressed air. A new piping run will be provided from the existing CA header in the main mechanical room to the new air receiver. Automatic drains, pressure regulators, and filters, will be added as required.

The air receiver will be installed in the new mechanical room.

A pressure sensor on the air receiver will installed for validation purposes and will be compatible with the Building Automation System.

Filtration will be installed for all compressed air points of use where air contacts the product or process/production equipment.

Based on preliminary calculations, the main will be 50 mm (2-inch) diameter pipe. The main supply pipe will be sloped towards the end of the network (On the opposite side of the Air Receiver Tank). Drains will be provided to remove any water condensation in the distribution piping.

Clean compressed air
This system is to provide Clean Compressed Air for process equipment or for process operations. Extra filtration is required when there is a possibility of introducing Compressed Air into the product. In this project, this system uses the same distribution network as Compressed Air but is protected by extra filtration at the points of use. After passing through the filtration step, we can consider this system Clean Compressed Air.

A sampling point will be installed at the critical process equipment for quality control purposes.

Specifications (preliminary)

- Piping up to 50 mm (2" NPS): Aluminium compressed air piping system (TOPRING or equivalent)
  - Copper - ACR/MED type L
- Stainless steel 316L:
  - For exposed piping in laboratories or cleanrooms
- Receiver:
  - Dry, for a nominal capacity of 1000 L (250 US gallons).
- Filters:
  - Filtration to achieve ISO 1.2.1 classification. Terminal filtration for clean compressed air at the points of use, as required.

6.5.9 Laboratory gases

Performance Requirements

Based on preliminary QC lab and production area requirements, these are the required laboratory gases:

- Carbon Dioxide
- Oxygen
- Nitrogen

System Description

For each gas type, a cylinder changeover station, including pressure regulator, isolation valve and pressure safety valve, will be provided. Gas cylinders will be provided by a third-party vendor. The distribution piping systems will provide the required gases to the production areas and lab equipment. Laboratory Gas station locations will be as close as possible to the points of use, to optimize the piping.

Preliminary Specifications

- Laboratory gases up to 50 mm (2" NPS):
  - Copper - ACR/MED type L
- Stainless steel 316L:
  - For exposed piping in laboratories or cleanrooms

6.5.10 Storm Water Drainage

Performance Requirements

Drain storm water from new roof to civil infrastructure on site. Water retention is required either on the roof or on site (TBD, but probably on the roof).

System Description

Roof drains are installed and dimensioned to remove peak water load based on the national building code. This requirement is to consider 26.5 mm of precipitation in 15 minutes for the Montreal area. Water retention will likely be on the roof of the new addition. Control flow roof drains will retain storm water on the roof to satisfy code requirements. Note that the code allows standing water on the roof for up to 24 hrs.

Preliminary Specifications

- PVC-DWV piping for the above and below ground storm water drainage system.
- All PVC piping in return-air plenums will be plenum rated

Insulation:

- Fiberglass with vapour barrier and PVC jacket to avoid condensation.

6.5.11 Sanitary Water Drainage and Venting

Performance Requirements
Provide drainage of all new sanitary fixtures for the CTMF. Sanitary drainage includes waste from the washrooms, locker rooms, sinks, hand sinks, janitor's closets, floor sinks and floor drains in non-production areas. Final fixture numbers and locations are to be finalised during detailed design.

System Description
Sanitary drainage is to be installed for all new sanitary fixtures. They will be connected to the existing under-slab sanitary drain in L4.

Preliminary Specifications:
The system is constructed with the following materials:

- Copper DWV or PVC up to 2-1/2 NPS.
- Cast iron and/or PVC - 3 NPS and up.
- Cast iron and/or PVC for buried service (minimum 3 NPS buried). Protect all buried piping from corrosion.
- Copper DWV or PVC for venting.
- Bronze floor drains and cleanouts.
- All PVC piping in return air plenums is plenum rated

6.5.12 Process Water Drainage and Venting

Performance Requirements
Provide drainage and drainage of chemical process effluents and biological process effluents. Provide pH neutralization and acceptable water treatment before draining to the municipal sanitary sewer system. Assure longevity of piping and materials within the drainage system.

System Description
Chemical and biological process drainage is installed for all laboratories and production areas including process equipment. Stainless Steel floor drains and hub drains with sanitary connections are proposed for process drainage.

Sump pit for biological process water drainage will be pumped to the kill tank (see Process) and then drained to the wastewater treatment system. New chemical process water will be drained to the existing acid resistant drainage systems and to the existing NRC central neutralization system.

Preliminary Specifications:
The system is constructed of the following materials:

- CPVC piping and venting.
- Stainless steel piping with sanitary connections.

6.5.13 Wastewater treatment system

Process drainage including drainage from the kill tank (post-treatment) will be drained to the existing buried acid-resistant drainage system in L4. It will be treated in the existing NRC central neutralization system (temperature and pH control) before draining to municipal drainage infrastructure.

Equipment:

- Above ground:
  - Stainless Steel 304 L or CPVC piping- 3 NPS and up.

6.6 HEATING, VENTILATING AND AIR-CONDITIONING (HVAC)

6.6.1 Scope

The new CTMF will be serviced by multiple all-new heating, ventilating, and air-conditioning (HVAC) systems. Existing HVAC systems serving the L4 ground floor will be decommissioned.

All occupied spaces, including technical areas, are supplied with minimum outdoor air volumes in accordance with relevant codes and standards.

The new building zones are classified as:

- Clean classified production areas, BSL CL2,
- Clean classified production, staging, and support areas,
- GMP Warehouse,
- Administrative (existing office),
- Laboratory,
- Technical Service areas.

6.6.2 Outdoor Design Criteria

Published outdoor climatic design criteria is used for heating and cooling load calculations necessary for the selection and sizing of HVAC equipment.

The reference for climatic design conditions is the ASHRAE Handbook – Fundamentals (2013), for the Montréal Pierre Elliott Trudeau airport (WMO: 711830), which is located close to the project site.

For GMP area systems, the design criteria have been selected to ensure interior operating conditions during extreme weather events. Even though they can be of relatively short duration, it is not considered acceptable to lose control of critical interior temperatures and relative humidity in production areas during extreme outdoor weather conditions.

Extreme temperatures have been witnessed often over the last decade, considering a warming trend on a global scale. For our project load calculations, the published 5-year extreme annual temperatures were considered for the Montreal region.

Exterior design conditions considered are therefore:

Winter:

- Dry Bulb Temperature: -30°C (-22°F)

Summer:

- Dry Bulb Temperature: 33.8°C (92.5°F)
- Wet Bulb Temperature: 27.4°C (81.3°F)

For non-GMP areas HVAC systems, the design criteria are based on ASHRAE criteria 0.4% for summer and 99.6% for winter.

Winter:

- Dry Bulb Temperature: -23.2°C (-9.8°F)

Summer:

- Dry Bulb Temperature: 30°C (86.1°F)
- Wet Bulb Temperature: 22.2°C (71.9°F)

6.6.3 Indoor Design criteria

Indoor temperature design conditions vary depending on production requirements and human comfort considerations.

All occupied areas are ventilated with outdoor air to maintain acceptable indoor air quality and offset exhaust air as per codes and relevant standards.

The following summarizes the primary zone types:

Classified Production Biosafety level 2 (BSL CL2) areas
Thermal zones are defined by the following temperatures:

- Room Classification Grade C.
  - Temperature is adjustable between 18 and 22°C.
  - Individual temperature control at room level.
  - Humidity control at room level.
    - Humidification set-point at 35% RH (at 22 deg C)
    - De-humidification set-point at 55% RH (at 18 deg C)

Classified Production areas
Thermal zones are defined by the following temperatures:

- Room Classification Grade C and Grade D.
  - Temperature is adjustable between 18 and 22°C.
  - Individual temperature control at room level.
  - Humidity control at zone level not room level.
    - Humidification set-point at 35% RH (at 22 deg C)
    - De-humidification set-point at 55% RH (at 18 deg C)

Laboratories (CL2)
The QC Lab will be set up in an existing laboratory on the 2nd floor. It will be modified to assure the required BSL CL2 and GMP requirements. The existing HVAC system will be modified to suit. Additional utilities will be supplied as required.

Warehouse (GMP)
The warehouse space is to have temperature and relative humidity conditions according to USP 34 10.30.60.

The following design criteria are used:

- Temperature set-point:
  - 22°C minimum, cooling
  - 22°C maximum, heating
- Humidity:
  - De-humidification set-point at 60% RH (at 22 deg C)
  - Humidification set-point at 35% RH (at 22 deg C)

Technical Rooms
These areas will include mechanical, electrical rooms and other technical rooms. They are not regularly occupied. The minimum outdoor air (based on ASHRAE 62.1) is supplied to the areas.

Generally, there is no mechanical cooling for these spaces. They will be conditioned using outdoor air.

- Temperature set-point:
  - 20°C minimum or ambient outdoor temperature +5°C
  - 20°C maximum, winter
- Humidity:
  - Not controlled

Administration

The existing administration office spaces on the 2nd floor will be used for the facility. No modifications to these spaces are considered in this study.

6.6.4 Air Filtration

Air Cleanliness Classification

Filtration is designed to achieve cleanliness requirements by reducing airborne particles. Rooms are classified based on the Particulate Limits allowable in the space. Classification types for this project are defined using the European Commission, 2008, Grade classifications for class A to D.

Controlled-Not-Classified (CNC) spaces are defined as per ISPE.

Air Filtration

Particulate concentration in clean classified rooms is controlled using a dilution ventilation strategy. Supply air is filtered and supplied to rooms in a diffuse pattern, encouraging mixing and replacing room air with filtered air.

The air supply rates required to maintain a grade of cleanliness are defined during basic design with air-changes per hour. Particle generation for each environment, depending on process activities, shall be evaluated to refine and validate design air-supply rates during the detailed design phase.

Classification	Air-Changes/hour	Filtration		
		AHU		Terminal
		Pre-Filter	Final-Filter	
C	30	MERV 8 (40%)	MERV 14 (90%)	HEPA
D	15	MERV 8 (40%)	MERV 14 (90%)	HEPA
CNC	6	MERV 8 (40%)	MERV 14 (90%)	N/A

6.6.5 Pressurization Criteria

Room Pressurization is required to ensure air flow from rooms of higher to lower classifications[1]. Pressure monitoring is installed to continuously measure the pressure differential between rooms of different classifications. This monitoring is installed across airlocks and other openings in the clean room enclosure (eg.: pass-throughs).

The minimum pressurization requirement between adjacent zones of different classifications is 10-15 Pa. This pressure differential assures adequate air flow and is of a magnitude great enough to allow for electronic monitoring.

[1] Volume 4, EU Guidelines to GMP, Annex 1: Manufacture of Sterile Medicinal Products.

Relative room pressure is measured across an airlock and the design is to ensure pressure is maintained if one air-lock door is opened. Airlock doors are to be interlocked to avoid simultaneous opening.

The pressure reference is to be the area of the lowest pressurization that is adjoining openings in the clean spaces. This is indicated as a 0. Consecutive pressurizations are indicated as a '+' sign which does not have a fixed magnitude but indicates the relative pressurization between spaces. The pressurization plan may also include relative pressure numerical values with 0 as the base.

All pressure readings will be recorded on a qualified data acquisition system, with visual or audible alarm warnings. Alarms are required near or at the lower acceptable differential pressure level.

The BSL CL2 rooms are to be negative pressure compared to the adjacent airlocks to limit the possibilities of cross-contamination. The filling room will nevertheless be in positive pressure to protect the product for contamination. All airlocks are to be designed as bubbles except the DSP and filling area airlocks to be designed as sinks. The airlocks from the warehouse are positive to avoid the possibility of dust infiltrating from the warehouse into the production areas.

Pressure requirements are maintained in classified spaces using the following strategy:

- Pressure is maintained by the Constant Volume Offset Method, as defined by the ISPE. Pressurization is created by a differential offset between the Supply Air Volume flow rate and the Return Air Volume flow rate.
- Supply and Return air are to be adjusted to a Constant Volumetric Flow Rate.
- The system is designed for constant air flow/variable temperature. There is no set-back flow rate for un-occupied hours.
- Air supply of the Airlock at the same air-change rate as the adjacent room of the highest classification.
- Classified rooms have Airlocks between adjacent rooms of different classification. Classified rooms have Airlocks between adjacent rooms of different classifications.
- Pressure cascades are maintained only when doors and other openings leading into the space are closed.

6.6.6 HVAC strategy

General

The facility will be heated, ventilated, and air-conditioned using zone-dedicated HVAC units located in the new mechanical room. Ventilation will be calculated based on code requirements and/or production requirements to assure the required biosafety classifications and building and zone pressurization. Total supply air will be calculated to maintain the required room grade classifications. Heating and cooling capacities will assure the required dehumidification, cooling and heating based on building loads and process loads.

A dedicated outdoor air system (DOAS) will pre-treat the outdoor air for distribution to production areas HVAC systems. Heat recovery from the centralized exhaust system will pre-heat the air. Final heating will be electric.

For BSL CL2 production areas, HVAC systems are dedicated air-handling units including recirculation, filtration, and temperature/humidity control. The recirculated air will be HEPA-filtered (to allow air recirculation in a CL2 area). Six air changes per hour will be assured, as recommended for the desired biosafety classification.

The production areas and warehouse HVAC systems are dedicated air-handling units including air recirculation, filtration, and temperature/humidity control.

Outdoor air is distributed to technical and non-classified spaces for minimum ventilation requirements. Chilled-water fan-coil units will be used for additional cooling as required.

Local general and sanitary exhaust will be provided as required.

Production rooms CL2, Grade C

Air-handling units for CL2 and Grade C zones are constant air-volume variable temperature systems with chilled-water cooling and electric heating coils. Fans are supplied with variable speed drives to maintain constant air flow in the supply and return ducts regardless of system pressure fluctuations. Return air will be HEPA filtered in bag-in bag-out (BIBO) modules to allow recirculation in the classified zones. Outdoor air will be supplied to assure room pressurization and the biosafety classification. Total air flow will assure the grade classification.

The system design is as follows:

- Exhaust air to the production exhaust system
- Return fan
- Bag in/Bag out HEPA filtration module.
- Outdoor air (pre-treated by the DOAS)
- Pre-filter MERV 8
- Final-filter MERV 14
- Cooling coil – chilled water
- Heating coil – Electric SCR
- Supply fan
- Steam humidifier

Most of the systems are dedicated to one production zone (single zone). The leaving temperature of the unit is based on the required room temperature set-point. For some systems supplying more than one room (including PAL & MAL), terminal air control devices will consist of constant air-volume non-motorized venturi type air valves with terminal electric heating coil to provide heating for individual rooms temperature control.

Terminal HEPA filters will be installed in radial-type air diffusers. Rooms are to have low return air intakes.

Cooling (and dehumidification if required) of the mixed air (return and DOAS air) is provided by the AHU cooling coil. Heating is provided by the air-handling unit heating coil, or the terminal electric heating coils. Humidification is provided by a clean steam humidifier installed inside of the air handling unit.

The required room pressurization is maintained using an air-volume offset strategy between supply and exhaust.

Exhaust air flows through the new central exhaust system with heat recovery.

Other classified production area

Air-handling units for classified areas are constant-volume variable temperature systems with chilled-water cooling and electric heating coils. Fans are supplied with variable speed drives to maintain constant air flow in the supply and return ducts regardless of pressure fluctuations.

The system design is as follows:

- Return fan
- Exhaust air to the production exhaust system

- Outdoor air (pre-treated by a DOAS)
- Pre-filter MERV 8
- Final-filter MERV 14
- Cooling coil – chilled water
- Heating coil – Electric SCR
- Supply fan
- Clean steam humidifier

Terminal air control devices consist of constant air-volume non-motorized air valves. An electric heating coil will provide re-heat for individual rooms. Terminal HEPA filters will be installed in radial-type air diffusers.

Grade C rooms are to have low return. Other production rooms are to have ceiling return.

Cooling (and dehumidification if required) of the mixed air (return and DOAS air) is provided by the cooling coil. Heating is provided by the Air-handling unit heating coil, or the terminal electric heating coils. Humidification is provided by a clean steam humidifier inside the air handling unit.

Exhaust air is extracted and rejected to the atmosphere by the laboratory and production exhaust system.

GMP Warehouse
This system will include an indoor air-handling unit located in the new mechanical room. Supply air is constant air-volume variable temperature to maintain room temperature set-point and reduce temperature stratification.

The system design is as follows:

- Constant-volume variable-temperature air-handling unit.
- Fans will have VFD.
- Pre filtration (MERV 8) and final filtration (MERV 14)
- Dehumidification and cooling of the mixed air (return and outdoor air) is provided by a chilled- water cooling coil (EWT 42°F).
- Heating provided by a electrical heating coil with modulating SCR control.
- Humidification is to be clean steam supplied to distribution manifold located in the air handling unit.
- Exhaust air is rejected to the outdoors by the main exhaust fans.

Technical Areas
Technical areas will be ventilated but not air-conditioned. The ventilation rate in summer and winter are based on the equipment heat dissipation and the indoor setpoint temperature. Outside air will be mixed with recirculated air. The recirculation damper and outside air dampers will modulate to maintain the room temperature. In winter, minimum outdoor air volumes will be maintained, and the air will be heated by an electric heating coil as required to maintain minimum space temperature conditions.

The return and supply fans will be direct drive axial fans.

Chilled water fan-coil units will be installed in critical technical areas that require mechanical cooling (IT room, electrical room, etc.)

Laboratory Area
The existing laboratory HVAC system will be modified to suit the new layout.

Production area exhaust system

Production areas exhaust will be ducted to a new heat recovery plenum on the existing roof. Three (3) laboratory exhaust fans all sized for 50% of the total required flow (n+1) and will be installed on the plenum. The fans will have VFD's to control pressure and maintain constant air flow in the system.

The heat recovery plenum will have glycol coil to recover the heat from the exhaust air. The plenum will also have a controlled outdoor-air relief damper so that the fans can operate at a constant air flow regardless of indoor variations and subsequently assuring the required exhaust air plume velocity and height.

The glycol run-around heat recovery system will include a steam-to-glycol heat exchanger to assure heating of the outdoor air in the DOAS during an electrical power outage (emergency heating). This will assure operation of the DOAS to maintain building pressurization and consequently the cleanliness grade, while avoiding the potential freezing of the building during cold weather.

Administration Area

No modifications to the administration area were considered in this study.

Existing loading Dock heating

This system will consist of electric heating air-curtain installed above the loading dock door. The air-curtain will be designed to maintain a minimum temperature of 19°C in the dock with the door closed.

6.6.7 HVAC Systems Outline Specifications

Dedicated Outdoor air system (DOAS)

- 100% Outdoor Air unit
- Packaged indoor air-handling unit is to be of semi-custom design, high pressure low leakage panels insulated to R-20 minimum.
- Exterior panels are to be Galvanised Steel
- Interior panels are to be Stainless Steel.
- Interior components (flashing, screws, etc.) are to be galvanized steel (Wipe down)
- Heat-recovery glycol pre-heating coil.
- Chilled-water cooling coil.
- Electric heating coil with modulating SCR control.
- MERV-8 pre-filtration, MERV-14 final-filtration.
- Vibration isolation of fans.
- All equipment CSA listed.

Indoor Air-Handlers

- Indoor air-handling equipment is to be packaged semi-custom design; high pressure low leakage panels insulated to R-20 minimum.
- Exterior panels are to be Galvanised Steel
- Interior panels are to be Stainless Steel.
- Interior components (flashing, screws, etc.) are to be galvanized steel (wipe down)
- Chilled water-cooling coil.
- Electric heating coil with modulating SCR control.
- Direct clean steam humidifier.
- MERV-8 pre-filtration, MERV-14 final-filtration.
- Terminal HEPA filtration in classified controlled zones (not in air-handler).
- Vibration isolation of fans.
- All equipment CSA listed.

6.7 BUILDING AUTOMATION SYSTEM (BAS)

6.7.1 Scope of work

The building automation system (BAS) is a Direct Digital Control (DDC) system for the energy management, the monitoring, and the control of mechanical and HVAC equipment. The system will be integrated into the existing Honeywell EBI system.

6.7.2 Design Criteria

The new facility controls will be integrated into the existing Honeywell EBI building automation system (BAS).

The BAS system will use the existing NRC Ethernet network and include the capability to email and/or text message in the case of critical situations. The BAS will use the standard Building and Floor level devices to maintain all set-point conditions. A BAS software installed in a server located on the corporate Ethernet network provides the interface for the system users as well as interfaces via an open protocol with other systems. The system will not be commissioned using Good Engineering Practices (GEP) but rather commissioned using standard engineering and industry standards. A separate Room monitoring system (RMS) will be installed in parallel to monitor the rooms conditioned and will be commissioned using Good Engineering Practices.

Communication involving control components (i.e. all types of controllers and operator interfaces) shall conform to ASHRAE 135-2010 BACnet standard.

The network architecture will be integrated into the existing Honeywell EBI system.

Appropriate software interface with the following optional functionalities shall be provided:

- Real-time graphical viewing and control of the BMS environment.
- Reporting of both real-time and historical information.
- Scheduling and override of building operations.
- Collection and analysis of historical data.
- Point database editing, storage and downloading of controller databases.
- Configuration of and navigation through default and personalized hierarchical "tree" views that include workstation and control system objects: Event reporting, routing, messaging, and acknowledgment.
- Definition and construction of dynamic color graphic displays.
- Online, context-sensitive help, including an index, glossary of terms, and the capability to search help via keyword or phrase.
- On-screen access to User Documentation, via online help or PDF-format electronic file.
- Automatic database backup at the operator interface for database changes initiated at Building Controllers.
- Display dynamic trend data graphical plot. Must be able to run multiple plots simultaneously.
- Must be able to command points from selection on dynamic trend plots.
- Must be able to plot real-time data without prior configuration.
- Must be able to plot both real-time and historical trend data simultaneously.
- Program editing.
- Remote notification via email or text messaging.

6.8 FIRE PROTECTION

6.8.1 Scope

The fire protection system consists of the following elements:

- A wet-pipe sprinkler system to protect the CTMF facility
- Hose connections in the warehouse
- A double-interlock pre-action system for the IT room.
- Portable fire extinguishers as per code.

6.8.2 Guidelines

The fire protection system will be designed in accordance with applicable codes, regulations, and guidelines including:

- Quebec Construc*tion Code- Chapter 1*
- NFPA 13 – *Installation of Sprinkler Systems*
- NFPA 20 – *Installation of Stationary Pumps for Fire Protection*
- NFPA 30 – *Flammable and Combustible Liquids Code*
- NFPA 10 – *Portable Fire Extinguishers*

6.8.3 Fire Protection Systems Description

The fire protection systems will be designed according to the specific occupancy and hazards of each section of the facility, as follows:

Offices if modified

The occupancy of the office area is classified as a Light Hazard Occupancy in accordance with NFPA 13. These areas will be protected by a wet-pipe sprinkler system designed to provide a density of 4.1 L/min/m^2 over the most remote 84 m^2 (0.10 gpm/ft^2 over the most remote 900 ft^2), using quick response sprinklers with an ordinary temperature rating. The maximum coverage area per sprinkler for this area will be 21 m2 (225 ft^2). The calculations for this area will include a hose allowance of 380 L/min (100 gpm). Each floor will have a separate control valve and flow detector.

Classified rooms and Laboratories

These areas, as well as certain production areas and mechanical rooms are classified as Ordinary Hazard, Group 1 Occupancy. These areas will be protected by a wet-pipe sprinkler system designed to provide a density of 6.1 L/min/m^2 over the most remote 139 m^2 (0.15 gpm/ft^2 over the most remote 1,500 ft^2), using standard response sprinklers with an ordinary temperature rating. The maximum coverage area per sprinkler for this area will be 12.1 m^2 (130 ft^2). The calculations for this area will include a hose allowance of 950 L/min (250 gpm). Each floor will have a separate control valve and flow detector.

For refrigerated rooms with possible temperatures below 4°C, to reduce the potential risk of freezing, pendant type dry sprinkler heads will be used.

In production areas, for rooms classified as clean rooms, the sprinkler heads will be of the gasketed-cover clean room type.

Warehouse

The warehouse will be used for storage of a variety of commodities complete with racking designed for two pallets high. These will include plastic products in cartons, which are deemed to be the most severe commodity (There will be no storage of exposed Group A plastic products). Sprinkler heads will be installed in the racking to provide adequate coverage only if necessary. No ESFR heads will be used and therefore no fire pump is expected to be required.

Portable Fire Extinguishers
Multipurpose dry chemical extinguishers (Class ABC) will be provided throughout the premises, placed strategically in accordance with the requirements of NFPA 10.

7 ELECTRICAL

7.1 SCOPE OF WORK

This section describes the electrical hardware required for the new Clinical trial material facility at NRC's facility.

The following electrical items and systems are included in the budgetary evaluation:

- Electrical distribution
  - Normal distribution
  - New electrical diesel generator and emergency distribution
  - Uninterruptible power supply and distribution
- Lighting
- Grounding
- Security and access control
- Airlock interlock system
- Fire alarm system
- Telecommunication
- Demolition

7.2 DESIGN CRITERIA

- New load is based on estimated process equipment, mechanical equipment, and service loads.
- Diversity factors are used for demand estimation.
- Emergency generator and uninterruptible power supply will feed the critical process and mechanical equipment.
  - The UPS will be used for the equipment that could not support the loss of power during the generator start-up and transfer time.
- All new equipment's are sized for at least 25% spare capacity.

7.3 ASSUMPTIONS

This design study is based on the following assumptions:

- Power capacity is available for the new load demand.
- Spare addresses and power capacity are available from the existing fire alarm panel.
- All process equipment complies with electrical Canadian standards.

7.4 APPLICABLE CODES AND STANDARDS

Applicable codes and standards listed below will be applied in the electrical design for this project.

- Code de construction du Québec, Chapitre V – Électricité 2018
- National Building Code of Canada, 2010

7.5 EXISTING INSTALLATION

7.5.1 Electrical Entrance

The main electrical entrance consists of an annex room post from Hydro-Quebec. Two 600/347V Hydro-Quebec transformers in the annex room feed a 6000 A switchgear trough a busduct, with a main breaker currently adjusted to around 4000 A.

The estimated peak load after the GMP Biomanufacturing expansion will be 4000A.

7.5.2 Emergency networks

There are two existing diesel generators, one 600 kW and one 500 kW.

The 600-kW actual peak load is estimated to 550 kW and there is no capacity on this generator.

The 500-kW actual peak load is estimated to 300 kW, with around 100 kW available.

There is no existing centralized uninterruptible power supply network.

7.6 NEW AND EXISTING LOAD

The following table shows the new estimated peak load on normal, generator and UPS networks:

	Peak load (kW)	Peak load (kVA)
Estimated loads after the vaccine plant run	3906	4145
Estimated loads removed from demolition	-125	-132
Added load on existing chiller	110	117
Added load on normal network	483	513
Added load on generator network	181	192
Added load on UPS network	25	27
Total load:	4580	4862

This table show the highest peak on the entrance during summer. The generator load includes the UPS load and the normal load includes the generator load.

The new peak load in amps is estimated at 4684 Amperes and the amperes demand shall not exceed 5000A for a 4MVA HQ. Therefore, the utilization factor of the entrance will be **93.6%** of the electrical entrance. This is very high, all heating equipment who can be using natural gas shall be switch on gas to lower the load on the electrical entrance.

7.7 ELECTRICAL DISTRIBUTION

7.7.1 Normal distribution

A 1600A existing feeder from the main switchgear supply a 1600 A switchboard for Laboratories 3 and 4 area. All new load for this project will be added to this power panel. This switchboard will supply the following items:

- One 200 A 600 V panel for electrical reheat.
- One 600 A 600 V panel for mechanical loads.
- One 200 A 600 V distribution panel for process loads.

    - 120/208 V transformer.
        - Main process 120/208 V panel feeding subpanels.
- 120/208 V service transformer.
    - Main service 120/208 V panel feeding subpanels.
- 277/480 V transformer for lighting.
    - 277/480 V lighting panel.
- 120/208V transformer.
    - 120/208 V panel for the packaging line.
- One 200 A 600 V warehouse service panel.
- One 100 A breaker connected to transfer switch for the life safety.
- One 400 A breaker connected the transfer switch for process and mechanical load connected to the emergency network.

7.7.2 Generator and emergency distribution

The existing generators do not have enough remaining capacity for the added loads.

A new 300 kW 375 kVA emergency standby diesel generator certified C282 will be installed outside the building in a thigh fit enclosure with integrated base fuel tank. The generator will supply a main 600 A 600 V generator panel. From this panel, a 100 A breaker is connected to an automatic transfer switch for life safety distribution (lighting). A 400 A breaker feeds a second automatic transfer switch for mechanical and process loads.

The automatic transfer switch for life safety distribution feeds the following.

- Transformer for emergency lighting and services.
    - Main panel for emergency lighting and services

The automatic transfer switch for mechanical and process charges is connected to a 400A panel that supplies the following:

- A 200 A 600 V panel for mechanical loads.
- 120/208 V process transformer.
    - Main process 120/208 V panel feeding subpanels.
- The UPS Transformer
    - Uninterruptible power supply and distribution.

7.7.3 Uninterruptible power supply and distribution

A new 60 kVA uninterruptible power supply will be fed by the main emergency distribution panel. 600 V UPS use internals transformers and have longer lead times.

The UPS will supply the following.

- A 120/208 V process transformer.
    - Main process 120/2008V panel feeding subpanels.

Spare capacity for IT loads has been considered on the total UPS capacity.

7.8 LIGHTING

LED source lighting will be used in all the area of this project. The long life of LED will reduce maintenance in the process rooms.

In all the clean production area recessed sealed cleanroom lighting fixtures will be integrated in the ceiling by the cleanroom manufacturer.

In the laboratories, recessed sealed cleanroom rated lighting fixtures with stainless steel overlapping door will be used.

All lighting will be at 120 V or 277 V single phase, with local switches used for each room. For process room, the switches will be in the corridors and control both the room and all associated airlocks.

Emergency lighting will be feed by a dedicated automatic transfer switch from the new generator.

The average illumination level by location are:

Location	Average Illumination
Office area	400 - 500 Lux
Mechanical space	200 - 300 Lux
Clean corridors, MAL, PAL	500 - 600 Lux
Clean manufacturing rooms	650 - 750 Lux
Warehouse	300 - 400 Lux
Emergency lighting	To illuminate egress pathways

7.9 SERVICES

- All electrical outlets in cleanrooms will be recessed and sealed.
- 120 V 5-15R electrical outlets will be duplex "Industrial Heavy Duty" and white in color.
- All electrical outlets located within 1.5 meters from a water source will be GFI protected.
- Emergency electrical outlets will be "Industrial Heavy Duty" and red in color.
- Electrical outlets fed by UPS will be "Industrial Heavy Duty" and blue or orange in color.

7.10 GROUNDING

- A ground loop of bare cooper wire with grounding rods will be installed around the part of the building and connected on the existing building ground loop. The ground loop will be connected to the steel columns of the extension.
- A ground bar will be installed in the new mechanical room and connected to the main building ground bar.
- Equipment grounding will be done through electrical bonding. EMT conduits shall have a green jacket ground conductor in every run to ensure positive electrical bonding.

7.11 SECURITY AND CONTROL ACCESS

- All new airlocks will have interlocked doors.
- All additions and modifications to the existing access control devices will be compatible with the existing access control system.

- Installation will include all existing controller modifications and all material and installation of push buttons, pull stations, door magnets, etc.
- Access to the production area, the warehouse and to the laboratory will be controlled by card readers.
- All new added controllers will include configuration.
- All new exterior doors will be monitored by the intrusion alarm system.
- New security cameras will be installed outdoor to monitor the perimeter of the extension.

7.12 FIRE ALARM SYSTEM

- Fire alarm devices (bell, strobes, manual red stations, etc.) will be installed as required by the building code.
- Fire alarm device in cleanrooms will be covered by polycarbonate protectors.
- All components will be installed on existing fire alarm panel using existing loops.
- Auxiliary power panels will be installed as needed for the signalisation.

7.13 TELECOMUNICATION

- Data outlets will be installed for the connections of computers and equipment.
- Data outlets in cleanrooms will be recessed and sealed.
- Conduct and Cat 6E Cables will be installed for data/telephone network installation.
- Recessed IP clean phones and wall clocks will be installed in the cleanrooms.

8 VALIDATION

8.1 ASSUMPTIONS

Health Human Therapeutics (HHT) Biomanufacturing Facility, located on Royalmount Avenue in Montreal, is committed to bring safe, effective, and high-quality products to a market that meet regulatory compliance and provide full user satisfaction. Validation, in accordance with Good Manufacturing Practice (GMP) principles, forms a key strategy in this commitment.

Current regulatory requirements will direct the philosophy, which will be used in the validation of CTMF facility and its systems and equipment. Validation requirements are established based upon criticality, where critical is defined as having the potential to impact product conformance to quality specifications and patient safety.

Refer to section 3 of the present report for applicable regulation, standard and best practices

Validation is the process of commissioning and qualifying (C&Q) by establishing documented evidence that provides a high degree of assurance that a specific piece of equipment, utility or system will consistently operate as designed, meeting a pre-determined set of specifications.

The inputs to the integrated C&Q process include product and process Critical Quality Attributes (CQAs) and Critical Process Parameters (CPP) that are established through research and development or technology transfer. CQAs and CPPs are to be used in qualification protocols to establish parameter to be verified and acceptance criteria.

8.2 SCOPE OF WORK

The "V-Model" will be used as the basis for the validation approach to be taken with the equipment and system. The V-Model is a simple and well-known tool that provides a life cycle approach demonstrating a progression from the design phase, to construction and implementation phase, to the qualification phase. Refer to picture below for a V-model representation.

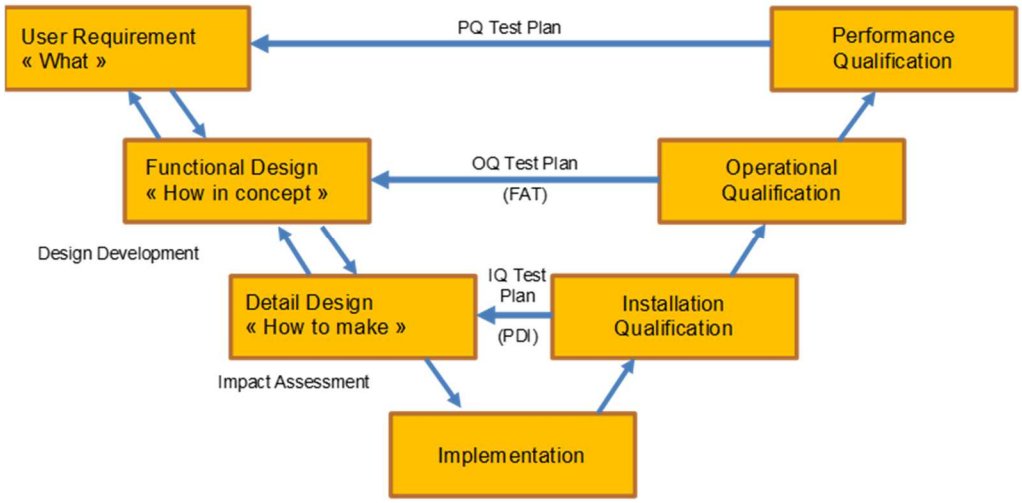


Figure 4: Validation V-model

All qualification studies are conducted according to pre-approved written protocols. Each protocol addresses the qualification of a specific system, piece of equipment, utility, or combination thereof and contains or references all the information necessary to complete the qualification study.

The validation effort consists of fundamentally the following elements:

- installation qualifications (IQ),
- operational qualifications (OQ),
- performance qualification (PQ) when required,
- process validation (PV) when required,
- analytical method validation when required

If possible, upstream phases of the system life cycles may be incorporated into the validation activities, including commissioning activities.

Equipment and system related to manufacture a product for human usage must be qualified. The System Classification is a tool used in the Validation Master Plan approach to establish whether a system or equipment has an impact on product quality and then should be subject to qualification. The equipment and system are categorized as direct impact or not direct impact, depending on its potential impact to product quality. Direct impact systems are commissioned and qualified while no impact system/equipment are commissioned only. For each direct impact equipment or system, the level of documentation and qualification is determined based on a risk assessment that takes into consideration the impact of an undetected change in the performance of the equipment or system may have on the products identity, safety, purity, strength and quality.

Once validated, all critical systems and processes are maintained in a validated state via systematic calibration, preventive maintenance, change control, monitoring and re-validation programs as developed by HHT SOPs.

9 AUTOMATION

9.1 GENERAL DESCRIPTION

The automation strategy will be based on the most cost-effective solutions to meet the projects requirements while making sure the solutions can be implemented in a fast-track schedule. The selection criteria for the level of automation are based on the client requirements, regulatory requirements, quality, costs, schedule, and safety requirements of the project. Also, the automation systems will be designed to comply with the current 21CFR part 11, GAMP 5, PIC/S data integrity guidance, ISA Standards, and best industry practices.

A structured approach will be taken for the design and risk assessment of the automated systems specifications (Specifications, F&DS, DDS, and traceability matrix). This documentation structure was proven much easier to maintain for the end user through the entire lifecycle of the automated systems compared to traditional documentation packages.

The automation strategy will be based on two (2) types of systems being used for the project:

- Specialized equipment will be specified and purchased with the automation designed and supplied by the equipment vendor. This type of systems will be provided with their own standard automation package which will contain a local PLC and operator interfaces. Basic automation requirements will be prepared to make sure those systems are compatible with the minimal integration required at go live (including connection to the centralized historian, production reports and security management on the AD) and that additional integration can be done subsequently. Specialized equipment is (without limitations): media prep mixers*, bioreactors, filtration systems (UF/DF), chromatography, bulk filling and process utilities systems.
- Other process systems will be manually operated.

Interactions between the systems (such as product transfer) will not be automated and will be managed manually by the operators.

***Note**: *The automation strategy must be confirmed during detailed design. However, because of the fast-track schedule, some equipment has already been purchased by the NRC. In this case, the automated systems specifications will be provided by the supplier (standard documentation).*

9.2 APPLICABLE REGULATIONS AND STANDARDS

Applicable codes and standards listed below will be applied in the automation design for this project:

- Health Canada – Good Manufacturing Practices guide for drug products, 2018 (GUI-0001).
- PIC/S Good Practices for Data Management and Integrity in Regulated GMP/GDP environments, 2016 (Referred by Health Canada GUI-0001).
- ISPE Guide: GAMP 5 A risk-based approach to Compliant GxP Computerized Systems, 2008.
- 21 CFR Part 11: "Electronic Records, Electronic Signatures".
- ISPE GAMP series of Good Practice Guides.
- ANSI/ISA-5.1-2009: "Instrument Symbols and Identification Standard".
- ANSI/ISA-88-2010: "Batch Control".

The following safety codes apply:

- CSA-Z432-04 (R2014): "Safeguarding of Machinery".
- ISO 12100, ISO 13849 and ISO 13852.

- IEC61511:2016: "Functional Safety – Safety Instrumented Systems for the Process Industry Sector".
- Commission de la Santé et Sécurité au Travail Québec (CSST).

9.3 MANUFACTURING IT

Manufacturing IT system must rely on a good IT infrastructure foundation. We must use good quality products that will ensure reliability, scalability, and stability. The infrastructure must be designed to offer performance and high availability where possible. Equipment from established vendors will be used.

IT equipment access must be limited. IT room must have a solid door with a proper locking mechanism, like a non-duplicable key hardware. All cabinets must have a proper locking mechanism.

The basic manufacturing IT components are grouped into four (4) major categories. Network infrastructure, Compute (servers), Storage and Power Distribution.

Network infrastructure components are configured to give good performance and stability:

- A centralized core switches are installed in the IT room.
- Industrial grade equipment is used.
- Ethernet based.
- All components will be redundant where possible.
- Signal distribution will be done through redundant links.
- Distribution switches are to be installed in wall cabinets (lockable).
- A firewall will be installed to ensure better security of infrastructure.

The servers will be furnished by one of the major venders such as DELL or HP. They will have adequate resources for performance and be scalable upon need:

- Windows-based servers.
- All specialized servers to be hosted on infrastructure (Data historian, EMS and other services).
- Virtualized by recognized vender.
- Part of a domain for security consideration.

The storage component will be sized for the capacity needed for plant requirement:

- The technology used in the hardware must meet stated needs.
- Sufficient size must be allocated.
- Must provide scalability and performance.
- Components must have redundancy.

Power distribution in each IT cabinet must meet requirements set forth by the plant.

- A centralized UPS will feed each cabinet.
- Proper power distribution units chosen to meet requirements.

The MIT infrastructure is a GMP system and will be validated.

9.4 PROCESS DATA HISTORIAN

The Data Historian system will serve as a central data repository for real-time process data, environmental conditions, alarms, and production events. The centralized Data Historian is used for high performance storage, data consolidation, efficient reporting and reliable security of critical plant and product data. The data is archived for a period of at least 10 years.

The Data Historian provides the following functions:

- Data acquisition
- Data recording
- Data reporting

The system will provide the capability of recording 2500 tags (expandable).

The production data will be accessible via the GMP Production Network by using software interfaces (such as OPC, ODBC and SQL). Historical data can be accessed from other systems (MES, BI and general applications such as Excel), for example to generate batch records or historical trending reports.

The Data Historian system's applications will reside on their own virtualized servers which will be hosted on the MIT infrastructure. The client station applications facilitate access to historical data for monitoring, reporting and analysis purposes.

The Data Historian is a GMP system. It will be validated and will comply with applicable codes and standards for data integrity, audit trail and electronic signatures.

9.5 QUALITY MANAGEMENT SOFTWARE

Quality Management Software (QMS) is used to manage the documentation required by Quality Assurance to meet regulatory expectations.

Solutions range in functionality; however, typical solutions automate the process of tracking some or all the following documents:

- Standard Operating Procedures (SOP)
- Personnel training
- Corrective And Preventive Actions (CAPA)
- Non-Conformances
- Complaints
- Audit Management

The documents are created, approved, and stored electronically. The QMS will also reinforce processes with approval workflows and calendar reminders.

The QMS system includes the software and supporting hardware and IT infrastructure. The system architecture will depend on vendor selection as both Server/Client and Cloud-based applications are available on the market. The QMS is related to product quality and must be validated.

9.6 MANUFACTURING EXECUTION SYSTEM

A Manufacturing Execution System (MES) oversees the manufacturing activities. It helps create flawless manufacturing processes, provide real-time feedback of requirement change and provide information at a single source.

The MES is presently excluded from the scope of this project.

9.7 ENVIRONMENTAL MONITORING SYSTEM

The Environmental Monitoring System (EMS) monitors and collects the critical environmental conditions. It allows real time monitoring of critical conditions such as:

- Differential room pressure
- Room humidity
- Room temperature
- Non-viable particles
- Critical equipment monitoring such as the temperature in incubators, cold rooms and freezers.

The core EMS functionalities that will be required for the selected solution are:

- Real-time views and Dashboards
- Data acquisition and archiving
- Alarm management
- Traceability and reporting
- Calibration management
- Compliance

The EMS applications will reside on their own virtualized servers which will be hosted on the MIT infrastructure. Critical environmental conditions will be displayed on HMI screens strategically located inside the CTMF manufacturing area.

The EMS is a GMP system. It will be validated and will comply with applicable codes and standards for data integrity, audit trail and electronic signatures.

The list of proposed monitored points list in the new CTMF Manufacturing at NRC's facility is presented in Appendix E.

9.8 LABORATORY INFORMATION MANAGEMENT SYSTEM

A Laboratory Information Management System (LIMS) is a software-based laboratory and information management system that allows you to effectively manage samples and associated data.

The LIMS is presently excluded from the scope of this project.

10 SCHEDULE

The schedule presented in Appendix I of the present study is based on timelines derived from previous projects and experiences. The schedule considers the following main activities for the project:

- Contract awarding: the month of December 2020 is dedicated to preparing and awarding contracts for construction management, construction, architecture, engineering, and validation.
- Detailed engineering: This phase of the project will include all the architectural and engineering work to be able to build the facility
- Construction
- Validation: validation is the last step to prepare for an authorization to produce in the facility. Even if it is the last step, activities still need to start way ahead of the facility being built.

Dates at which PO should be awarded to different services or equipment suppliers have been indicated for information only and serve to provide a better comprehension of the related tasks and timeline to be respected.

Refer to Appendix I for preliminary schedule.

11 BUDGET

11.1 BUDGET PREPARATION

The budget was prepared using budget quotations from equipment suppliers when possible and an internal data bank of construction costs including cost estimating guides. Whenever available, alternatives to recognized suppliers were used to reduce costs.

Equipment installation includes the field work required to install and connect the equipment to the required utilities.

The conceptual budget was prepared at a ± 15% precision level.

11.2 PROJECT BUDGET

Refer to Appendix H for project budget details.

The cost budget for the new CTMF facility is approximatively 28.9 M$ CAD (± 15% contingency included) including process equipment.

The cost presented do not include OPEX costs such as testing material required for validation, cleaning validation costs, process validation costs, QC laboratory consumables, various offices consumables, environmental monitoring costs, all costs related to submittal of files to Health Canada, production consumables, maintenance costs, routine testing costs (for example for purified water, water for injection and pure steam) as well as any NRC internal costs linked to the execution of the project.

11.3 EXCLUSION

1. This study does not take into account the presence of potential hazardous materials in wall and in furniture such as asbestos.
2. This study does not take into account the feasibility around installing the goods lift where it is proposed. Further structural study should be performed.

12 APPENDICES

A. PLANT LAYOUT

- NRC-14_LAY-110 - Ground Level - Proposed Layout
- NRC-14_LAY-120 - Second Level - Proposed Layout
- NRC-14_A-110 AILE F H3 - Fermentation lab to H3 – Proposed layout

B. FLOW DRAWINGS

- NRC-14_FLU-110 - Ground Level – Material Flow
- NRC-14_FLU-111 - Ground Level – Personnel Flow
- NRC-14_FLU-120 - Second Level – Material Flow
- NRC-14_FLU-121 - Second Level – Personnel Flow

C. GRADE CLASSIFICATION AND AIR FLOWS DRAWINGS

- NRC-14_FLU-112 - Ground Level – Zoning and air flows
- NRC-14_FLU-122 - Second Level – Zoning and air flows

D. PROCESS

- NRC-14-LIST-01-00 (Room and Equipment List)
- NRC-14-LIST-03-00 (Gowning)
- NRC-14-NDC-01-00 (Mass balance Viral vector)
- NRC-14-NDC-03-00 (Mass balance mAb)

E. MECHANICAL

F. ELECTRICAL

No Appendix

G. BUDGET

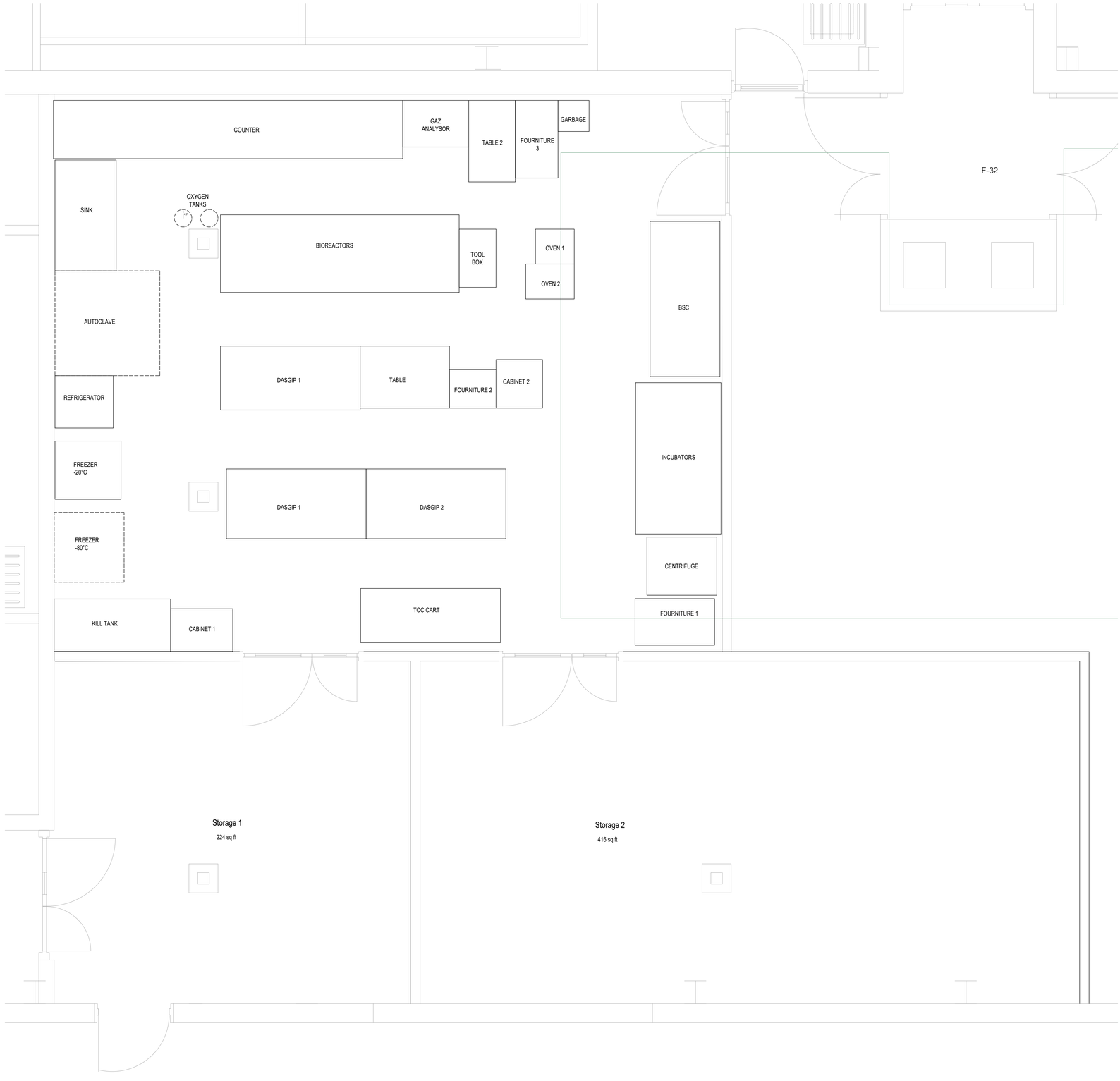
H. SCHEDULE

I. CALCULATIONS

- NRC-14-NDC-02-00 (Warehouse capacity)
- NRC-14-LIST-02-00 (Human resources)
- NRC-14-NDC-04-00 (Temperature requirements)
- NRC-14-NDC-05-00 (WFI Simulation)
- NRC-14-NDC-06-00 (Biological effluents)
- NRC-14-NDC-07-00 (Solid waste)
- NRC-14-NDC-08-00 (PW Simulation)

J. FEASIBILITY STUDY – MOVING MICROBIAL SUITE (Document provided by NRC)

APPENDIX A: PLANT LAYOUT

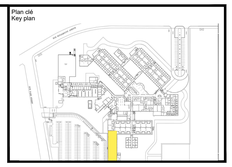


Equipment provided on October 19th, 2020

Equipment provided on November 11th, 2020

MEZZANINE

Plan clé
Key plan



Notes:

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00	2020-11-27	N.C.	ISSUED FOR FEASIBILITY STUDY	J.M.C.

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MATERIAL FACILITY

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Dessin
Drawing
NRC-14
MOVING OF FERMENTATION
LAB

Date	2020-11-04	Échelle Scale	1:20	Format Size	A0
Projet Project	NRC-14	Dessin Drawing	LAY-110-F	Rév. Rev.	00

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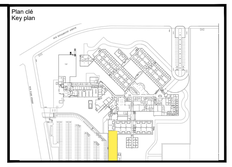
Plan clé
Key plan



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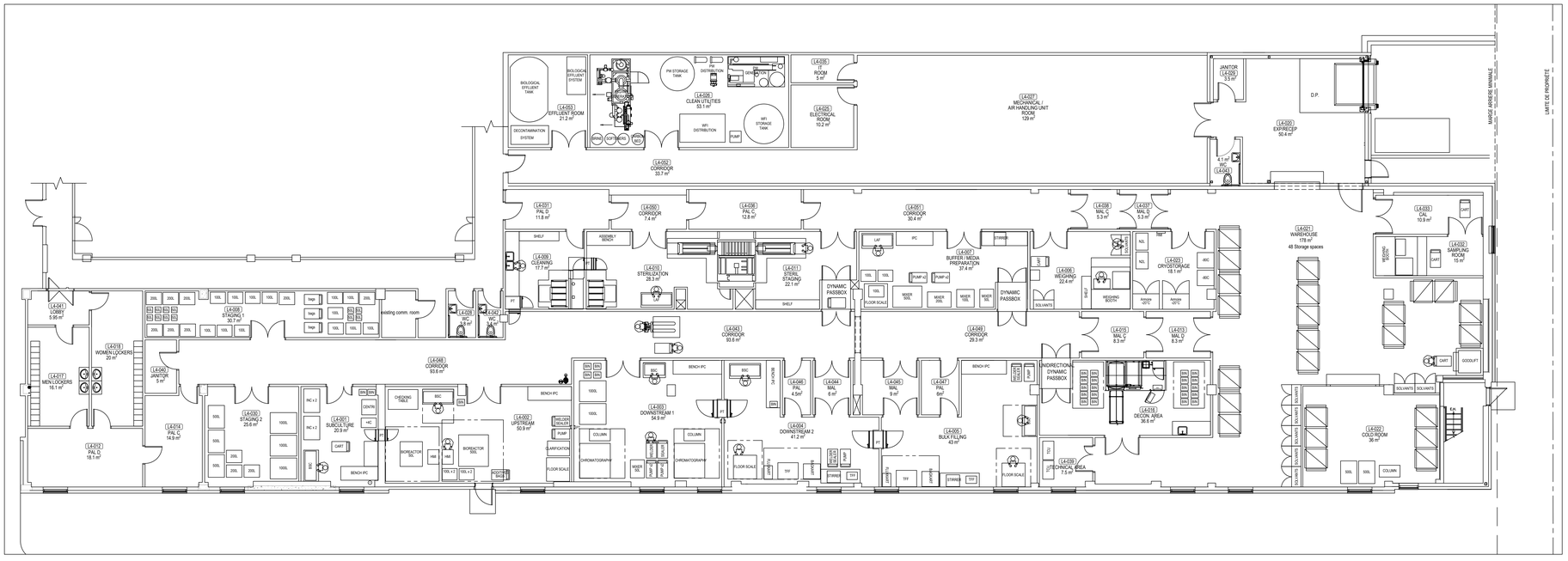

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Dessin
Drawing

CTMF-L4
GROUND FLOOR
LAYOUT

Date	2020-11-04	Échelle Scale	1:100	Format Size	A0

Projet Project	NRC-14	Dessin Drawing	LAY-110	Rév. Rev.	00

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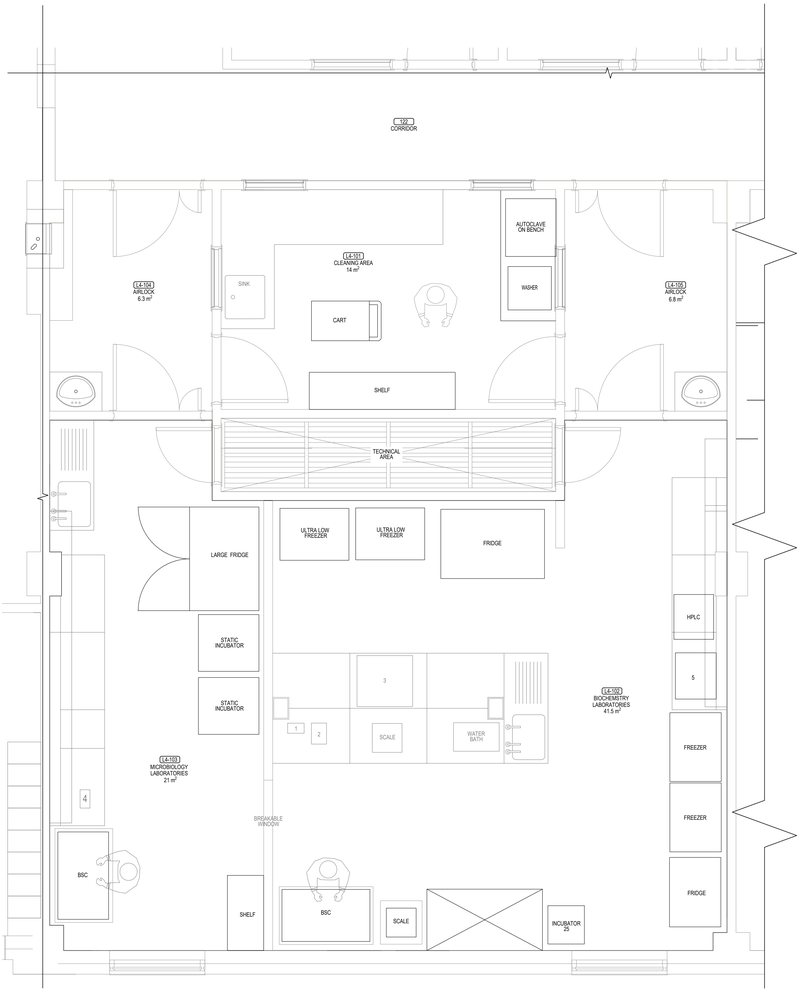
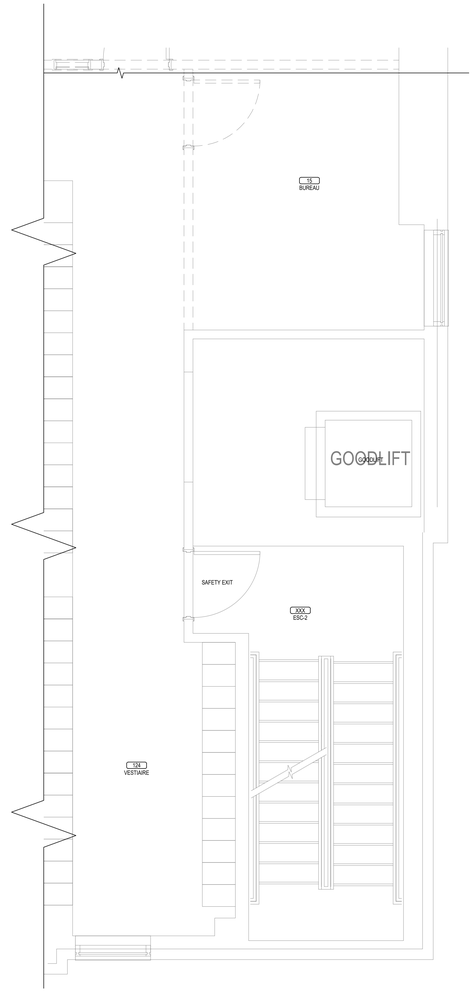
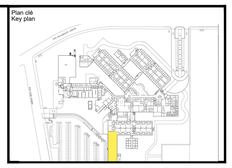


QC-LAB
ÉCHELLE 1:30



GOODLIFT
ÉCHELLE 1:30

Plan clé
Key plan



Notes:

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N°	Date	Par Drawn by	Révision Revision	Vér. par CHK'd by

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Dessin
Drawing
CTMF-L4
SECOND FLOOR
LAYOUT

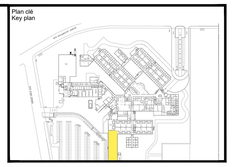
Conçu par / Designed by	Dessiné par / Drawn by	
Date 2020-11-24	Échelle Scale 1:30	Format Size A0

Projet Project	Dessin Drawing	Rév. Rev.
NRC-14	LAY-120	00

50 10 0
50 10 0 mm

APPENDIX B: FLOW DRAWINGS

Plan clé
Key plan

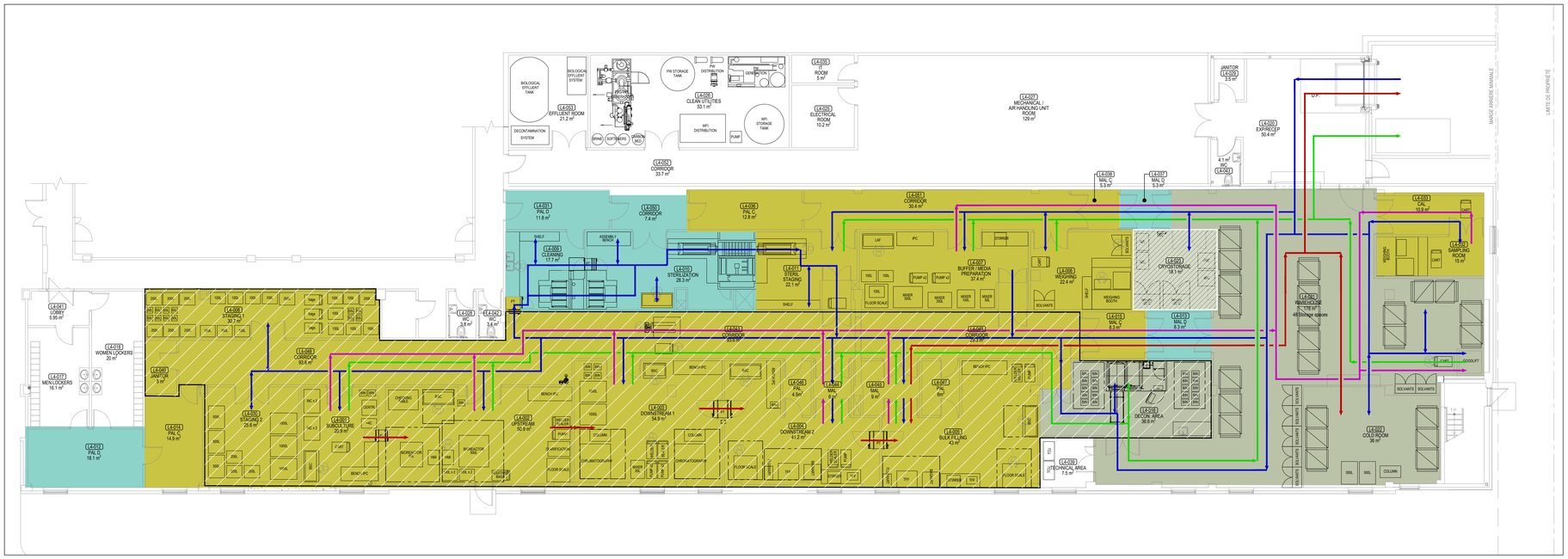


Notes:

NOTE 1 : INCLUDING SEEDS, RAW MATERIALS, DISPOSABLES, MEDIA, BUFFERS, RE-USABLE MATERIALS

LEGEND :

- RAW MATERIAL (NOTE 1)
- PRODUCT
- WASTE
- SAMPLE
- GRADE C
- GRADE D
- CNC
- CNC ANOXIA RISK
- BIOCONTAINMENT LEVEL 2



00	2020-11-27	J.P.	ISSUED FOR FEASIBILITY STUDY	J.M.C.
N°	Date	Par Drawn by	Révision Revision	Vér. par Ch'd by

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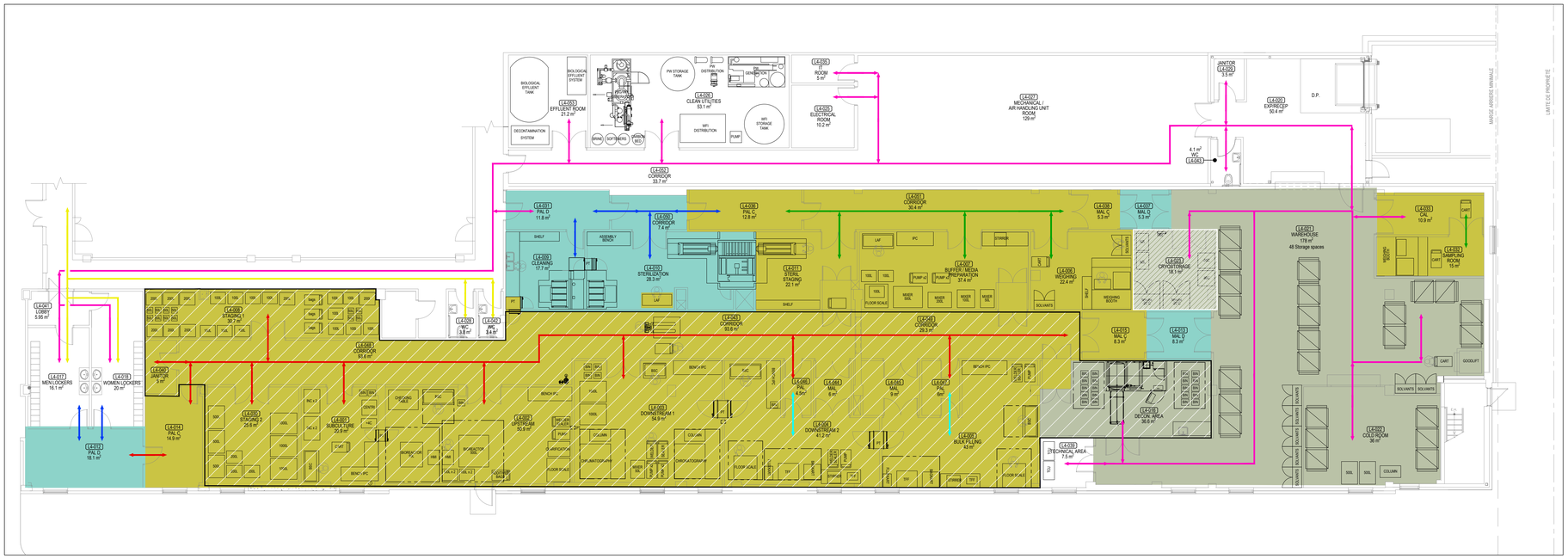
Dessin Drawing: CTMF-L4 MATERIAL FLOWS LAYOUT

Date 2020-11-04 | Échelle Scale | Format Size A0

Projet Project NRC-14 | Dessin Drawing FLU-110 | Rév. Rev. 00

50 10 0 mm

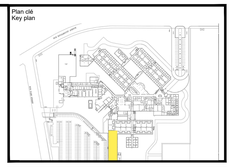


LEGEND :

- CITY CLOTHES
- GRADE D CLOTHES
- GRADE C CLOTHES
- PLANT CLOTHES
- GRADE C / CL-2 CLOTHES
- GRADE C / CL -2 VIRUS FREE CLOTHES (NOTE1)

- GRADE C
- GRADE D
- CNC
- CNC ANOXIA RISK
- BIOCONTAINMENT LEVEL 2

Plan clé
Key plan



Notes:

1- VIRUS FREE IN CASE OF mAb PRRODUCTION

00	2020-11-27	F.A.S.	ISSUED FOR FEASIBILITY STUDY	J.M.C.
N°	Date	Par Drawn by	Révision Revision	Ver. par CN/G by

Approuvé Approved	Date

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FOR CLINICAL TRIAL
MATERIAL FACILITY

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Dessin
Drawing

CTMF-L4
PERSONNEL FLOWS
LAYOUT

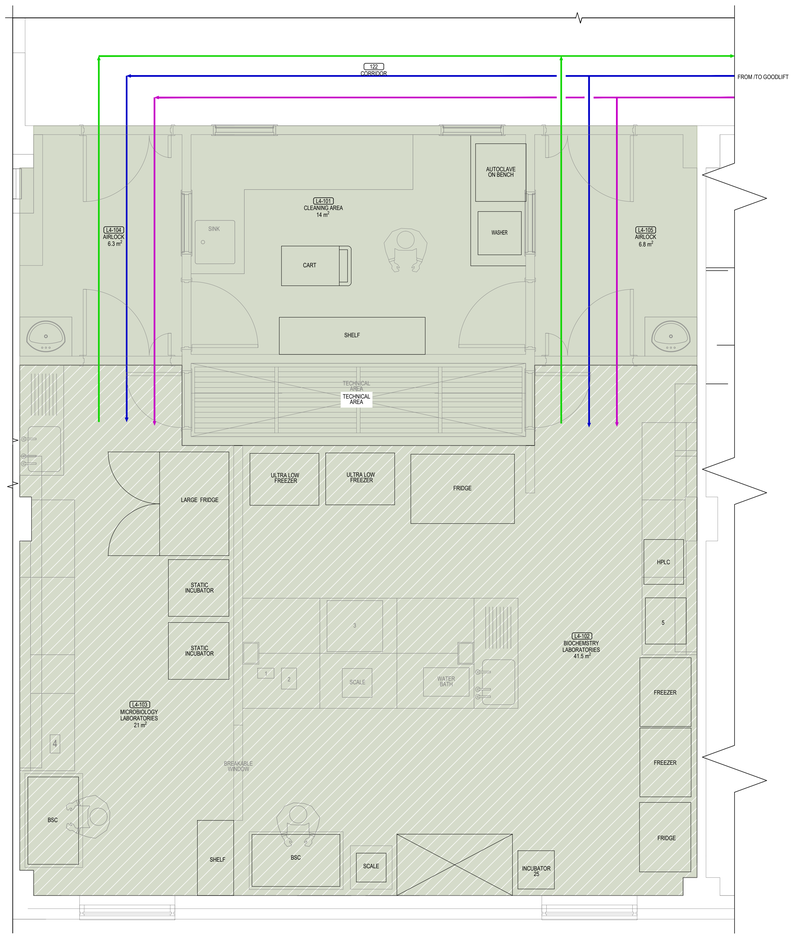
Date	2020-11-04	Échelle Scale	1:100
		Format Size	A0

Projet Project	NRC-14	Dessin Drawing	FLU-111
		Rév. Rev.	00

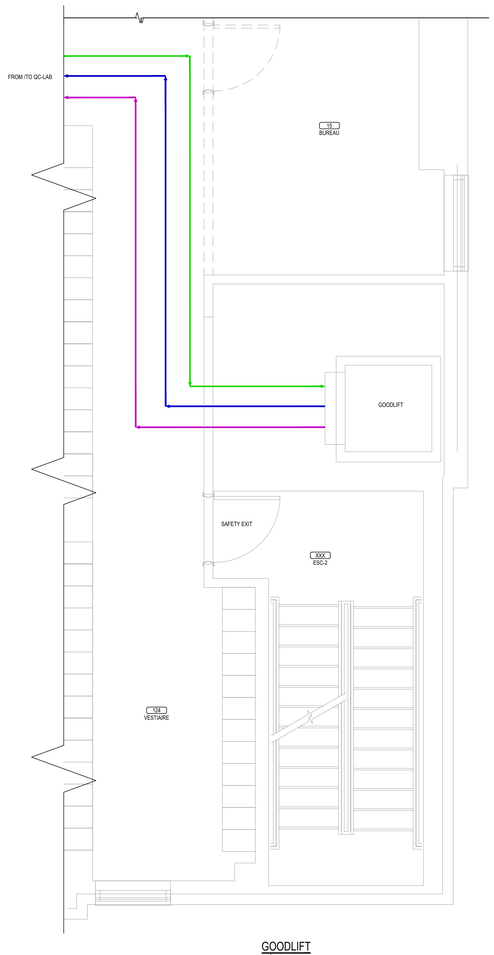
50 10 0 mm

LEGEND :

- RAW MATERIAL
- WASTE
- SAMPLE
- CNC
- BIOCONTAINMENT LEVEL 2

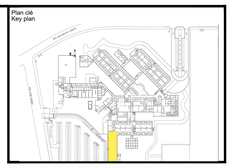


QC-LAB
ÉCHELLE 1:30



GOODLIFT
ÉCHELLE 1:30

Plan clé
Key plan



Notes:

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Dessin
Drawing
CTMF-L4
MATERIAL FLOWS
LAYOUT

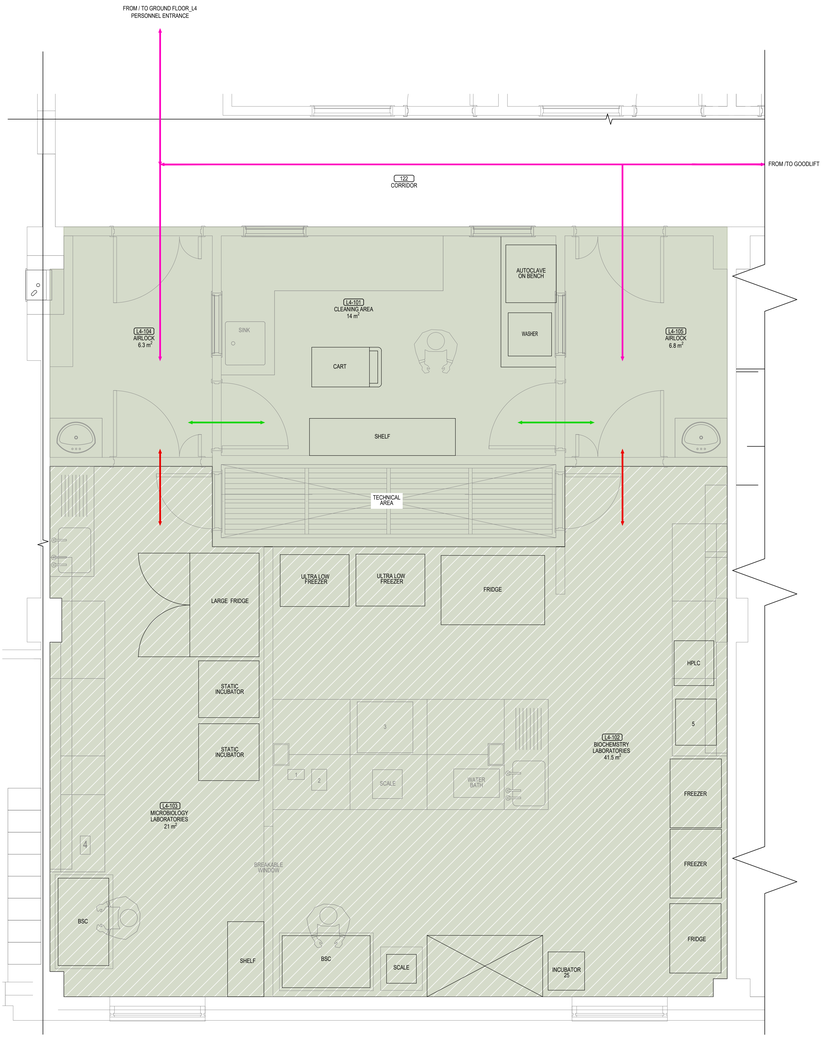
Date	2020-11-24	Échelle Scale	1:30	Format Size	A0

Projet Project	NRC-14	Dessin Drawing	FLU-120	Rév. Rev.	00

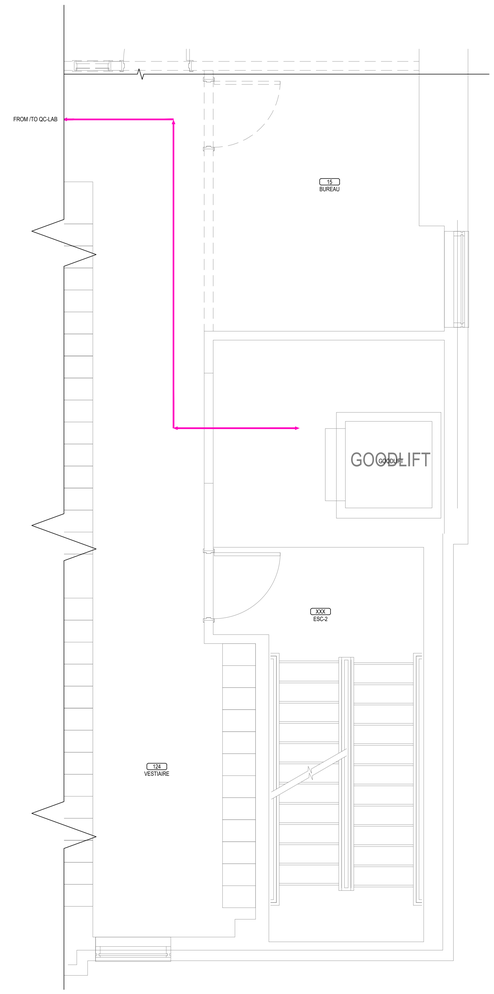
50 10 0 mm

LEGEND :

- PLANT CLOTHES
- LAB CLOTHES
- LAB / CL-2 CLOTHES
- CNC
- BIOCONTAINMENT LEVEL 2

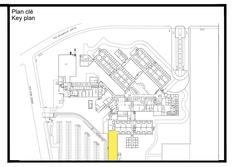


QC-LAB
ÉCHELLE 1:30



GOODLIFT
ÉCHELLE 1:30

Plan clé
Key plan



Notes:

N°	Date	Par Drawn by	Révision Revision	Vér. par. Ch'd by
00	2020-11-27	J.P.	ISSUED FOR FEASIBILITY STUDY	J.M.C.

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Dessin
Drawing

CTMF-L4
PERSONAL FLOWS
LAYOUT

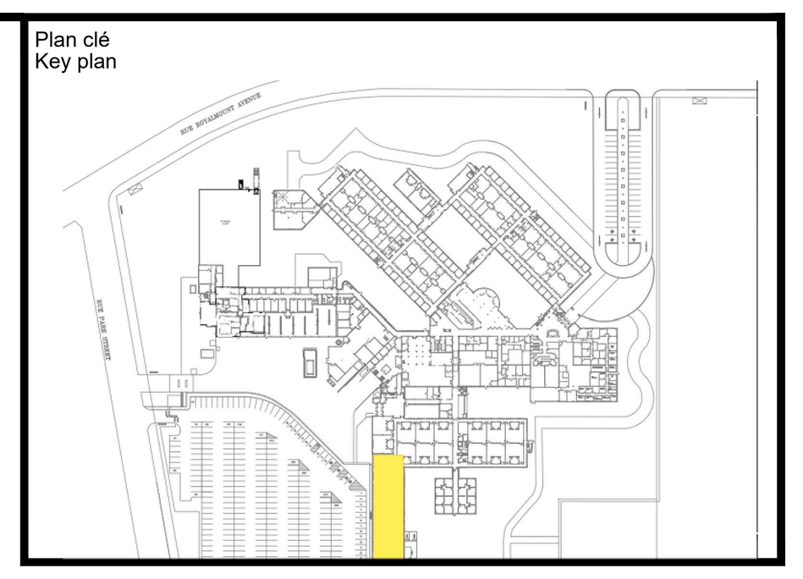
Date	Échelle Scale	Format Size
2020-11-24	1:30	A0

Projet Project	Dessin Drawing	Rév. Rev.
NRC-14	FLU-121	00

50 10 0 mm

APPENDIX C: GRADE CLASSIFICATION AND PRESSURIZATION DRAWINGS

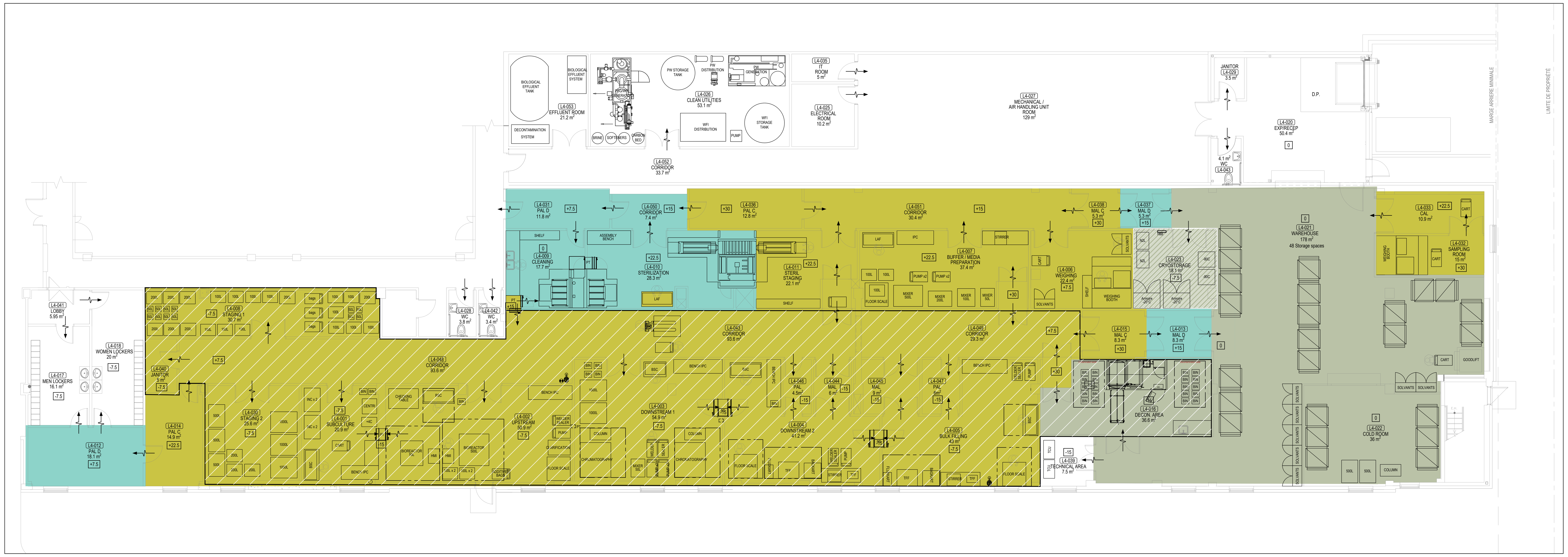
Plan clé
Key plan



Notes:

LEGEND :

- GRADE C
- GRADE D
- CNC
- CNC ANOXIA RISK
- BIOCONTAINMENT LEVEL 2
- AIR FLOW



N°	Date	Par / Drawn by	Révision / Revision	Ver. par / Chk'd by
00	2020-11-27	F.A.S.	ISSUED FOR FEASIBILITY STUDY	J.M.C.

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Projet / Project: FEASABILITY STUDY FOR CLINICAL TRIAL MATERIAL FACILITY

Dessin / Drawing: CTMF-L4 ZONING AND AIR FLOW LAYOUT

Date: 2020-11-04 | Échelle / Scale: 1:100 | Format / Size: A0

Projet / Project: NRC-14 | Dessin / Drawing: FLU-112 | Rév. / Rev.: 00

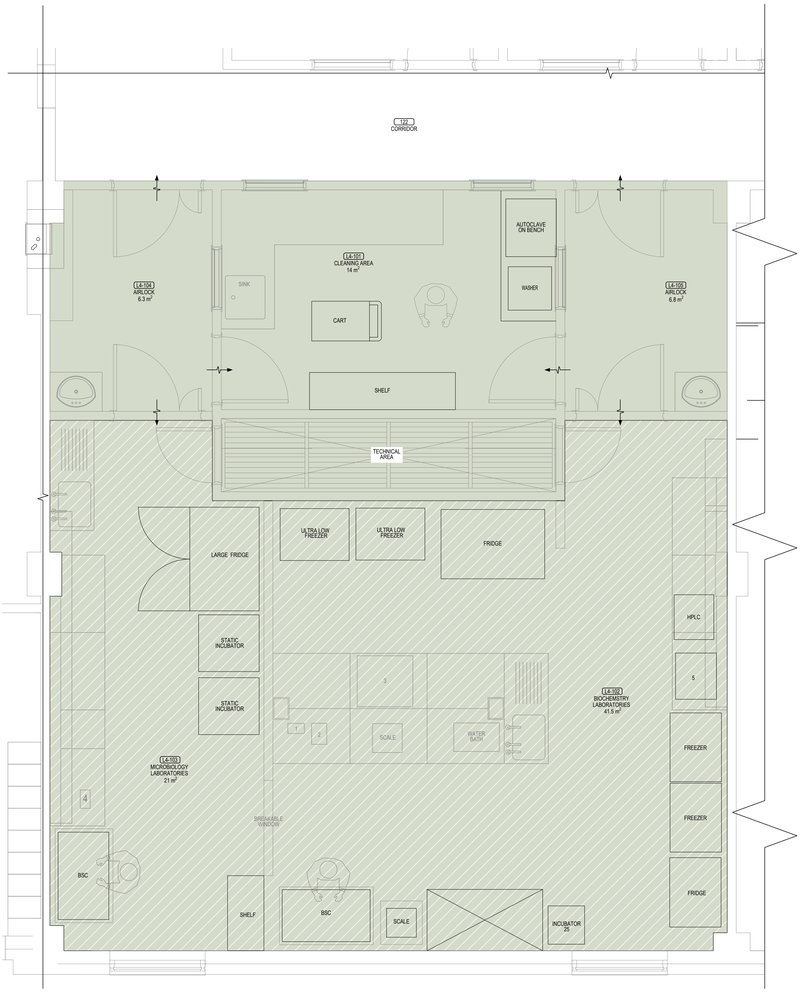
LEGEND :

CNC

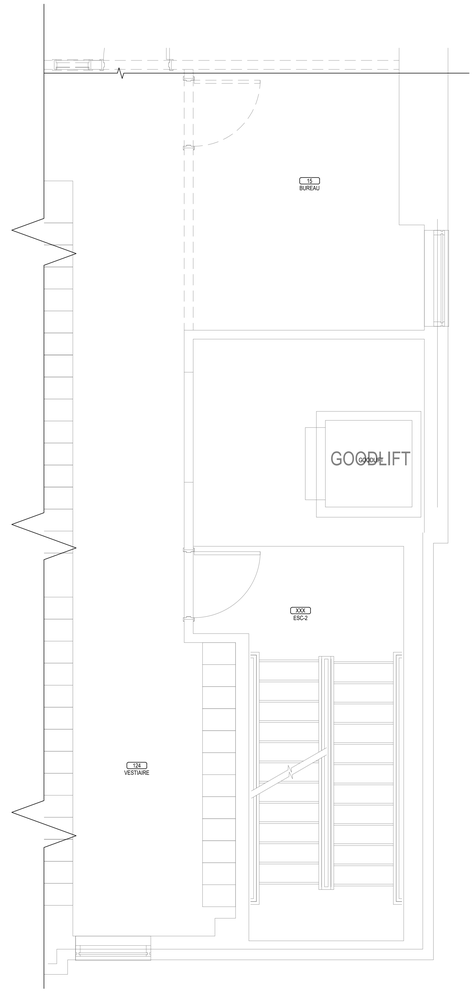
BIOCONTAINMENT LEVEL 2

AIR FLOW

XPa PRESSURE



QC-LAB
ÉCHELLE 1:30



GOODLIFT
ÉCHELLE 1:30

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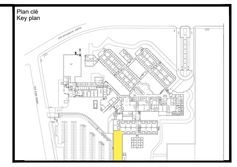
Plan clé
Key plan



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FOR CLINICAL TRIAL
MATERIAL FACILITY

Dessin Drawing
CTMF-L4
PRESSION FLOWS AND ZONING
LAYOUT

Date	Échelle Scale	Format Size
2020-11-24	1:30	A0

Projet Project	Dessin Drawing	Rév. Rev.
NRC-14	FLU-122	00

50 10 0 mm

APPENDIX D: PROCESS

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

2020-11-27

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-001	GF	Production	Subculture	ROOM	C	CL-2	Lab	30	20,9	N/A	N/A	N/A
L4-001	GF	Production	Subculture	Large Stackable Incubated Orbital Shaker #1	N/A	N/A	Equipment	605 x 846 x 635 mm	N/A	298,5	To be purchased	Thermo Scientific™ MaxQ™ 8000 Incubated/Refrigerated Stackable Shakers
L4-001	GF	Production	Subculture	Large Stackable Incubated Orbital Shaker #2	N/A	N/A	Equipment	605 x 846 x 635 mm	N/A	298,5	To be purchased	Thermo Scientific™ MaxQ™ 8000 Incubated/Refrigerated Stackable Shakers
L4-001	GF	Production	Subculture	Large Stackable Incubated Orbital Shaker #3	N/A	N/A	Equipment	605 x 846 x 635 mm	N/A	298,5	To be purchased	Thermo Scientific™ MaxQ™ 8000 Incubated/Refrigerated Stackable Shakers
L4-001	GF	Production	Subculture	Biosafetycabinet	N/A	N/A	Equipment	800 x 1300 x 1568 mm	N/A	280	To be purchased	ThermoFisher 6' (1300 A2)
L4-001	GF	Production	Subculture	Media storage - fridge	N/A	N/A	Equipment	610 x 962 x 1473 mm	N/A	164	To be purchased	Thermo Scientific™ TSX2305SA
L4-001	GF	Production	Subculture	Cell counter Cedex	N/A	N/A	Equipment	405 x 535 x 465 mm	N/A	26,9	To be purchased	Cedex Hires
L4-001	GF	Production	Subculture	Microscope	N/A	N/A	Equipment	235 x 560 x 560 mm	N/A	5	To be purchased	ZEISS Axio Vert.A1
L4-001	GF	Production	Subculture	Pipetman	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-001	GF	Production	Subculture	Balance - under BSC	N/A	N/A	Equipment	N/A	N/A	10	To be purchased	Sartorius Cubis-II TBench top balance
L4-001	GF	Production	Subculture	Water Bath Flask culture	N/A	N/A	Equipment	394 x 632 x 249 mm	N/A	20	To be purchased	Fisherbrand™ Isotemp™ Shaking Water Baths
L4-001	GF	Production	Subculture	Centrifuge for Cell thaw	N/A	N/A	Equipment	1075 x 720 x 1400 mm	N/A	71	To be purchased	Heraeus™ Megafuge™ 8 Small Benchtop Centrifuge Series
L4-001	GF	Production	Subculture	Bench IPC	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-001	GF	Production	Subculture	Bench IPC	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-001	GF	Production	Subculture	Mobil Cart	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-002	GF	Production	Upstream	ROOM	C	CL-2	Lab	70	50,9	N/A	N/A	N/A
L4-002	GF	Production	Upstream	500L SU Bioreactor	N/A	N/A	Equipment	1440 x 2230 x 2380 mm	N/A	1170	Existing	Xcellerex 500 L + deux balances de plancher (pour perfusion)
L4-002	GF	Production	Upstream	500L SU Bioreactor HMI	N/A	N/A	Equipment	600 x 780 x1440 mm	N/A	146	Existing	X-Station
L4-002	GF	Production	Upstream	50L SU Bioreactor	N/A	N/A	Equipment	1110 x 710 x 735 mm	N/A	600	Existing	Xcellerex 50 L
L4-002	GF	Production	Upstream	50L SU Bioreactor HMI	N/A	N/A	Equipment	600 x 780 x 1440 mm	N/A	146	Existing	X-Station
L4-002	GF	Production	Upstream	Biosealer	N/A	N/A	Equipment	391 x 115 x 147 mm	N/A	3	To be purchased	Bioselect TC sartorius
L4-002	GF	Production	Upstream	Bioreactor room BioWelder	N/A	N/A	Equipment	555 x 261 x 69 mm	N/A	15,9	To be purchased	Sartorius
L4-002	GF	Production	Upstream	Balance for bioreactor operation	N/A	N/A	Equipment	1500 x 1250 x 45 mm	N/A	N/A	Existing	foot print only
L4-002	GF	Production	Upstream	Biosafetycabinet for sample preparation	N/A	N/A	Equipment	800 x 1300 x 1568 mm	N/A	280	To be purchased	ThermoFisher 6' (1300 A2)
L4-002	GF	Production	Upstream	Millistak+ Depth filter holder / Clarification	N/A	N/A	Equipment	1574 x 2540 x 762 mm	N/A	N/A	Existing	Millipore
L4-002	GF	Production	Upstream	Continious centrifuge (Upstream?)	N/A	N/A	Equipment	N/A	N/A	N/A	Future	Ksep - Model to be confirmed by Julien
L4-002	GF	Production	Upstream	Water Bath Flask culture	N/A	N/A	Equipment	394 x 632 x 249 mm	N/A	30	To be purchased	Fisherbrand™ Isotemp™ Shaking Water Baths

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

2020-11-27

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-002	GF	Production	Upstream	Centrifuge for Cell thaw	N/A	N/A	Equipment	1075 x 720 x 1400 mm	N/A	71	To be purchased	Heraeus™ Megafuge™ 8 Small Benchtop Centrifuge Series
L4-002	GF	Production	Upstream	Blood gas analyzer	N/A	N/A	Equipment	305 x 1362 x 39 mm	N/A	8,2	To be purchased	Stat Profile Prime ES Plus analyzer
L4-002	GF	Production	Upstream	Analyzer metabolite	N/A	N/A	Equipment	550 x 720 x 480 mm	N/A	38,6	To be purchased	Cedex Bio
L4-002	GF	Production	Upstream	Jacketed 500L tank	N/A	N/A	Equipment	1245 x 805 x 572 mm	N/A	600	To be purchased	Palletank® Jacketed
L4-002	GF	Production	Upstream	Bench IPC	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-002	GF	Production	Upstream	Cart for pump	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-002	GF	Production	Upstream	Cart for welder and sealer	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-002	GF	Production	Upstream	Mobil table for assembly checking	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	ROOM	C	NC	Lab	60	54,9	N/A	N/A	N/A
L4-003	GF	Production	Downstream 1	Biosafetycabinet	N/A	N/A	Equipment	800 x 1300 x 1568 mm	N/A	280	Existing	Thermo1300
L4-003	GF	Production	Downstream 1	AKTA Ready Chromatography System – I	N/A	N/A	Equipment	N/A	N/A	250	Existing	Akta ready gradiant
L4-003	GF	Production	Downstream 1	AKTA Ready Chromatography System – II	N/A	N/A	Equipment	N/A	N/A	250	Existing	Akta ready gradiant
L4-003	GF	Production	Downstream 1	Balance - 8 kg	N/A	N/A	Equipment	N/A	N/A	10	Existing	Sartorius Cubis-II TBench top balance
L4-003	GF	Production	Downstream 1	Masterflex I/P Digital Pump system	N/A	N/A	Equipment	320 x 85 x 116 mm	N/A	20	Existing	Masterflex I/P Digital Pump system
L4-003	GF	Production	Downstream 1	Pump Head I/P	N/A	N/A	Equipment	N/A	N/A	N/A	Existing	Pump Head I/P
L4-003	GF	Production	Downstream 1	Orion star A215 pH and Conductivity meter (pH meter 1)	N/A	N/A	Equipment	300 x 300 mm	N/A	1	Existing	Orion star A215 pH and Conductivity meter (pH meter 1)
L4-003	GF	Production	Downstream 1	Conductivity Calibration Kit	N/A	N/A	Equipment	N/A	N/A	N/A	Existing	Conductivity Calibration Kit
L4-003	GF	Production	Downstream 1	Magnetic stirrer - sampling management	N/A	N/A	Equipment	500 x 500 mm	N/A	2	Existing	TBD
L4-003	GF	Production	Downstream 1	Magnetic stirrer - intermediate product	N/A	N/A	Equipment	500 x 510 mm	N/A	2	To be purchased	20L carboy custom made
L4-003	GF	Production	Downstream 1	PMAT 3P pressure monitor with single-use pressure sensor (for clarification Upstream room also)	N/A	N/A	Equipment	57 x 200 x 115 mm	N/A	5	Existing	PMAT 3P pressure monitor with single-use pressure senso - Cole Parmer
L4-003	GF	Production	Downstream 1	Masterflex I/P Digital Pump system	N/A	N/A	Equipment	320 x 85 x 116 mm	N/A	20	Existing	Masterflex I/P Digital Pump system
L4-003	GF	Production	Downstream 1	Pump Head I/P	N/A	N/A	Equipment	N/A	N/A	N/A	Existing	Pump Head I/P
L4-003	GF	Production	Downstream 1	Masterflex L/S Pump system	N/A	N/A	Equipment	320 x 85 x 116 mm	N/A	20	To be purchased	Masterflex L/S Digital Pump system
L4-003	GF	Production	Downstream 1	Pump Head L/S	N/A	N/A	Equipment	N/A	N/A	N/A	Existing	Pump Head I/P
L4-003	GF	Production	Downstream 1	Quantum 600 Peristaltic Pump	N/A	N/A	Equipment	297 x 736 x 231 mm	N/A	N/A	Existing	Quantum 600 Peristaltic Pump
L4-003	GF	Production	Downstream 1	Pipetman G_P200G 1	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	Pipetman G_P200G 2	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	Pipetman G_P1000G 1	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	Pipetman G_P1000G 2	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	Biosealer	N/A	N/A	Equipment	391 x 115 x 147 mm	N/A	3	Existing	Bioselect TC sartorius

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

2020-11-27

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-003	GF	Production	Downstream 1	Mixer 10/50L	N/A	N/A	Equipment	750 x 650 x 975 mm	N/A	106	To be purchased	Mobius mixer Millipore + load cell + 10L adaptator
L4-005	GF	Production	Downstream 1	Floor scale	N/A	N/A	Equipment	1500 x 1250 x 45 mm	N/A	N/A	To be purchased	500kg scale
L4-003	GF	Production	Downstream 1	Bench IPC	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	Cart for 2 x pump	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	Cart for 2 x pump	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-003	GF	Production	Downstream 1	Cart for sealer	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-004	GF	Production	Downstream 2	ROOM	C	NC	Lab	30	41,2	N/A	N/A	N/A
L4-004	GF	Production	Downstream 2	Sartocheck plus - Filter integrity tester	N/A	N/A	Equipment	348 x 379 x 286 mm	N/A	16,8	To be purchased	Sartocheck 4 or 5 plus
L4-004	GF	Production	Downstream 2	Biosealer	N/A	N/A	Equipment	391 x 115 x 147 mm	N/A	3	Existing	Bioselect TC sartorius
L4-004	GF	Production	Downstream 2	Orion star A215 pH and Conductivity meter (pH meter 2)	N/A	N/A	Equipment	300 x 300 mm	N/A	1	Existing	Orion star A215
L4-004	GF	Production	Downstream 2	Magnetic stirrer - sampling management	N/A	N/A	Equipment	500 x 500 mm	N/A	2	Existing	TBD
L4-004	GF	Production	Downstream 2	Magnetic stirrer - carboy product	N/A	N/A	Equipment	500 x 510 mm	N/A	2	To be purchased	20L carboy custom made
L4-004	GF	Production	Downstream 2	AKTA Flux 6 (Small Scale TFF - 50L GMP Backup Equipment)	N/A	N/A	Equipment	460 x 400 mm	N/A	53	Existing	AKTA Flux 6
L4-004	GF	Production	Downstream 2	Biosafetycabinet	N/A	N/A	Equipment	800 x 1300 x 1568 mm	N/A	280	Existing	ThermoFisher 6' (1300 A2)
L4-004	GF	Production	Downstream 2	AKTA Ready Flux (TFF system)	N/A	N/A	Equipment	Main system : 1100 × 1520 × 880 mm Bagkart : 910 × 1550 × 810 mm Flux kart : 720 × 1000 × 450 mm	N/A	407	Existing	AKTA Ready Flux
L4-005	GF	Production	Downstream 2	Floor scale	N/A	N/A	Equipment	1500 x 1250 x 45 mm	N/A	N/A	To be purchased	500kg scale
L4-004	GF	Production	Downstream 2	Bench IPC	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-004	GF	Production	Downstream 2	Cart for pump	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-004	GF	Production	Downstream 2	Cart for sealer	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-005	GF	Production	Bulk filling	ROOM	C	NC	Lab	30	43	N/A	N/A	N/A
L4-005	GF	Production	Bulk filling	Filter capsule cart	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-005	GF	Production	Bulk filling	Bulk bag cart	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-005	GF	Production	Bulk filling	Floor scale	N/A	N/A	Equipment	1500 x 1250 x 45 mm	N/A	N/A	To be purchased	500kg scale
L4-005	GF	Production	Bulk filling	Biosafetycabinet	N/A	N/A	Equipment	800 x 1300 x 1568 mm	N/A	280	To be purchased	ThermoFisher 6' (1300 A2)
L4-005	GF	Production	Bulk filling	Biosealer	N/A	N/A	Equipment	391 x 115 x 147 mm	N/A	3	To be purchased	multisize sealer - sartorius
L4-005	GF	Production	Bulk filling	BioWelder TC	N/A	N/A	Equipment	555 x 261 mm	N/A	10	To be purchased	Biowelder - diffrent adaptor for tube size

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-005	GF	Production	Bulk filling	Mixer 50L for stabilizer addition	N/A	N/A	Equipment	750 x 650 x 975 mm	N/A	106	To be purchased	Mobius mixer Millipore 50L + load cell + 10L adaptator
L4-005	GF	Production	Bulk filling	Sartocheck plus - Filter integrity tester	N/A	N/A	Equipment	348 x 379 x 286 mm	N/A	16,8	To be purchased	Sartocheck 4 or 5 plus
L4-005	GF	Production	Bulk filling	Bench	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-005	GF	Production	Bulk filling	Cart for pump	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-005	GF	Production	Bulk filling	Cart for welder and sealer	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-006	GF	Support	Powder dispensing/ weighing	ROOM	C	NC	Lab	10	22,4	N/A	N/A	N/A
L4-006	GF	Support	Powder dispensing/ weighing	1 x weighing booth	N/A	N/A	Equipment	2100 x 2750 mm	N/A	1000	To be purchased	TBD
L4-006	GF	Support	Powder dispensing/ weighing	carts	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	TBD
L4-006	GF	Support	Powder dispensing/ weighing	Solvent cabinet	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	TBD
L4-006	GF	Support	Powder dispensing/ weighing	Storage (shelf)	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	TBD
L4-007	GF	Support	Powder dispensing/ weighing	Balance 35kg max	N/A	N/A	Equipment	N/A	N/A	40	To be purchased	Sartorius Cubis
L4-007	GF	Support	Powder dispensing/ weighing	Balance 12kg max	N/A	N/A	Equipment	N/A	N/A	20	To be purchased	Sartorius Cubis
L4-007	GF	Support	Powder dispensing/ weighing	Analytical Balance	N/A	N/A	Equipment	N/A	N/A	5	To be purchased	Sartorius Cubis
L4-007	GF	Support	Buffer preparation	ROOM	C	NC	Lab	40	37,4	N/A	N/A	N/A
L4-007	GF	Support	Buffer preparation	500L Mobius Power Mix with Load cell	N/A	N/A	Equipment	1680 x 1120 x 990 mm	N/A	600	To be purchased	500L Mobius Power Mix with Load cell
L4-007	GF	Support	Buffer preparation	200L Mobius Power Mix with Load cell	N/A	N/A	Equipment	1240 x 970 x810 mm	N/A	250	To be purchased	200L Mobius Power Mix with Load cell
L4-007	GF	Support	Buffer preparation	100L Mobius Power Mix with Load cell	N/A	N/A	Equipment	1220 x 890 x 790 mm	N/A	150	To be purchased	100L Mobius Power Mix with Load cell
L4-007	GF	Support	Buffer preparation	10/50L Mobius Power Mix with Load cell	N/A	N/A	Equipment	975 x 750 x 650 mm	N/A	110	To be purchased	10/50L Mobius Power Mix with Load cell
L4-007	GF	Support	Buffer preparation	Floor balance	N/A	N/A	Equipment	1500 x 1250 x 45 mm	N/A	N/A	To be purchased	500kg scale
L4-007	GF	Support	Buffer preparation	Balance 12kg max - for small volum	N/A	N/A	Equipment	N/A	N/A	20	To be purchased	Sartorius
L4-007	GF	Support	Buffer preparation	Magnetic stirrer plate	N/A	N/A	Equipment	500 x 510 mm	N/A	2	To be purchased	TBD
L4-007	GF	Support	Buffer preparation	Pump Masterflex 77420-10	N/A	N/A	Equipment	320 x 85 x 116 mm	N/A	20	To be purchased	Masterflex 77420-10
L4-007	GF	Support	Buffer preparation	Pump Masterflex 77602-10	N/A	N/A	Equipment	320 x 85 x 116 mm	N/A	20	To be purchased	Masterflex 77602-10
L4-007	GF	Support	Buffer preparation	Pump Masterflex 07522-20	N/A	N/A	Equipment	320 x 85 x 116 mm	N/A	20	To be purchased	Masterflex 07522-20
L4-007	GF	Support	Buffer preparation	Pump Masterflex 77800-60	N/A	N/A	Equipment	320 x 85 x 116 mm	N/A	20	To be purchased	Masterflex 77800-60
L4-007	GF	Support	Buffer preparation	Orion star A215 pH and Conductivity meter (pH meter 2)	N/A	N/A	Equipment	300 x 300 mm	N/A	1	To be purchased	VSTAR-50
L4-007	GF	Support	Buffer preparation	Laminar air flow	N/A	N/A	Equipment	N/A	4ft	100	To be purchased	2' Purifier HEPA-Filtered Enclosure with Airflow Monitor

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-007	GF	Support	Buffer preparation	Sartocheck plus - Filter integrity tester	N/A	N/A	Equipment	348 x 379 x 286 mm	N/A	16,8	To be purchased	Sartocheck 4 or 5 plus
L4-007	GF	Support	Buffer preparation	Extraction arm	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Filter holder	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	FlexAct to be confirmed
L4-007	GF	Support	Buffer preparation	Mobile Cart for 10-20L medium bags	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Flexstation 100L x 6	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Flexstation 200L x1	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Flexstation 50L x 2	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Bench for small preparation	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Bench for IPC	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Cart for 2x pumps	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-007	GF	Support	Buffer preparation	Cart for 2x pumps	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-008	GF	Support	Staging 1 - solution/equipment	ROOM	C	NC	Lab	20	30,7	N/A	N/A	N/A
L4-008	GF	Support	Staging 1 - solution/equipment	Flexstation 1000L	N/A	N/A	Equipment	1200 x 1000 x 1260 mm	N/A	1300	To be purchased	FlexStation 1000
L4-008	GF	Support	Staging 1 - solution/equipment	Flexstation 1000L	N/A	N/A	Equipment	1200 x 1000 x 1260 mm	N/A	1300	To be purchased	FlexStation 1000
L4-008	GF	Support	Staging 1 - solution/equipment	BioWelder TC	N/A	N/A	Equipment	555 x 261 mm	N/A	10	To be purchased	Biowelder - different adaptor for tube size
L4-008	GF	Support	Staging 1 - solution/equipment	FS1000 SS Mobile cart	N/A	N/A	Equipment	1200 x 1000 x 1260 mm	N/A	1300	To be purchased	FlexStation 1000
L4-008	GF	Support	Staging 1 - solution/equipment	FS1000 SS Mobile cart with load cells	N/A	N/A	Equipment	1200 x 1000 x 1260 mm	N/A	1300	To be purchased	FlexStation 1000
L4-008	GF	Support	Staging 1 - solution/equipment	Flexstation 500L x 5	N/A	N/A	Equipment	1200 x 800 x 915 mm	N/A	650	To be purchased	FlexStation 500
L4-008	GF	Support	Staging 1 - solution/equipment	Flexstation 200L x 10	N/A	N/A	Equipment	810 x 610 x 840 mm	N/A	300	To be purchased	FlexStation 200
L4-008	GF	Support	Staging 1 - solution/equipment	Flexstation 100L x 10	N/A	N/A	Equipment	810 x 610 x 840 mm	N/A	300	To be purchased	FlexStation 100
L4-008	GF	Support	Staging 1 - solution/equipment	QuaDrum 50L with bottom drain x 10	N/A	N/A	Equipment	N/A	N/A	60	To be purchased	Quadrum 50
L4-008	GF	Support	Staging 1 - solution/equipment	Flex station SS Pallet Truck	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-009	GF	Support	Cleaning (dirty)	ROOM	D	NC	Lab	20	17,7	N/A	N/A	N/A
L4-009	GF	Support	Cleaning	Washer	N/A	N/A	Equipment	2083 x 2388 x 953 mm	N/A	1338	To be purchased	Steris Reliance 480 PG
L4-009	GF	Support	Cleaning	Sink 1	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-009	GF	Support	Cleaning	Sink 2	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-009	GF	Support	Cleaning	Shelf	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-009	GF	Support	Cleaning	Cart	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-010	GF	Support	Sterilization (dirty)	ROOM	D	NC	Lab	20	28,3	N/A	N/A	N/A
L4-010	GF	Support	Sterilization	Sterilisation autoclave	N/A	N/A	Equipment	2428 x 2041 x 2003 mm	N/A	1908 kg installation weight, 2859 kg filled	To be purchased	FINN-AQUA BPS GMP STEAM STERILIZER 6915 WITH DOUBLE DOORS
L4-010	GF	Support	Sterilization	Assembly and wraping bench	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-010	GF	Support	Sterilization	Laminar air flow	N/A	N/A	Equipment	N/A	4ft	100	To be purchased	2' Purifier HEPA-Filtered Enclosure with Airflow Monitor
L4-010	GF	Support	Sterilization	Pass-Through from cleaning to sterilization	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-011	GF	Support	Staging - material / Steril staging	ROOM	C	NC	Lab	20	22,1	N/A	N/A	N/A
L4-012	GF	Production	PAL D (from locker to production corridor)	ROOM	C	NC	Lab	5	18,1	N/A	N/A	N/A
L4-012	GF	Production	PAL D (from locker to production corridor)	Sink	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-013	GF	Production	MAL D (from warehouse to MAL C)	ROOM	C	NC	Lab	10	8,3	N/A	N/A	N/A
L4-014	GF	Production	PAL C (from PAL D to production corridor)	ROOM	C	NC	Lab	5	14,9	N/A	N/A	N/A
L4-015	GF	Production	MAL C (from MAL D to production corridor)	ROOM	C	NC	Lab	5	8,3	N/A	N/A	N/A
L4-016	GF	Waste	Waste magenement / deconta. area	ROOM	NC	CL-2	Mechanical	50	36,6	N/A	N/A	N/A
L4-016	GF	Waste	Waste storage / outside	Decontamination autoclave	N/A	N/A	Equipment	3038 x 2051 x 2305 mm	N/A	2855 kg empty 4692 kg filled	To be purchased	FINN-AQUA BPS GMP STEAM STERILIZER 9912 single door
L4-016	GF	Waste	Waste storage / outside	Sink	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	TBD
L4-017	GF	Admin	Lockers M	ROOM	NC	NC	Admin	20	16,1	N/A	N/A	N/A
L4-017	GF	Admin	Lockers M	20 lockers	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-017	GF	Admin	Lockers M	Bench	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-017	GF	Admin	Lockers M	Sink	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-018	GF	Admin	Lockers W	ROOM	NC	NC	Admin	20	20	N/A	N/A	N/A
L4-018	GF	Admin	Lockers W	20 lockers	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-018	GF	Admin	Lockers W	Bench	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-018	GF	Admin	Lockers W	Sink	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-101	R+1	QC lab	Cleaning/stérilization	ROOM	NC	NC	Lab	15	14	N/A	N/A	N/A
L4-101	R+1	QC lab	Cleaning/stérilization	Glass washer	N/A	N/A	Equipment	600 x 600 x 835 mm	N/A	56	To be purchased	Miele PG 8504
L4-101	R+1	QC lab	Cleaning/stérilization	Wet bench - sink	N/A	N/A	Furniture	340 x 290 x 440 mm	N/A	N/A	To be purchased	N/A
L4-101	R+1	QC lab	Cleaning/stérilization	Small sterililization autoclave	N/A	N/A	Equipment	880 x 700 x 967 mm	N/A	50	To be purchased	Tuttnauer 5075 EL/ML

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-101	R+1	QC lab	Cleaning/stérilization	bench	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-101	R+1	QC lab	Cleaning/stérilization	shelf	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-101	R+1	QC lab	Cleaning/stérilization	cart	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-102	R+1	QC lab	CL2-lab	ROOM	NC	CL-2	Lab	100	41,4	N/A	N/A	N/A
L4-102	R+1	QC lab	CL2-lab	Biosafetycabinet	N/A	N/A	Equipment	800 x 1300 x 1568 mm	N/A	280	To be purchased	ThermoFisher 6' (1300 A2)
L4-102	R+1	QC lab	CL2-lab	automatic pipette	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-102	R+1	QC lab	CL2-lab	pH-Meter /conductivity meter	N/A	N/A	Equipment	TBD	N/A	N/A	To be purchased	N/A
L4-102	R+1	QC lab	CL2-lab	HPLC /UPLC with fluorescence	N/A	N/A	Equipment	550 x 620 x 820 mm	N/A	110	To be purchased	Thermo Scientific™ Vanquish™ UHPLC system
L4-102	R+1	QC lab	CL2-lab	automated Cell counter	N/A	N/A	Equipment	228 x 139 x 228 mm	N/A	3,6	To be purchased	Countess II
L4-102	R+1	QC lab	CL2-lab	analytical Balance + printer (marbre plate)	N/A	N/A	Equipment	412 x 400 mm	N/A	N/A	To be purchased	TBD
L4-102	R+1	QC lab	CL2-lab	Top load Balance + printer	N/A	N/A	Equipment	412 x 400 mm	N/A	N/A	To be purchased	TBD
L4-102	R+1	QC lab	CL2-lab	Water bath	N/A	N/A	Equipment	394 x 632 x 249 mm	N/A	30	To be purchased	Fisherbrand™ Isotemp™ Shaking Water Baths
L4-102	R+1	QC lab	CL2-lab	TOC	N/A	N/A	Equipment	N/A	N/A	1	To be purchased	QbD1200
L4-102	R+1	QC lab	CL2-lab	ELISA Plate reader with temperature control	N/A	N/A	Equipment	210 x 290 x 400 mm	N/A	80	To be purchased	MULTISKAN FC
L4-102	R+1	QC lab	CL2-lab	microcentrifuge refrigerated	N/A	N/A	Equipment	770 x 706 x 456 mm	N/A	141	To be purchased	ROTANTA 460 R
L4-102	R+1	QC lab	CL2-lab	Conductivity meter for low conductivity water	N/A	N/A	Equipment	N/A	N/A	0,5	To be purchased	TBD
L4-102	R+1	QC lab	CL2-lab	EndoSafe Nexgen-PTS	N/A	N/A	Equipment	254 x 137 x 70 mm	N/A	1	To be purchased	EndoSafe Nexgen-PTS
L4-102	R+1	QC lab	CL2-lab	oven - furnace 25 or 100 - 400 °C - drying, depyrogeneization	N/A	N/A	Equipment	565 x 640 x 820 mm	N/A	100	To be purchased	Heratherm™ General Protocol Ovens
L4-102	R+1	QC lab	CL2-lab	Shelf	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-102	R+1	QC lab	CL2-lab	Large fridge - stability and retained	N/A	N/A	Equipment	960 x 1435 x 1994 mm	N/A	282	To be purchased	Thermo Scientific TSX Series Model TSX5005GA
L4-102	R+1	QC lab	CL2-lab	Large freezer - stability and retained	N/A	N/A	Equipment	953 x 711 x 1996 mm	N/A	280	To be purchased	Thermo Scientific TSX Series High-Performance (TSX2320FA)
L4-102	R+1	QC lab	CL2-lab	Large ultralow freezer - stability and retained	N/A	N/A	Equipment	955 x 719 x 1981 mm	N/A	260	To be purchased	Thermo Scientific TSX60086A 28.8 cu.ft. Ultra-Low
L4-102	R+1	QC lab	CL2-lab	incubator 25°C - stability and retained	N/A	N/A	Equipment	505 x 530 x 635 mm	N/A	150	To be purchased	TBD
L4-102	R+1	QC lab	CL2-lab	Medium Fridge 4°C - sampling	N/A	N/A	Equipment	962 x 711 x 1996 mm	N/A	164	To be purchased	Thermo Scientific™ TSX2305SA
L4-102	R+1	QC lab	CL2-lab	Medium Freezer - sampling	N/A	N/A	Equipment	953 x 711 x 1996 mm	N/A	280	To be purchased	Thermo Scientific TSX Series High-Performance (TSX2320FA)
L4-102	R+1	QC lab	CL2-lab	Ultralow freezer - sampling	N/A	N/A	Equipment	955 x 719 x 1981 mm	N/A	260	To be purchased	Thermo Scientific TSX60086A 28.8 cu.ft. Ultra-Low
L4-102	R+1	QC lab	CL2-lab	Sink	NC	CL-2	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-103	R+1	QC lab	Microbiology (env.)	ROOM	TBD	CL-2	Lab	70	20,8	N/A	N/A	N/A
L4-103	R+1	QC lab	Microbiology (env.)	Biosafetycabinet	N/A	N/A	Equipment	800 x 1300 x 1568 mm	N/A	280	To be purchased	ThermoFisher 6' (1300 A2)

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-103	R+1	QC lab	Microbiology (env.)	static incubator 35degC	N/A	N/A	Equipment	838 x 787 x 2032 mm	N/A	150	To be purchased	Forma™ 3960 Series Environmental Chamber, 821.2 L, Stainless Steel
L4-103	R+1	QC lab	Microbiology (env.)	incubator 25degC	N/A	N/A	Equipment	838 x 787 x 2032 mm	N/A	150	To be purchased	Forma™ 3960 Series Environmental Chamber, 821.2 L, Stainless Steel
L4-103	R+1	QC lab	Microbiology (env.)	bench	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-103	R+1	QC lab	Microbiology (env.)	Large fridge	N/A	N/A	Equipment	960 x 1435 x 1994 mm	N/A	282	To be purchased	Thermo Scientific TSX Series Model TSX5005GA
L4-104	R+1	QC lab	PAL Microbio	ROOM	NC	NC	Lab	5	6,3	N/A	N/A	N/A
L4-104	R+1	QC lab	PAL Microbio	sink	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-105	R+1	QC lab	PAL Biochemestry	ROOM	NC	NC	Lab	5	6,8	N/A	N/A	N/A
L4-104	R+1	QC lab	PAL Biochemestry	sink	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-020	GF	Warehouse	Loading dock/ exp/recep	ROOM	NC	NC	Plant	10	46,1	N/A	N/A	N/A
L4-021	GF	Warehouse	Warehouse	ROOM	NC	NC	Storage	155	167	N/A	N/A	N/A
L4-021	GF	Warehouse	Warehouse	Palet racking (2 levels)	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-022	GF	Warehouse	Cold room	ROOM	NC	NC	Storage	15	36	N/A	N/A	N/A
L4-023	GF	Warehouse	Cryostorage	ROOM	NC	NC	Storage	10	18,1	N/A	N/A	N/A
L4-023	GF	Warehouse	Cryostorage	Liquid N2 Cell storage 797L	N/A	N/A	Equipment	diam 1067 mm	N/A	469	To be purchased	CryoExtra™ High-Efficiency Cryogenic Storage Systems
L4-023	GF	Warehouse	Cryostorage	Liquid N2 Cell storage - back up 797L	N/A	N/A	Equipment	diam 1067 mm	N/A	469	To be purchased	CryoExtra™ High-Efficiency Cryogenic Storage Systems
L4-023	GF	Warehouse	Cryostorage	Liquid nitrogen supply tank	N/A	N/A	Equipment	diam 1067 mm	N/A	469	To be purchased	CryoExtra™ High-Efficiency Cryogenic Storage Systems
L4-023	GF	Warehouse	Cryostorage	Large freezer - 20	N/A	N/A	Equipment	N/A	N/A	260	Existing	Thermo Scientific TSX Series High-Performance (TSX2320FA)
L4-023	GF	Warehouse	Cryostorage	Large freezer - 20 back up	N/A	N/A	Equipment	N/A	N/A	260	To be purchased	Thermo Scientific TSX Series High-Performance (TSX2320FA)
L4-023	GF	Warehouse	Cryostorage	Large ultralow freezer -80	N/A	N/A	Equipment	955 x 719 x 1981 mm	N/A	260	Existing	Thermo Scientific TSX60086A 28.8 cu.ft. Ultra-Low
L4-023	GF	Warehouse	Cryostorage	Large ultralow freezer - 80 back up	N/A	N/A	Equipment	955 x 719 x 1981 mm	N/A	260	Existing	Thermo Scientific TSX60086A 28.8 cu.ft. Ultra-Low
L4-024	GF	Waste	Waste storage / outside	ROOM	NC	NC	Mechanical	20	36,6	N/A	N/A	N/A
L4-024	GF	Waste	Waste storage / outside	Compactor	N/A	N/A	Equipment	N/A	N/A	TBD	Existing	TBD
L4-025	GF	Mechanical	Electrical	ROOM	NC	NC	Mechanical	20	10,2	N/A	N/A	N/A
L4-025	GF	Mechanical	Electrical	Electrical panel	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-025	GF	Mechanical	Electrical	Uniterruptible power generator	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-026	GF	Mechanical	Clean utilities	ROOM	NC	NC	Mechanical	200	53,2	N/A	N/A	N/A
L4-026	GF	Mechanical	Clean utilities	WFI system / pure steam generator	N/A	N/A	Equipment	including connections : 4262 x 914 x 4572 mm	N/A	full : 2500 kg empty : 1900 kg	To be purchased	Combi Stilmas
L4-026	GF	Mechanical	Clean utilities	WFI storage	N/A	N/A	Equipment	84" diam (height: 118" including legs)	N/A	N/A	To be purchased	Stilmas
L4-026	GF	Mechanical	Clean utilities	WFI distribution system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-026	GF	Mechanical	Clean utilities	Purified water system	N/A	N/A	Equipment	Pretreatment: Skid approximate size: 140” L X 40” W X 91” H LSX Skid size: 120” L X 66”W X 79” H Carbon Tank Size: 86”H X 26” D	N/A	Pretreatment: Skid Wet Weight: 4,300 LBS LSX Skid Wet Weight: 6,265 LBS - DRY WEIGHT: 4,480 LBS Carbon Wet Weight: 1,400 LBS	To be purchased	LSX
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	ROOM	NC	NC	Mechanical	129	129	N/A	N/A	N/A
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-027	GF	Mechanical	Air Handling Unit room / Mechanical Room	Ventilation system	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-028	GF	Admin	WC 1	Toilets + showers	NC	NC	Admin	5	3,8	N/A	N/A	N/A
L4-029	GF	Warehouse	Janitor	ROOM	NC	NC	Mechanical	2	3,5	N/A	N/A	N/A
L4-030	GF	Production	Staging - solution/equipment 2	ROOM	C	NC	Lab	20	25,6	N/A	N/A	N/A
L4-030	GF	Production	Staging - solution/equipment 2	Mobile support for 10-20L medium bags	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-030	GF	Production	Staging - solution/equipment 2	Flexstation 100L x 6	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-030	GF	Production	Staging - solution/equipment 2	Flexstation 200L x1	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-030	GF	Production	Staging - solution/equipment 2	Flexstation 50L x 2	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	N/A
L4-030	GF	Production	Staging - solution/equipment 2	Mobile VHP decontamination station	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	Steris Victory
L4-030	GF	Production	Staging - solution/equipment 2	Portable air sampler	N/A	N/A	Equipment	N/A	N/A	N/A	To be purchased	TBD
L4-031	GF	Support	PAL D (from general corridor to support grade D corridor)	ROOM	D	NC	Lab	5	11,8	N/A	N/A	N/A
L4-032	GF	Warehouse	Sampling room	ROOM	D	NC	Lab	10	15	N/A	N/A	N/A
L4-032	GF	Warehouse	Sampling room	1 x weighing booth	N/A	N/A	Equipment	N/A	N/A	1000	To be purchased	TBD
L4-033	GF	Warehouse	Sampling room CAL	ROOM	D	NC	Lab	6	10,9	N/A	N/A	N/A
L4-035	GF	Mechanical	IT room	ROOM	NC	NC	Mechanical	5	5	N/A	N/A	N/A
L4-036	GF	Support	PAL C (from support grade D corridor to support grade C corridor)	ROOM	C	NC	Lab	5	12,8	N/A	N/A	N/A

APPENDIX E - NRC-14 - CTMF - ROOM & EQUIPMENT LIST

Item #	Level	Area	Room description	Main Equipment - Phase I&II scale	Grade	Biosafety level	Type	Surface estim. (roon: sqm / equipment: cm)	Surface layout (sqm)	Weight (kg)	Statut	Model
L4-037	GF	Support	MAL D (from warehouse to MAL D)	ROOM	C	NC	Lab	10	5,3	N/A	N/A	N/A
L4-038	GF	Support	MAL C (from MAL D to support)	ROOM	C	NC	Lab	5	5,3	N/A	N/A	N/A
L4-039	GF	Mechanical	Technical area	ROOM	NC	NC	Mechanical	10	7,5	N/A	N/A	N/A
L4-039	GF	Mechanical	Technical area	500L Bioreactor TCU	N/A	N/A	Equipment	TBD	N/A	TBD	To be purchased	TBD
L4-039	GF	Mechanical	Technical area	500L tank TCU	N/A	N/A	Equipment	TBD	N/A	TBD	To be purchased	TBD
L4-039	GF	Mechanical	Technical area	50L Bioreactor TCU	N/A	N/A	Equipment	TBD	N/A	TBD	To be purchased	TBD
L4-040	GF	Production	Janitor	ROOM	C	CL-2	Lab	3	5	N/A	N/A	N/A
L4-040	GF	Production	Janitor	Portable VHP biodecontamination system for cleanroom	N/A	N/A	Equipment	TBD	N/A	TBD	To be purchased	TBD
L4-041	GF	Production	Lobby	ROOM	NC	NC	Lab	5	5,95	N/A	N/A	N/A
L4-043	GF	Warehouse	WC	ROOM	NC	NC	Mechanical	5	4,1	N/A	N/A	N/A
L4-046	GF	Support	PAL C (from corridor to Downstream 2)	ROOM	C	NC	Lab	5	4,5	N/A	N/A	N/A
L4-047	GF	Support	PAL C (from corridor to Bulkfilling)	ROOM	C	NC	Lab	5	6	N/A	N/A	N/A
L4-048	GF	Circulation	Corridor production	ROOM	C	CL-2	Lab	N/A	93,6	N/A	N/A	N/A
L4-049	GF	Circulation	Corridor production	ROOM	C	CL-2	Lab	N/A	29,3	N/A	N/A	N/A
L4-050	GF	Circulation	Corridor support	ROOM	D	NC	Lab	N/A	7,4	N/A	N/A	N/A
L4-051	GF	Circulation	Corridor support	ROOM	C	NC	Lab	N/A	30,4	N/A	N/A	N/A
L4-052	GF	Circulation	Corridor mechanical/warehouse access	ROOM	NC	NC	Mechanical	N/A	40	N/A	N/A	N/A
L4-053	GF	Mechanical	Effluent room	ROOM	NC	CL-2	Mechanical	30	21,2	N/A	N/A	N/A
L4-053	GF	Mechanical	Effluent room	Kill Tank System	N/A	N/A	Equipment	3000 x 1000 x 2600 mm	N/A	ULT1,000 (full) = 1,800 lbs	To be purchased	Actini Ultimate 500 (price included above)
L4-053	GF	Mechanical	Effluent room	Sink	N/A	N/A	Furniture	N/A	N/A	N/A	To be purchased	N/A
L4-053	GF	Mechanical	Effluent room	Kill Tank Storage tank	N/A	N/A	Equipment	2250 diam x 3190 mm	N/A	Tank 8,000L (Full)) = 22,000 lbs	To be purchased	Actini Ultimate 500 (price included above)

Appendix E - NRC-14-LIST-03-00

Gowning example

Client: National Research Council
Date: 2020-11-27

N°	Type	Picture	Gowing Items	Comment
0	Ville	N/A	N/A	
1	NC Area / visitor		City clothes Safety shoes and/or shoe cover	NRC personnel and external visitor
2	NC technical area		Safety shoes Working clothes with longue sleeves and pants Proper individual protection based on operation risk analysis	Could be different color for different services (e.g. maintenance vs supply)
3	QC lab		City clothes (pants) under lab coton lab coat Safety shoes Safety glasses	
4	QC lab _ CL2		City clothes (pants) under lab polyester lab coat Safety shoes Safety glasses Lab hairnet Gloves	
5	Grade D		Clean room facility uniform (one or two pieces) Clean room safety shoes Hairnet Beard mask if required	
6	Grade C		Grade D clothes Tyvek grade C Safety glasses Gloves Mask Shoe cover Beard mask if required	

National Research Council Canada

PROCESS MASS BALANCE - Viral Vector

Feasability study - Clinical Trial Manufacturing Facility

Revision 00
Issued for approval

Client: National Research Council

Date: 2020-11-04

[NRC-14] *Subculture of HEK293*

Hypothesis: based on NRC-09-NDC-01		
Doubling time:	30	hours
Working volume:	1/5	volume
Initial concentration	3,00E+05	cells/mL
Viability:	90%	

USP DATA SHEET

Could be replace by bioreactor 10L volum

THAWING		PHASE 1					PHASE 2					PHASE 3					PHASE 3					
Volum (mL)	Qty	Volum (mL)	Qty0	C0	Time (days)	Qtyf	Volum (mL)	Qty0	C0	Time (days)	Qtyf	Volum (mL)	Qty0	C0	Time (days)	Qtyf	Volum (mL)	Qty0	C0	Time (days)	Qtyf	
							50	8,64E+07	1,73E+06	4	2,49E+09											
		50	1,00E+07	2,00E+05	4	2,88E+08	**50**	8,64E+07	1,73E+06	4	2,49E+09	**400**	5,04E+09	1,26E+07	4	1,45E+11	**1000**	6,53E+10	6,53E+07	4	1,88E+12	
							50	8,64E+07	1,73E+06	4	2,49E+09						**1000**	6,53E+10	6,53E+07	4	1,88E+12	
1,8	1,00E+07						**50**	8,64E+07	1,73E+06	4	2,49E+09	**400**	5,04E+09	1,26E+07	4	1,45E+11	**1000**	6,53E+10	6,53E+07	4	1,88E+12	
		50	1,00E+07	2,00E+05	4	2,88E+08	**50**	8,64E+07	1,73E+06	4	2,49E+09						**1000**	6,53E+10	6,53E+07	4	1,88E+12	
							50	8,64E+07	1,73E+06	4	2,49E+09	**400**	5,04E+09	1,26E+07	4	1,45E+11	**1000**	6,53E+10	6,53E+07	4	1,88E+12	
1,8	1,00E+07																					
							50	8,64E+07	1,73E+06	4	2,49E+09						**1000**	6,53E+10	6,53E+07	4	1,88E+12	
		50	1,00E+07	2,00E+05	4	2,88E+08	**50**	8,64E+07	1,73E+06	4	2,49E+09	**400**	5,04E+09	1,26E+07	4	1,45E+11	**1000**	6,53E+10	6,53E+07	4	1,88E+12	
1,8	1,00E+07						**50**	8,64E+07	1,73E+06	4	2,49E+09						**1000**	6,53E+10	6,53E+07	4	1,88E+12	
Sécurity bank												**25**	3,02E+09	2,42E+07	4	8,71E+10	**50**	3,48E+10	6,97E+08	4	1,00E+12	
Could be used for MVSS preparation																	**50**	3,48E+10	6,97E+08	4	1,00E+12	
							25	2,33E+08	9,33E+06	4	6,72E+09	**25**	3,02E+09	2,42E+07	4	8,71E+10	**50**	3,48E+10	6,97E+08	4	1,00E+12	Total security (cells)
																	50	3,48E+10	6,97E+08	4	1,00E+12	8,02E+12
1,8	1,00E+07	**25**	1,80E+07	7,20E+05	4	5,18E+08						**25**	3,02E+09	2,42E+07	4	8,71E+10	**50**	3,48E+10	6,97E+08	4	1,00E+12	
																	50	3,48E+10	6,97E+08	4	1,00E+12	
							25	2,33E+08	9,33E+06	4	6,72E+09	**25**	3,02E+09	2,42E+07	4	8,71E+10	**50**	3,48E+10	6,97E+08	4	1,00E+12	
																	50	3,48E+10	6,97E+08	4	1,00E+12	

TOTAL:	**Qty cells:**	**Qty flask:**	**Qty cells:**	**Qty flask:**	**Qty cells:**	**Qty flask:**	**Qty cells:**	**Qty flask:**	**Qty cells:**	**TOTAL TIME**
Working	**3,00E+07**	**3**	**8,64E+08**	**9**	**2,24E+10**	**4**	**5,80E+11**	**8**	**1,50E+13**	**16**
		150		450		1600		8000		

Client: National Research Council
Date: 2020-11-04

[NRC-14] *Final cell amplification and Virus production based on NRC-09-NDC-01 (500l scale production client 62)*

Legend: Validation ref. Process Volumes // Ad5 Process Model
Ref. NRC Ad5 Process Model
Ref. Initial drug product requirement

USP DATA SHEET

Cellules	TD (H)	C_0 ensemencement (cells/mL)	Ratio	Viabilité (%)
HEK293	**30**	**3,00E+05**	**1/5**	**90%**
Process Step	Temps de culture	Scale (L)	Qté initiale théorique (cells)	Qté finale théorique (cells)
Cell amplification	3	**50**	1,50E+10	7,13E+10
	Process Step - Level 2	Medium type	Volume/final production volume (L)	Total Volume (L)
	Medium set up	HEK293 medium D0	0,45	22,5
	Medium increase	HEK293 medium D1	0,5	25
	Feed 4	4% NaOH, 9% NaHCO3	0,05	2,5
Process Step	Temps de culture	Scale (L)	Qté initiale théorique (cells)	Qté finale théorique (cells)
Virus production	4	**500**	6,41E+10	5,30E+11
	Process Step - Level 2	Medium type	Volume/final production volume (L)	Total Volume (L)
	Medium set up	HEK293 medium D0	0,4	200
	Medium increase	HEK293 medium D1	0,4	200
	Feed 3	Glutamine 4mM	0,05	25
	Feed 4	4% NaOH, 9% NaHCO3	0,05	25
Process Step	Process Step - Level 2	Solution type	Volume/final production volume (L)	Total Volume (L)
Cell lysis	Resuspension	mM Hepes, 2mM MgCl2, 300mM NaCl 2% Sucrose pH7	0,023	11,5
DNAse treatment	DNAse	Benzonase	0,001	0,462
	Buffer	Saline buffer	0,077	38,5
	Expected Potein Yield %	Expected Final volume	Expected Final IVP productivity (ivp/cell)	Expected Final Total ivp Amount (ivp)
	70%	**500,5**	2,20E+06	4,08E+17
Process Step	Flow rate (LMH)	Secondary Filter Name	Guard Filter Name	Final Filter Name
Filtration	**300**	TBD	0.45/0.22 µm PES Filter	0.22 µm PES or PVDF Filter
+ bioburden reduction	Filter surface area (m2)*			
	3	**2**	0,5	
	Process Step - Level 2	Medium type	Volume (L)/m2	Total Volume (L)
	Pre-Flush	WFI	100	300
	Equilibration	mM Hepes, 2mM MgCl2, 300mM NaCl 2% Sucrose pH7	30	90
	Loading	Cell culture supernatant	N/A	500,5
	Rinse	**WFI**	15	45
	Expected Potein Yield %	Expected Final volume	Expected Final IVP concentration (ivp/mL)	Expected Final Total ivp Amount (ivp)
	90%	**546**	6,74E+11	3,68E+17

SOLUTION PREPARATION DATA SHEET

Security factor	Medium, Buffer Type	Buffer Volume / Buffer type	Container type	Palletank number	Buffer Weight (Kg) /Palletank	Component #1 Name	Component #1 weight (g) / 1 Kg buffer	Component #1 weight (g)	Component #2 Name	Component #2 weight (g) / 1 Kg buffer	Component #2 weight (g)	Component #3 Name	Component #3 weight (g) / 1 Kg buffer	Component #3 weight (g)	Component #4 Name	Component #4 weight (g) / 1 Kg buffer	Component #4 weight (g)
1,1	**Cell amplification**																
	HEK293 medium D0	25	50	1	25	HEK293 media	23,72	587,07	Sodium bicarbonate	2,2	54,45						
	HEK293 medium D1	28	50	1	28	HEK293 media	23,72	652,30	Sodium bicarbonate	2,2	60,50						
	4% NaOH, 9% NaHCO3	3	10	1	3	Sodium hydroxyde	40	110,00	Sodium bicarbonate	90	247,50						
	Virus production																
	HEK293 medium D0	220	300	1	220	HEK293 media	23,72	5 218,40	Sodium bicarbonate	2,2	484,00						
	HEK293 medium D1	220	300	1	220	HEK293 media	23,72	5 218,40	Sodium bicarbonate	2,2	484,00						
	Glutamine 4mM	28	50	1	28	READY TO USE											
	4% NaOH, 9% NaHCO3	28	50	1	28	Sodium hydroxyde	40	1 100,00	Sodium bicarbonate	90	2 475,00						
	Cell lysis																
	10mM Hepes, 2mM MgCl2, 300mM NaCl 2% Sucrose pH7.5	13	20	1	13	Sodium chloride	17,532	221,78	Hepes 1M	11,915	150,72	MgCl2 1M	0,190422	42,23	Sucrose	20	3 014,50
	Benzonase	1	10	1	1	READY TO USE											
	Saline buffer	42	50	1	42	READY TO USE											
	Filtration																
	10mM Hepes, 2mM MgCl2, 300mM NaCl 2% Sucrose pH7.5	99	100	1	99	Sodium chloride	17,532	1 735,67	Hepes 1M	11,915	1 179,59	MgCl2 1M	0,190422	330,51	Sucrose	20	23 591,70
	WFI	380	N/A	N/A	N/A												

Client: National Research Council

Date: 2020-11-04

[NRC-14] *Purification steps based on NRC-09-NDC-01 (500L scale production client 62)*

Legend: Validation ref. Process Volumes (500L scale) NRC
Ref. NRC Ad5 Process Model
Ref. Initial drug product requirement

DSP DATA SHEET

Process Step - Level 1	Technology Name*	VP load (L/L)	Gel volume (L)	Run Number	Effective Elution volume*	Expected Virus Yield (%)*	Expected Final viral Concentration (ivp/mL)	Expected Final Total ivp Amount (ivp)	Expected Final Volume (L)	Débit skid (L/h)
Anion Exchange Chromatography	Q Sepharose HP	40	13,6	1	0,9	85%	**2,55E+13**	**3,12E+17**	**12**	79,2
column 450 mm diam / 20 cm bed height	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	VC	Linear flow rate (cm/h)*	Time (H) / step	Time/run (H)	Buffer volume (L)		
	RUN	Rinse	WFI	3	50	0,52	**2**	41		
		Sanitisation	1N NaOH	4,6	50	0,80		63		
		Sanitisation	1N NaOH	#N/A	#N/A	0,5		#N/A		
		Regeneration	50mM Hepes pH7.5, 2M NaCl	3	50	0,52		41		
		Equilibration	50mM Hepes, 2mM MgCl2, 300mM NaCl 2% Sucrose pH7.5	5	50	0,87		69		
		Load	0.45µm filtered clarified harvest	#N/A	50	6,89		546		
		Wash 1	50mM Hepes, 2mM MgCl2, 300mM NaCl 2% Sucrose pH7.5	5	50	0,87		69		
		Wash 2	50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5 + 450mM NaCl	5	50	0,87		69		
		Elution	50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5 + 600mM NaCl	5	50	0,87		69		
		Strip 1	50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5 + 1M NaCl	5	50	0,87		69		
		Strip 2	50mM Hepes pH7.5, 2M NaCl	5	50	0,87		69		
		Sanitisation	1N NaOH	3	50	0,52		41		
		Sanitisation	1N NaOH	#N/A	#N/A	0,50		#N/A		
		Regeneration	50mM Hepes pH7.5, 2M NaCl	3	50	0,52		41		
		Storage	20% Ethanol	3	50	0,52		41		

Adjustment 1 and filtration	Filter capacity (L/m^2)	Filter surface (m2)	Expected Protein Yield (%)*	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)
	100	0,79	98%	**1,84E+16**	**3,06E+17**	**17**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type*	Volume (L)/m2 or *Equivalent*	Buffer volume (L)	
	ADJ	pH adjustment	50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5	0,4	4,4	
	FILTER	Equilibration	50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5	30	23,8	
		Loading	Adjusted product	N/A	16,6	

Affinity Chromatography	Technology Name	Capacity (L/L)*	Membrane (L) volume	Run Number*	Effective Elution volume*	Expected Virus Yield (%)*	Expected Final viral Concentration (ivp/mL)	Expected Final Total ivp Amount (ivp)	Expected Final Volume (L)
- Mode FT	Capto Core 700	0,66	**19**	1	0,7	85%	**2,00E+13**	**2,60E+17**	**13,0**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	MV*	Linear flow rate (L/min)	Time (H) / step Level 3	Time (H) / step Level 2	Buffer volume / Step	
	PRE	Rinse	WFI	3	0,88	1,06	4	56	
		Sanitisation	1N NaOH	4,6	1,18	1,62		86	
		Regeneration	50mM Hepes pH7.5, 2M NaCl	3	1,18	1,06		56	
	RUN	Equilibration	50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5,0.5M NaCl	5	1,77	1,76	4	93	
		Load	AEX eluat adjusted and filtered	#N/A	1,7	0,31		17	
		Buffer flush	50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5,0.5M NaCl	5	1,7	1,76		93	
		Strip	50mM Hepes pH7.5, 2M NaCl	3	1,7	0,04		2	
		Sanitisation	1N NaOH	4,6	1,18	0,06		3	
		Regeneration	50mM Hepes pH7.5, 2M NaCl	3	1,18	0,04		2	
	POS	Storage	20% ethanol	3	0,88	1,06	1	56	

Diafiltration	Technology Name	Inlet flow rate (LMM)	Membrane (s.m)	Targeted Protein Concentration (g/L) before DF	DV (L)	Expected Virus Yield (%)*	Expected Final viral Concentration (ivp/mL)	Expected Final Total ivp Amount (ivp)	Expected Final Volume (L)
	50kDa Pellicon 2	5	2	6,00E+12	**6,0**	70%	**1,82E+13**	**1,82E+17**	**10**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Volume (L/sq m or *DV*)	Linear flow rate (L/min)	Time (H) / step Level 3	Time (H) / step Level 2	Buffer volume / Step	
	PRE	Rinse	WFI	60	10	0,20	1	120	
		Sanitisation	0.5M NaOH (WFI)	20	10	0,07		40	
		Sanitisation	0.5M NaOH	#N/A	#N/A	0,50		#N/A	
		Rinse	WFI	30	10	0,10		60	
	RUN	Equilibration	50mM Hepes pH 7.5, 2mM MgCl2, 0.5M NaCl	10	10	0,03	0,1	20	
		Load	AFF eluat	#N/A	10	0,00		13,02	
		Diafiltration	20mM Tris pH8.0, 25mM NaCl,2.5% glycerol	*7*	10	0,07		42	
		Diafiltration finale	20mM Tris pH8.0, 25mM NaCl,2.5% glycerol	*1*	10	0,01		6	
		Rinse	20mM Tris pH8.0, 25mM NaCl,2.5% glycerol	*2*	10	0,01		4	

Adjustment 2	Targeted stabilizer concentration (g/L)*	Targeted ivp Concentration (ivp/L)	Dilution Factor	Expected Virus Yield (%)*	Expected Final viral Concentration (ivp/mL)	Expected Final Total ivp Amount (ivp)	Expected Final Volume (L)
	0,4	6,00E+12	**3,0**	100%	**6,00E+12**	**1,82E+17**	**30**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Buffer volume / Step			
	RUN	**Stabilizer**	Stabilizer	0			
		Virus concentration adjustement	20mM Tris pH8.0, 25mM NaCl,2.5% glycerol	20			

Security factor: 1,1

PREPARATION Data Sheet

Medium, Buffer Type	Buffer Volume / Buffer type	Container type	Tank number	Buffer Weight (Kg) /Palletank	Component #1 Name	Component #1 weight (g) / 1 Kg buffer	Component #1 weight (g)	Component #2 Name	Component #2 weight (g) / 1 Kg buffer	Component #2 weight (g)	Component #3 Name	Component #3 weight (g) / 1 Kg buffer	Component #3 weight (g)	Component #4 Name	Component #4 weight (g) / 1 Kg buffer	Component #4 weight (g)
Anion Exchange Chromatography																
WFI	45	N/A	N/A	N/A	READY TO USE											
1N NaOH	114	200	1	115	Sodium hydroxide	40	4 576									
50mM Hepes pH7.5, 2M NaCl	166	200	1	167	Sodium chloride	11,688	1 941	Hepes 1M	11,915	1 979						
50mM Hepes, 2mM MgCl2, 300mM NaCl 2% Sucrose pH7.5	152	200	1	152	Sodium chloride	17,532	2 661	Magnesium chloride 1M	0,190422	29	Hepes 1M	11,915	1 809	Sucrose	20	578
50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5 + 450mM NaCl	76	100	1	76	Sodium chloride	26,298	1 996	Magnesium chloride 1M	0,190422	14	Hepes 1M	11,915	904	Sucrose	20	289
50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5 + 600mM NaCl	76	100	1	76	Sodium chloride	35,064	2 661	Magnesium chloride 1M	0,190422	14	Hepes 1M	11,915	904	Sucrose	20	289
50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5 + 1M NaCl	76	100	1	76	Sodium chloride	58,44	4 436	Magnesium chloride 1M	0,190422	14	Hepes 1M	11,915	904	Sucrose	20	289
20% Ethanol	45	50	1	46	READY TO USE											
Adjustment 1 and filtration																
50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5	31	50	1	31	Hepes 1M	11,915	369	Magnesium chloride 1M	0,190422	6	Sucrose	20	619			
Affinity Chromatography																
WFI	61	N/A	N/A	N/A	READY TO USE											
1N NaOH	98	100	1	98	Sodium hydroxide	40	3 906									
50mM Hepes pH7.5, 2M NaCl	66	100	1	66	Sodium chloride	11,688	771	Hepes 1M	11,915	786						
50mM Hepes, 2mM MgCl2, 2% Sucrose pH7.5,0.5M NaCl	205	300	1	205	Sodium chloride	29,22	5 977	Magnesium chloride 1M	0,190422	39	Hepes 1M	11,915	2 437	Sucrose	20	4 100
20% ethanol	61	100	1	62	READY TO USE											
Diafiltration																
WFI	198	200	1	198	READY TO USE											
0.5M NaOH (WFI)	44	50	1	44	Sodium hydroxide	20	880									
20mM Tris pH8.0, 25mM NaCl,2.5% glycerol	57	100	1	58	Sodium chloride	0,01461	1	Tris 1M	2,4228	139	Glycerol	2,5	143			
50mM Hepes pH 7.5, 2mM MgCl2, 0.5M NaCl	22	50	1	22	Sodium chloride	29,22	643	Magnesium chloride 1M	0,190422	4	Hepes 1M	11,915	262	Sucrose	20	440
Adjustment 2																
Stabilizer	0	10	1	1	TBD											
20mM Tris pH8.0, 25mM NaCl,2.5% glycerol	20	20	1	20	TBD											

Client: National Research Council
Date: 2020-11-11

[NRC-14]

Process Water Balance

Legend: Worst case
Total for 1 batch

Room	SUBCULTURE	UPSTREAM				DOWNSTREAM 1			DOWNSTREAM 2		TOTAL
Process Step	Subculture	Cell amplification	Virus production	Cell lysis	Harvest and clarification	Anion Exchange Chromatography	Adjustment 1 and filtration	Affinity Chromatography	Diafiltration	Adjustment 2	
Total volum of solution (L) *Needs in prepration room*	11	55	495	56	99	705	31	430	123	20	2024
Total WFI direct (L) *Needs in production rooms*	0	0	0		380	45	0	61	198	0	684
Final Volum (L)	8	50	450	501	546	12	17	13	10	30	N/A
Liquide Waste (L)	3	5	45	5	383	1283	27	495	324	0	2570

National Research Council Canada

PROCESS MASS BALANCE - mAb

Feasability study - Clinical Trial Manufacturing Facility

Revision 00
Issued for approval

Date: 2020-11-11

[NRC-14] *Subculture of CHO*

Hypothesis:	CHO cell lines
Doubling time:	24 hours
Working volume:	1/5 volume
Initial concentration	5,00E+05 cells/mL
Viability:	90%
Viability post thawing:	70%

USP DATA SHEET

THAWING		PHASE 1					PHASE 2					PHASE 3					PHASE 3						
Volum (mL)	Qty	Volum (mL)	Qty0	C0	Time (days)	Qtyf	Volum (mL)	Qty0	C0	Time (days)	Qtyf	Volum (mL)	Qty0	C0	Time (days)	Qtyf	Volum (mL)	Qty0	C0	Time (days)	Qtyf		
							50	1,07E+07	2,14E+05	2	3,85E+07												
		50	7,00E+06	1,40E+05	2,5	3,56E+07	**50**	1,07E+07	2,14E+05	2	3,85E+07	**400**	7,79E+07	1,95E+05	2,5	3,97E+08	**1000**	2,38E+08	2,38E+05	3	1,71E+09		
							50	1,07E+07	2,14E+05	2	3,85E+07												
1,8	1,00E+07						**50**	1,07E+07	2,14E+05	2	3,85E+07	**400**	7,79E+07	1,95E+05	2,5	3,97E+08	**1000**	2,38E+08	2,38E+05	3	1,71E+09		
		50	7,00E+06	1,40E+05	2,5	3,56E+07	**50**	1,07E+07	2,14E+05	2	3,85E+07												
							50	1,07E+07	2,14E+05	2	3,85E+07	**400**	7,79E+07	1,95E+05	2,5	3,97E+08	**1000**	2,38E+08	2,38E+05	3	1,71E+09		
1,8	1,00E+07						**50**	1,07E+07	2,14E+05	2	3,85E+07												
		50	7,00E+06	1,40E+05	2,5	3,56E+07	**50**	1,07E+07	2,14E+05	2	3,85E+07	**400**	7,79E+07	1,95E+05	2,5	3,97E+08	**1000**	2,38E+08	2,38E+05	3	1,71E+09		
1,8	1,00E+07						**50**	1,07E+07	2,14E+05	2	3,85E+07												
Banque de sécurité												**25**	4,72E+07	3,78E+05	2	1,70E+08	**50**	6,80E+07	1,36E+06	3	4,90E+08		
																	50	6,80E+07	1,36E+06	3	4,90E+08		
							25	2,92E+07	1,17E+06	2	1,05E+08	**25**	4,72E+07	3,78E+05	2	1,70E+08	**50**	6,80E+07	1,36E+06	3	4,90E+08	Total security (cells)	
																	50	6,80E+07	1,36E+06	3	4,90E+08	3,92E+09	
1,8	1,00E+07	**25**	1,80E+07	7,20E+05	2	6,48E+07						**25**	4,72E+07	3,78E+05	2	1,70E+08	**50**	6,80E+07	1,36E+06	3	4,90E+08		
																	50	6,80E+07	1,36E+06	3	4,90E+08		
							25	2,92E+07	1,17E+06	2	1,05E+08	**25**	4,72E+07	3,78E+05	2	1,70E+08	**50**	6,80E+07	1,36E+06	3	4,90E+08		
																	50	6,80E+07	1,36E+06	3	4,90E+08		
TOTAL:	**Qté cells:**	**nbr de flacons:**				**Qté cells:**	**nbr de flacons:**				**Qté cells:**	**nbr de flacons:**				**Qté cells:**	**nbr de flacons:**				**Qté cells:**	**nbr totale jours:**	
Working	**2,10E+07**	**3**				**1,07E+08**	**9**				**3,46E+08**	**4**				**1,59E+09**	**4**				**6,86E+09**	**10**	

Client: National Research Council
Date: 2020-11-11

[NRC-14] *Upstream process*

Hypothesis: all process parameters and solution formulation are based on typical mAb process // must be confirmed by NRC

USP DATA SHEET

Process Step - Level 1	Technology Name	Scale (L)	Expected final cell quantity (cells)	Time (hrs)
Cell amplification	XDR50	**50**	**7,76E+10**	84
	Process Step - Level 2	Medium type	Volume/final production volume (L) or Volume (L)/m2	Total Volume (L)
	Medium set up	BalanCD CHO Growth A Medium D-01	0,4	20
	Medium increase	BalanCD CHO Growth A Medium D00	0,5	25
	Feed	7.5% Sodium Bicarbonate	0,1	5
Process Step - Level 1	Technology Name	Scale (L)	Protein Titer (g/L)	Bioreactor number
mAb production	XDR500	**500**	**4**	TBD
	Process Step - Level 2	Medium type	Volume/final production volume (L) or Volume (L)/m2	Total Volume (L)
	Medium set up	BalanCD CHO Growth A Medium D-01	0,4	200
	Medium increase	BalanCD CHO Growth A Medium D00	0,3	150
	Feed 1	Cell boost a	0,2	100
	Feed 2	Cell boost b	0,02	10
	Feed 3	Glucose 450 g/L	0,04	20
	Feed 4	7.5% Sodium Bicarbonate	0,04	20
Process Step - Level 1	Primary Filter Name	Secondary Filter Name	Guard Filter Name	Final filer area (m2)
Harvest and clarification	D0HC	MX0HC	0.45/0.22 µm PES Filter	0.22 µm PES or PVDF Filter
	Filter surface area (m2)			
	5,5	2,5	0,8	0,8
	Process Step - Level 2	Medium type	Volume (L)/m2	Total Volume (L)
	Pre-Flush	WFI	100	550
	Equilibration	DPBS	50	275
	Loading	Cell culture supernatant	500	500
	Rinse	WFI	20	110
	Expected Potein Yield %	**Expected Final volume (L)**	**Expected Final IgG concentration (g/L)**	**Expected Final Total protein Amount (g)**
	95%	**610**	**3,45**	**2105**

SOLUTION PREPARATION DATA SHEET

Security factor: **1,1**

Medium, Buffer Type	Buffer Volume / Buffer type	Container type	Palletank number	Buffer Weight (Kg) /Palletank	Component #1 Name	Component #1 weight (g) / 1 Kg buffer	Component #1 weight (g)	Component #2 Name	Component #2 weight (g) / 1 Kg buffer	Component #2 weight (g)
Cell amplification										
BalanCD CHO Growth A Medium D-01	50	50	2	25	Balance CD growth A	23,72	1 174,14	Sodium bicarbonate	2,2	108,90
7.5% Sodium Bicarbonate	6	10	2	3	Sodium bicarbonate	75	412,50			0,00
mAb production										
BalanCD CHO Growth A Medium D-01	220	500	2	110	Balance CD growth A	23,72	5 218,40	Sodium bicarbonate	2,2	484,00
BalanCD CHO Growth A Medium D00	165	200	2	83	Balance CD growth A	23,72	3 913,80	Sodium bicarbonate	2,2	363,00
Cell boost a	110	200	2	55	Cell Boost 7a	181,04	19 914,40	5N NaOH	18,6	2 046,00
Cell boost b	11	20	2	6	Cell Boost 7b	94,6	1 040,60	5N NaOH	160,5	1 765,50
Glucose 450 g/L	22	50	2	11	D-Glucose	450	9 900,00			0,00
7.5% Sodium Bicarbonate	22	50	2	11	Sodium bicarbonate	75	1 650,00			0,00
Harvest and clarification										
WFI	726	500	2	363			0,00			0,00
DPBS	303	500	2	152			0,00			0,00

Client: National Research Council
Date: 2020-11-11

[NRC-14] *Downstream process*
Hypothesis: all process parameters and solution formulation are based on typical mAb process // must be confirmed by NRC
If multiple runs are required for chromatography _ only one sanitization between run will be done

DSP DATA SHEET

Process Step - Level 1											
Affinity chromatography	Technology Name	Protein Load (g/L)	Resin (L) volume	Run Number	Effective Elution volume	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)	Column diameter (cm)	Bed heigh (cm)
B/E Mode	MabSelect SuRe	40	**53**	**2**	1,7	85%	**4**	**1789**	**495**	45	20
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	VC or MV	Linear flow rate (cm/h)	Time (H) / step Level 3	Time (H) / step Level 2	Time (H) / step Level 1	Buffer volume / Step	RTP Column volum (L)	Skid
	PRE	Rinse	WFI	10	200	1,00	7,9	42,4	319	31,81	Akta ready gradiant
		Equilibration	0.4 M NaCl	10	200	1,00			319		
		Packing assessment	1.0 M NaCl	0,025	20	0,03			1		
		Rinse	WFI	10	200	1,00			319		
		Sanitisation	0.5 M NaOH	10	200	1,00			319		
		Sanitisation	0.5 M NaOH	#N/A	#N/A	0,50			#N/A		
		Rinse	WFI	10	200	1,00			319		
		Regeneration	2.0 M NaCl	10	200	1,00			319		
		Rinse	WFI	10	200	1,00			319		
		Storage	20% EtOH	3	200	0,30			96		
	RUN	Rinse	WFI	10	200	1,00	11,5		319		
		Equilibration	25mM Tris, 25mM NaCl, pH 7.1	10	200	1,00			319		
		Load	**0.22µm filtered clarified harvest**	#N/A	200	1,92			**610**		
		Wash 1	25mM Tris, 25mM NaCl, pH 7.1	3	200	0,30			96		
		Wash 2	25mM Tris, 1.2M NaCl, pH 7.1	3	200	0,30			96		
		Wash 3	25mM Tris, 25mM NaCl, pH 5.0	3	200	0,30			96		
		Elution	5mM Sodium formate, 0.2M Arginine, pH3.1	3	200	0,30			96		
		Neutralisation	1M Tris pH 9	3	200	0,30			96		
		Stripping	2.0 M NaCl	3	200	0,30			96		
	POS	Rinse	WFI	10	200	1,00	5,8		319		
		Sanitisation	0.5M NaOH	10	200	1,00			319		
		Sanitisation	0.5M NaOH	#N/A	#N/A	0,50			N/A		
		Rinse	WFI	10	200	1,00			319		
		Regeneration	2.0M NaCl	10	200	1,00			319		
		Rinse	WFI	10	200	1,00			319		
		Storage	20% Ethanol	3	200	0,30			96		

Adjustment 1	Technology Name	Equivalent volume	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)
	SUM	0,02	100%	**4**	**1789**	**505**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Time (H) / step Level 3	Buffer volume / Step	
	RUN	pH adjustment	2M acetic acid	0,5	10	

Viral Inactivation	Technology Name	Targeted Protein Concentration (g/L) before next step	Equivalent volume	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)
	SUM	#N/A	0,1	100%	**3**	**1789**	**560**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Time (H) / step Level 3	Time (H) / step Level 2	Time (H) / step Level 1	Buffer volume / Step
	RUN	Inactivation	20% Octoxynol-100	0,5	8	8,56	50
		Inactivation hold	N/A	7			N/A
		Neutralisation	1M Tris pH 9	0,5			56

Adjustment 2	Technology Name	Targeted Protein Concentration (g/L) before next step	Equivalent volume	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)	Pump flowrate (LPM)
	SUM	#N/A	0,5	100%	**2,1**	**1789**	**840**	26
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Time (H) / step Level 3	Buffer volume / Step			
	RUN	Conductivity adjustement	20mM Sodium Acetate, 30mM NaCl, pH 6.0	0,2	280			

Cation Exchange Chromatography	Technology Name	Protein Load (g/L)	Resin (L) or Membrane (L or s.m.) volume	Run Number	Effective Elution volume	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)	Column diameter (cm)	Bed heigh (cm)
	Capto S	90	20	1	5	90%	**16**	**1611**	**99**	35,9	20
B/E Mode	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	VC or MV	Linear flow rate (cm/h or MV/min) or LMH	Time (H) / step Level 3	Time (H) / step Level 2	Time (H) / step Level 1	Buffer volume / Step	RTP Column volum (L)	Skid
	PRE	Rinse	WFI	10	200	0,98	8	19	199	20,24	Akta ready gradiant
		Equilibration	0.4M NaCl	10	200	0,98			199		
		Packing assessment	1.0M NaCl	0,025	200	0,00			1		
		Rinse	WFI	10	200	0,98			199		
		Sanitisation	0.5M NaOH	10	200	0,98			199		
		Sanitisation	0.5M NaOH	#N/A	#N/A	0,5			#N/A		
		Rinse	WFI	10	200	0,98			199		
		Regeneration	2.0M NaCl	10	200	0,98			199		
		Rinse	WFI	10	200	0,98			199		
		Storage	0.2M Sodium Acetate/20% Ethanol	3	200	0,30			60		
	RUN	Rinse	WFI	10	200	0,98	6		199		
		Equilibration	20mM Sodium Acetate, 30mM NaCl, pH 6.0	10	200	0,98			199		
		Load	Inactivated product adjusted to 5 mS/cm	#N/A	200	2,08			420		
		Wash 1	20mM Sodium Acetate, 30mM NaCl, pH 6.0	13	200	1,28			259		
		Elution	20mM Tris, 160mM NaCl, pH 7.0	3	200	0,30			60		
		Stripping	2.0 M NaCl	3	200	0,30			60		
	POS	Rinse	WFI	10	200	0,98	6		199		
		Sanitisation	0.5M NaOH	10	200	0,98			199		
		Sanitisation	0.5M NaOH	#N/A	#N/A	0,5			N/A		
		Rinse	WFI	10	200	0,98			199		
		Regeneration	2.0M NaCl	10	200	0,98			199		
		Rinse	WFI	10	200	0,98			199		
		Storage	0.2M Sodium Acetate/20% Ethanol	3	200	0,30			60		

SOLUTION PREPARATION DATA SHEET

Security factor	Medium, Buffer Type	Buffer Volume /	Container type	Palletank number	Buffer Weight (Kg) /Palletank	Component #1 Name	Component #1 weight (g) / 1	Component #1 weight (g)	Component #2 Name	Component #2 weight (g) / 1 Kg	Component #2 weight (g)	Component #3 Name	Component #3 weight (g) / 1 Kg buffer	Component #3 weight (g)	Component #4 Name	Component #4 weight (g) / 1 Kg buffer	Component #4 weight (g)
1,1	Affinity chromatography																
	WFI	4211	500	9	468			0			0			0			0
	0.4 M NaCl	351	500	1	351	Sodium chloride	23,378	8 203			0			0			0
	1.0 M NaCl	1	10	1	2	Sodium chloride	58,44	64			0			0			0
	0.5 M NaOH	1053	500	3	351	Sodium hydroxide	20	21 054			0			0			0
	2.0 M NaCl	1264	500	3	422	Sodium chloride	116,88	147 725			0			0			0
	20% Ethanol	317	500	1	317	EtOH	0,158	50			0			0			0
	25mM Tris, 25mM NaCl, pH 7.1	913	500	2	457	Tris	3,03	2 766	Sodium chloride	1,46	1 333			0			0
	25mM Tris, 1.2M NaCl, pH 7.1	211	500	1	212	Tris	3,03	640	Sodium chloride	70,13	14 811			0			0
	5mM Sodium formate, 0.2M Arginine, pH3.1	211	500	1	212	Sodium formate	0,34	72	L-Arginine	34,84	7 358	37% Hydrogen chloride		0			0
	1M Tris pH 9	211	500	1	212	Tris	121,14	25 585	37% Hydrogen chloride		0			0			0
	25mM Tris, 25mM NaCl, pH 5.0	211	500	1	212	Tris	3,03	640	Sodium chloride	1,46	308			0			0
	Adjustment 1																
	2M acetic acid	11	20	1	11	Sodium formate	0,34	4			0			0			0
	Viral Inactivation																
	20% Octoxynol-100	61	100	1	62	Triton X100	200	12 212			0			0			0
	1M Tris pH 9	61	100	1	62	Tris	121,14	7 397			0			0			0
	Adjustment 2																
	20mM Sodium Acetate, 30mM NaCl, pH 6.0	308	500	1	309	Sodium acetate	2,72	838	Sodium chloride	1,75	539			0			0
	Cation Exchange Chromatography																
	WFI	1751	500	4	438			0,00			0,00			0,00			0,00
	0.4M NaCl	219	500	1	219	Sodium chloride	23,378	5 117,44			0,00			0,00			0,00
	1.0M NaCl	1	10	1	2	Sodium chloride	58,44	64,28			0,00			0,00			0,00
	0.5M NaOH	438	500	1	438	Sodium hydroxide	20	8 756,00			0,00			0,00			0,00
	0.2M Sodium Acetate/20% Ethanol	132	200	1	132	Sodium acetate	27,22	3 593,04	EtOH	166	21 912,00			0,00			0,00
	20mM Sodium Acetate, 30mM NaCl, pH 6.0	504	500	2	252	Sodium acetate	2,72	1 370,34	Sodium chloride	1,75	881,65			0,00			0,00
	20mM Tris, 160mM NaCl, pH 7.0	66	100	1	66	Tris	2,42	159,72	Sodium chloride	9,35	617,10			0,00			0,00
	2.0M NaCl	504	500	2	252	Sodium chloride	116,88	58 884,14			0,00			0,00			0,00

Client: National Research Council
Date: 2020-11-11

[NRC-14] *Downstream process*
Hypothesis: all process parameters and solution formulation are based on typical mAb process // must be confirmed by NRC
If multiple runs are required for chromatography _ only one sanitization between run will be done

DSP DATA SHEET

Process Step - Level 1

Adjustment 3	Technology Name	Osmolality adjustement (mOsm/kg)	Targeted Protein Concentration (g/L) before Osmo adjust.	Dilution Factor for protein concent. Adj.	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)	Pump flowrate (LPM)
	SUM	200	10	**N/A**	100%	**6,1**	**1611**	**266**	26
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Time (H) / step Level 1	Time (H) / step Level 2	Buffer volume / Step			
	RUN	Protein concentration adjustement	20mM Tris, 160mM NaCl, pH 7.0	0,1	0,2	62			
		Osmolality adjustment	50mM Tris, pH8.15	0,1		105			

Anion Exchange Chromatography	Technology Name	Protein liberation (g/MV)	Resin (L) or Membrane (L) volume	Run Number	Capsule type	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)	Débit skid (L/h)
FT Mode	Mustang Q	500	**3,2**	1	5,0	90%	**5,0**	**1449**	**291**	**193**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	VC or MV	Linear flow rate (cm/h or MV/min) or LMH	Time (H) / step Level 3	Time (H) / step Level 2	Time (H) / step Level 1	Buffer volume / Step	
	PRE	Rinse	WFI	50	1	0,83	4,3	4,4	250	
		Sanitisation	0.5M NaOH	50	1	0,83			250	
		Rinse	WFI	50	1	0,83			250	
		Regeneration	2.0M NaCl	50	5	0,17			250	
		Rinse	WFI	50	1	0,83			250	
		Storage	20mM Tris/83mM NaCl, pH8.0	50	1	0,83			250	
	RUN	Equilibration	20mM Tris/83mM NaCl, pH8.0	5	10	0,01	0,1		25	
		Load	CEX eluat adjusted to 10 mS/cm	#N/A	10	0,09			266	
		Buffer flush	20mM Tris/83mM NaCl, pH8.0	5	10	0,01			25	

Nanofiltration	Technology Name	Protein Load (MV)	Membrane (s.m.) volume	Targeted Protein Concentration (g/L) before DF	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)	
	A1HC/Viresolve Pro	1500	**1**	20	90%	**4,1**	**1305**	**316**	
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Volume (L/sq m)	Linear flow rate (cm/h or MV/min) or LMH	Time (H) / step Level 3	Time (H) / step Level 2	Buffer volume / Step	
	RUN	Rinse	WFI	100	90	1,11	4,90	100	
		Equilibration	30mM trisodium citrate, 122mM NaCl, pH6.0	25	90	0,28		25	
		Load	AEX eluat	NA	90	3,23		291	
		Buffer flush	30mM trisodium citrate, 122mM NaCl, pH6.0	25	90	0,28		25	

Ultrafiltration/ Diafiltration	Technology Name	Protein Load (g/s.m.)	Membrane (s.m.) volume	Targeted Protein Concentration (g/L)	DV (L)	Diafiltration Factor	Expected Protein Yield (%)	concentration théorique initiale (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)
	50kDa Pellicon 2 BioMax	150	**9**	**110**	**12,0**	**26,3**	95%	**4**	**1239**	**12**
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Volume (L/sq m)	Linear flow rate (LMH)	Time (H) / step Level 3	Time (H) / step Level 2	Time (H) / step Level 1	Buffer volume / Step	
	PRE	Rinse	WFI	60	50	1,20	2,30	6,99	540	
		Sanitisation	0.5M NaOH (WFI)	25	240	0,10			225	
		Sanitisation	0.5M NaOH	#N/A	#N/A	0,5			N/A	
		Rinse	WFI	60	240	0,25			540	
		Storage	0.1M NaOH (WFI)	60	240	0,25			540	
	RUN	Rinse	WFI	60	50	1,20	3,50		540	
		Equilibration	30mM trisodium citrate, 122mM NaCl, pH6.0	20	50	0,40			180	
		Load	NAN permeat	N/A	50	0,70			316	
		Rinse	30mM trisodium citrate, 122mM NaCl, pH6.0	60	50	1,20			540	
	POS	Rinse	WFI	60	240	0,25	1,19		540	
		Sanitisation	0.5M NaOH	25	240	0,10			225	
		Sanitisation	0.5M NaOH	60	#N/A	0,5			0	
		Rinse	WFI	60	240	0,25			540	
		Storage	0.1M NaOH ((WFI)	20	240	0,08			180	

Adjustment 4	Technology Name	Targeted 80PS concentration (g/L)	Targeted Protein Concentration (g/L)	Dilution Factor	Expected Protein Yield (%)	Expected Final Protein Concentration (g/L)	Expected Final Total Protein Amount (g)	Expected Final Volume (L)	Pump flowrate (LPM)
	SUM	0,4	100,0	**1,5**	100%	**49,2**	**1305**	25	26
	Process Step - Level 2	Process step - Level 3	Solution or Buffer type	Time (H) / step Level 3	Time (H) / step Level 2	Buffer volume / Step			
	RUN	80PS adjustement	10 g/L PS80	0,1	0,2	1			
		Protein concentration adjustement	30mM trisodium citrate/122mM NaCl/400 mg/L	0,1		13			

SOLUTION PREPARATION DATA SHEET

Security factor	Medium, Buffer Type	Buffer Volume /	Container type	Palletank number	Buffer Weight (Kg) /Palletank	Component #1 Name	Component #1 weight (g) / 1	Component #1 weight (g)	Component #2 Name	Component #2 weight (g) / 1 Kg	Component #2 weight (g)	Component #3 Name	Component #3 weight (g) / 1 Kg buffer	Component #3 weight (g)	Component #4 Name	Component #4 weight (g) / 1 Kg buffer	Component #4 weight (g)
1,1	Adjustment 3																
	20mM Tris, 160mM NaCl, pH 7.0	68	100	1	68	Tris	2,42	164,08	Sodium Chloride	9,35	633,94			0,00			0,00
	50mM Tris, pH8.15	115	200	1	116	Tris	3,42	393,82			0,00			0,00			0,00
	Anion Exchange Chromatography																
	WFI	825	500	2	413			0,00			0,00			0,00			0,00
	0.5M NaOH	275	500	1	275	Sodium hydroxide	20	5 500,00			0,00			0,00			0,00
	2.0M NaCl	275	500	1	275	Sodium chloride	58,44	16 071,00			0,00			0,00			0,00
	20mM Tris/83mM NaCl, pH8.0	330	500	1	330	Tris	2,42	798,60	Sodium chloride	4,85	1 600,50			0,00			0,00
	Nanofiltration																
	WFI	110	200	1	110			0,00			0,00			0,00			0,00
	30mM trisodium citrate, 122mM NaCl, pH6.0	55	100	1	55	Sodium citrate	7,65	420,75	Citric acid	0,84	46,20	Sodium chloride	7,13	392,15			0,00
	Ultrafiltration/ Diafiltration																
	WFI	2970	500	6	495			0,00			0,00			0,00			0,00
	0.5M NaOH (WFI)	495	500	1	495	Sodium hydroxide	20	9 900,00			0,00			0,00			0,00
	0.1M NaOH (WFI)	792	500	2	396	Sodium chloride	58,44	46 284,48			0,00			0,00			0,00
	30mM trisodium citrate, 122mM NaCl, pH6.0	792	500	2	396	Sodium citrate	7,65	6 058,80	Citric acid	0,84	665,28	Sodium chloride	7,13	2 823,48			0,00
	Adjustment 4																
	10 g/L PS80	1	10	1	1	Sodium citrate	7,65	4,21	Citric acid	0,84	0,46	Sodium chloride	7,13	7,13	PS80	10	42,08
	30mM trisodium citrate/122mM NaCl/400 mg/L polysorbate 80, pH 6.0,	14	20	1	14	Sodium citrate	7,65	106,87	Citric acid	0,84	11,73	Sodium chloride	7,13	99,82	10g/L PS80	40,32	4 309,02

Client: National Research Council
Date: 2020-11-11

[NRC-14] *Process Water Balance*

Legend: Worst case
Total for 1 batch

Hypothesis: solution using for step preparation are not concidering as biological contaminated liquid waste

Room	SUBCULTURE	UPSTREAM			DOWNSTREAM 1			DOWNSTREAM 2					BULK FILLING		TOTAL
Process Step	Subculture	Cell amplification	mAb production	Harvest and clarification	Affinity chromatography	Adjustment 1	Viral Inactivation	Adjustment 2	Cation Exchange Chromatography	Adjustment 3	Anion Exchange Chromatography	Nanofiltration	Adjustment 4	Ultrafiltration/ Diafiltration	
Total volum of solution (L) *Needs in prepration room*	7	50	550	303	4743	11	122	308	1863	183	880	55	15	2079	11168
Total WFI direct (L) *Needs in production rooms*	0	0	0	726	4211	0	0	0	1751	0	825	110	0	2970	10593
Final Volum (L)	4	50	500	610	495	505	560	840	99	266	291	316	25	12	N/A
Liquide Waste (L)	3	0	50	919	9069	1	67	28	4355	17	1680	140	305	5062	21696
including Biological waste (L)	3	0	0	0	2924	0	0	0	2153	0	25	0	0	2893	7998

NRC-10-PRO-NDC-06

Production Schedule

Date: 2020-11-18

Area	Room	Equipment	Activity	Production Day D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19	D20	D21	D22	D23	D24	D25	D26	D27	D28	D29	D30	D31	D32	D33	D34	D35	D36	D37	D38	D39	D40	D41	D42	D43	D44	D45	D46	D47	D48	D49
Support	**Weighing**		Powder																																																	
		Small volum system	10L Media for Subculture																																																	
			6L 7.5% Sodium Bicarbonate - Cell amplification																																																
			1L 1,0M NaCl - Affinity Chromatography																																																
			1L 1,0M NaCL- Cation exchange chromatography																																																
			7L 30mM trisodium citrate, 122mM NaCl, pH6,0																																																
			1L 10g/L PS80 - Adjustment 4																																																
		Mixer 50L	50L BalanCD CHO Growth A Medium D-01 - Cell amplification																																																
			11L Cell boost b - mAb production																																																
			22L Glucose 450 g/L - mAb production																																																
			22L 7.5% Sodium Bicarbonate - mAB production																																															
			11L 2M acetic acid - Adjustment 1																																															
			13L 30mM trisodium citrate/122mM NaCl/400 mg/L polysorbate 80, pH 6.0, - Adjustment 4																																															
		Mixer 100L	105L 2,0M NaCL - Affinity Chromatography stripping run 1																																															
			105L 2,0M NaCL - Affinity Chromatography stripping run 2																																															
			61L 20% Octoxynol-100 - Viral Inactivation																																														
			61L 1M Tris pH9 - Viral Inactivation																																														
			66L 20mM Tris, 160mM NaCl, pH7,0 - Cation exchange chromatography																																														
			68L 20mM Tris, 160mM NaCl, pH 7,0 - Adjustument 3																																														
			55L - 30mM trisodium citrate, 122mM NaCl, pH6.0 - Nanofiltration																																														
		Mixer 200L	110L Cell boost a - mAb production																																														
			211L 25mM Tris, 1,2M NaCl, pH 7,1 - Affinity Chromatography run 1 +2																																														
			211L 5mM Sodium formate, 0.2M Arginine, pH3.1 - Affinity Chromatography run 1 +2																																														
			211L 1M Tris pH 9 - Affinity Chromatography run 1 +2																																														
			211L 25mM Tris, 25mM NaCl, pH 5.0 - Affinity Chromatography run 1 +2																																														
	Preparation 1		132L 0,2M Sodium Acetate / 20 %Ethanol - Cation exchange chromatography																																														
			115L 50mM Tris, pH 8,15 - Adjustment 3																																														
		Mixer 500L	385L BalanCD CHO Growth A Medium - mAb production																																														
			300L DPBS - Harvest and clarification																																															
			351L 0,4M NaCl - Affinity Chromatography																																														
			351L 0,5M NaOH - Affinity Chromatography prep																																														
			351L 0,5M NaOH - Affinity Chromatography sanit run 1																																														
			351L 0,5M NaOH - Affinity Chromatography sanit run 2																																														
			351L 2,0M NaCL - Affinity Chromatography prep																																														
			351L 2,0M NaCL - Affinity Chromatography sanit run 1																																														
			351L 2,0M NaCL - Affinity Chromatography sanit run 2																																														
			457L 25mM Tris, 25mM NaCl, pH 7.1 - Affinity chromatography run 1																																														
			457L 25mM Tris, 25mM NaCl, pH 7.1 - Affinity chromatography run 2																																														
			308L 20mM Sodium Acetate, 30 mM NaCl, pH6,0 - adjustment 2																																														
			219L 0,4M NaCl - Cation exchange chromatography																																														
			438L 0,5M NaOH - Cation exchange chromatography																																														
			504L 20mM Sodium Acetate, 30mM NaCl, pH 6.0 - Cation exchange chromatography																																														
			504L 2,0M NaCl - Cation exchange chromatography																																														
			275L 0,5M NaOH - Anion exchange chromatography																																														
			275L 2,0M NaCl - Anion exchange chromatography																																														
			330L 20mM Tris/83mM NaCl, pH 8,0 - Anion exchange chromatography																																														
			495L 0,5M NaOH - UF/DF																																														
			396L 0,1M NaOh - UF/DF																																														
			396L 0,1M NaOh - UF/DF																																														
			396L 30mN trisodium citrate, 122mM NaCl, pH6 - UF/DF																																														
			396L 30mN trisodium citrate, 122mM NaCl, pH6 - UF/DF																																														
	Decontamination		Autoclave																																														
	Cleaning		Reusable glassware cleaning for SUbculture																																														
			DSP small part cleaning																																														
			Prepration small parts cleaning																																														
	Sterlization		Stérilisation montage																																														

NRC-10-PRO-NDC-06

Production Schedule

Client: National Research Council
Date: 2020-11-18

Area	Room	Equipment	Activity	Production Day D1	D2	D3	D4	D5	D6	D7	D8	D9	D10	D11	D12	D13	D14	D15	D16	D17	D18	D19	D20	D21	D22	D23	D24	D25	D26	D27	D28	D29	D30	D31	D32	D33	D34	D35	D36	D37	D38	D39	D40	D41	D42	D43	D44	D45	D46	D47	D48	D49
PRODUCTION 1	**Subculture**		Room preparation																																																	
			Cell thawing (37°C, SS5min)																																																	
			SUb-culture erlen 50mL (37°C, 5% CO2)																																																
			SUb-culture erlen 50mL (37°C, 5% CO2)																																																
			SUb-culture erlen 400mL (37°C, 5% CO2)																																																
			SUb-culture erlen 1000L (37°C, 5% CO2)																																																
			Room clearance																																																	
	Upstream		Room preparation																																																
			SU Bioreactor 50L preparation																																																	
			SU Bioreactor 50L inoculation and expansion																																																
			Culture transfer to 500L bioreactor																																																
			SU Bioreactor 50L clearance																																																
			SU Bioreactor 500L preparation																																																
			SU Bioreactor 500L medium addition																																															
			SU Bioreactor 500L inoculation and expansion																																															
			SU Bioreactor 500L clearance																																															
			Harvest through clarification																																															
			Product storage in jacketed tank																																															
			Transfer to DSP																																															
			Room clearance																																																
	Downstream 1		Room preparation																																															
			Affinity Chromatography preparation																																															
			Affinity Chromatography run 1																																															
			Affinity Chromatography Sanitisation																																															
			Affinity Chromatography run 2																																															
			Affinity Chromatography Sanitisation																																															
			Adjustment 1																																															
			Viral Inactivation																																															
			Transfer to DSP 2																																															
			Room clearance																																															
	Downstream 2		Room preparation																																															
			Reception/pooling - adjustment 2																																															
			Cation Exchange Chromatography preparation																																															
			Cation Exchange Chromatography run 1																																															
			Cation ExchangeChromatography Sanitisation																																															
			Adjustment 3																																															
			Anion Exchange Chromatography preparation																																															
			Anion Exchange Chromatography run 1																																															
			Anion ExchangeChromatography Sanitisation																																															
			Nanofiltration																																															
			Transfert to Bulk Filling room																																															
			Room clearance																																															
	Bulk Filling		Room preparation																																															
			Reception																																																
			UF/DF preparation																																															
			Concentration diafiltration UF/DF																																															
			Product adjustment 4 and exipient addition																																															
			Filtration 0,22micron and DS bag filling																																															
			Transfert to IP storage or cold room																																															
			Room clearance																																															

Hypothesis:

1- 2h for one preparation then 4 preparation per shift
2- 20 days of Subculture
3- Preparation could be in parallel of production (dedicated team)
4- 2 days of batch preparation (room cleaning, raw material Supply)
5- 1 day room clearance after batch
6- No Support operation during weekend
7- Production 7j/7
8- Similar preparation schedule per week
9- 15 days of mAb production
10- Maximum 5 preparations per day

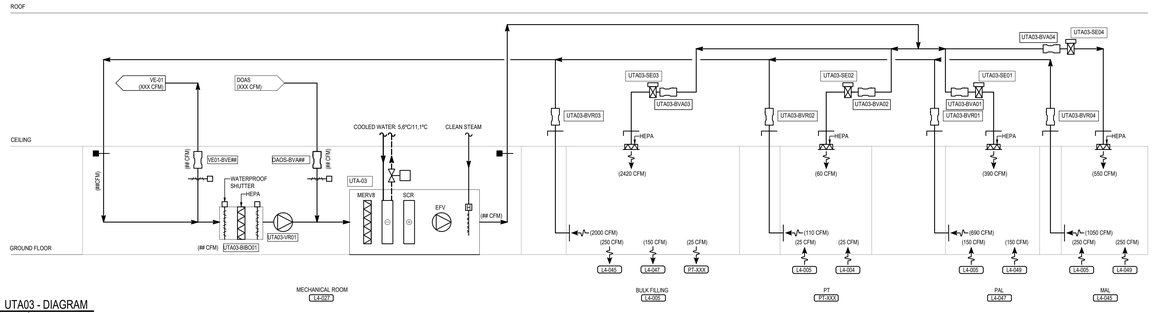
Legend:

- Support
- Product batch suite 1
- Equipment preparation/clearance
- Room preparation/clearance
- Minimum worker time
- Worstcase week - basis of design

References:

NRC-14-NDC-03 (mass balance mAb)

APPENDIX E: MECHANICAL



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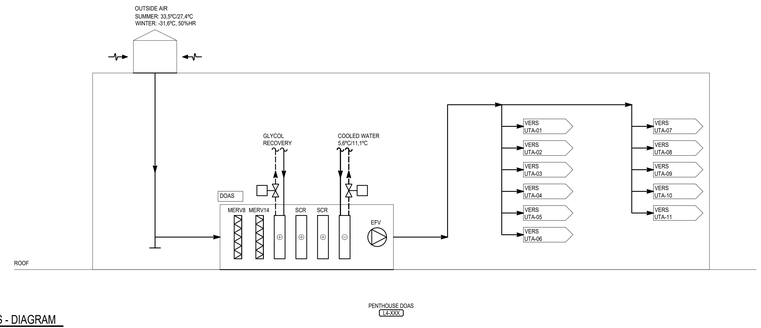
ÉCHELLE: N.T.S.



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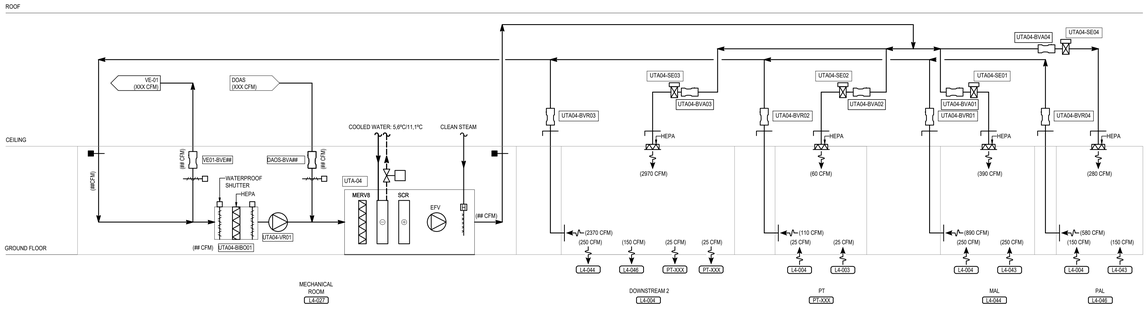

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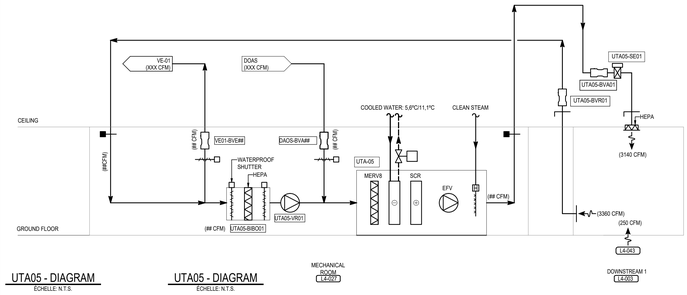

UTA05 - DIAGRAM
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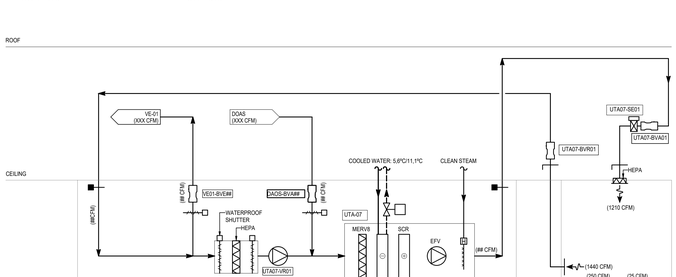

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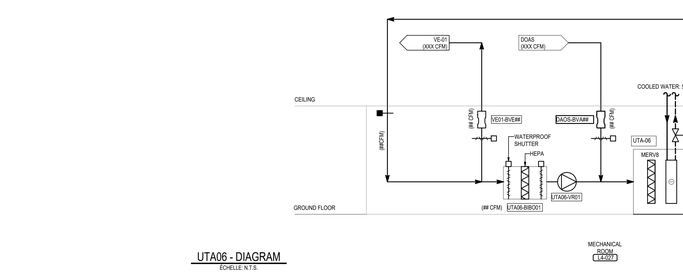

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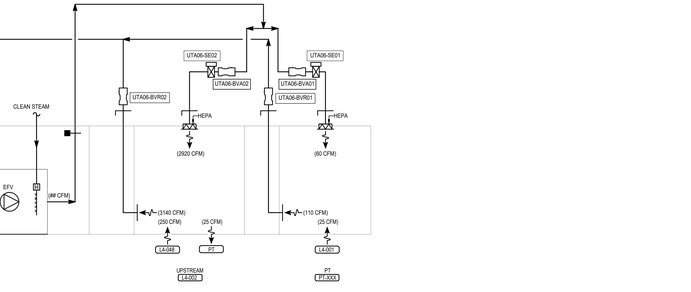

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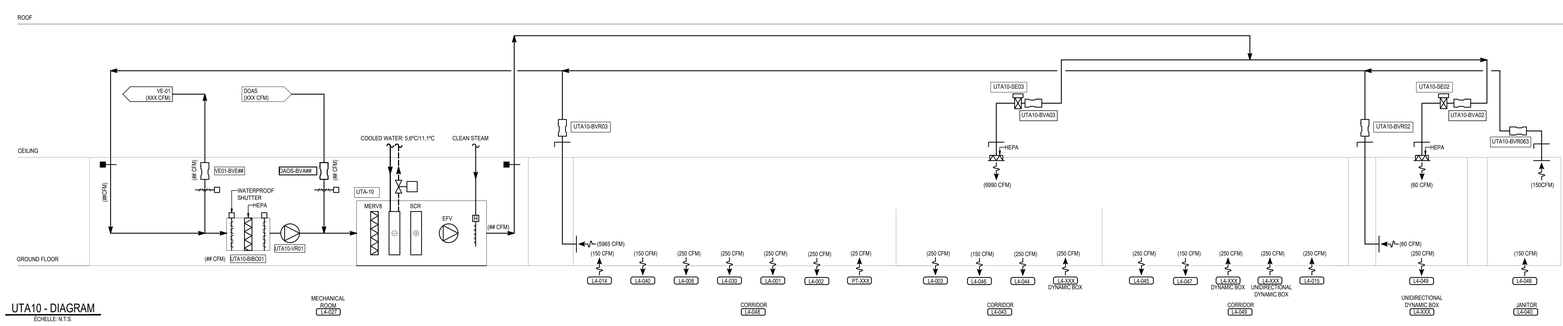

UTA10 - DIAGRAM
ÉCHELLE: N.T.S.

UTA06 - DIAGRAM
ÉCHELLE: N.T.S.

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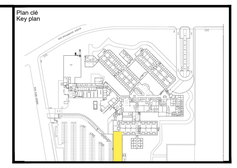
Plan clé
Key plan



Notes:

N°	Date	Par Drawn by	Révision Revision	Ver. par. Ch'd by
00	2020-11-27	J.P.	ISSUED FOR FEASIBILITY STUDY	J.M.C.

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Approuvé Approved	Date

Sceaux
Seals

Canada
NRC·CNRC

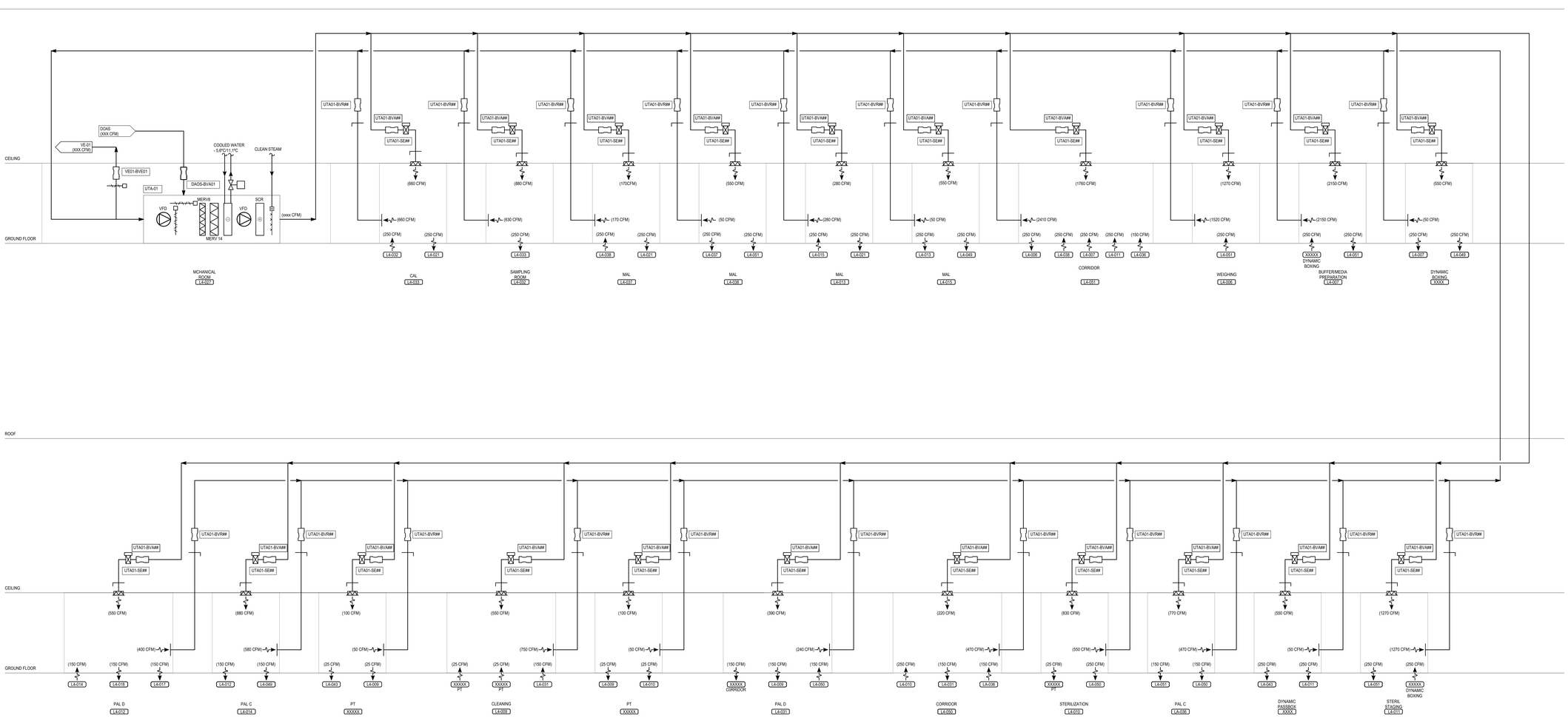
Projet
Project
FEASIBILITY STUDY
FOR CLINICAL TRIAL
MATERIAL FACILITY

Dessin
Drawing
VENTILATION
DIAGRAM DOAS
UTA-03/04/05/06/07/08/09/10

Date	2020-11-25	Échelle Scale	AS NOTED	Format Size	A0

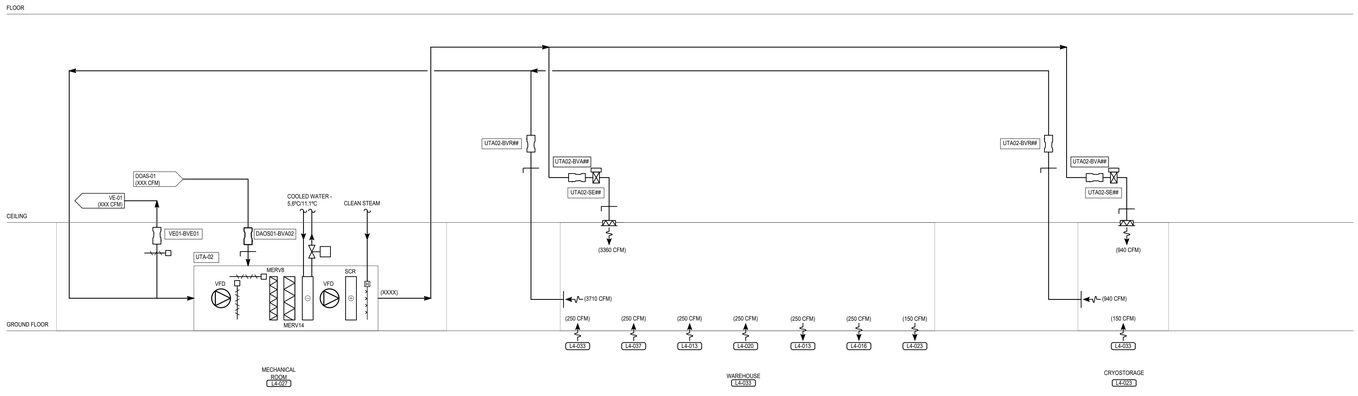
Projet Project	NRC-14	Dessin Drawing	VEN-001	Rév. Rev.	00

50 10 0 mm



UTA01 - DIAGRAM

SCALE: N.T.S.



UTA02 - DIAGRAM

SCALE: N.T.S.

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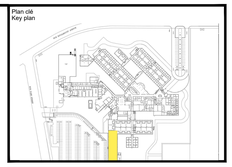
Plan clé
Key plan



Notes:

N°	Date	Par Drawn by	Révision Revision	Ver. par CM'd by
00	2020-11-27	F.A.S.	ISSUED FOR FEASIBILITY STUDY	D.G.

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Approuvé Approved	Date

Sceaux Seals

Canada NRC·CNRC

Projet Project: FEASIBILITY STUDY FOR CLINICAL TRIAL MATERIAL FACILITY

Dessin Drawing: VENTILATION UTA-01 / UTA-02 DIAGRAM

Date	Échelle Scale	Format Size
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Projet Project	Dessin Drawing	Rév. Rev.
NRC-14	VEN-002	00

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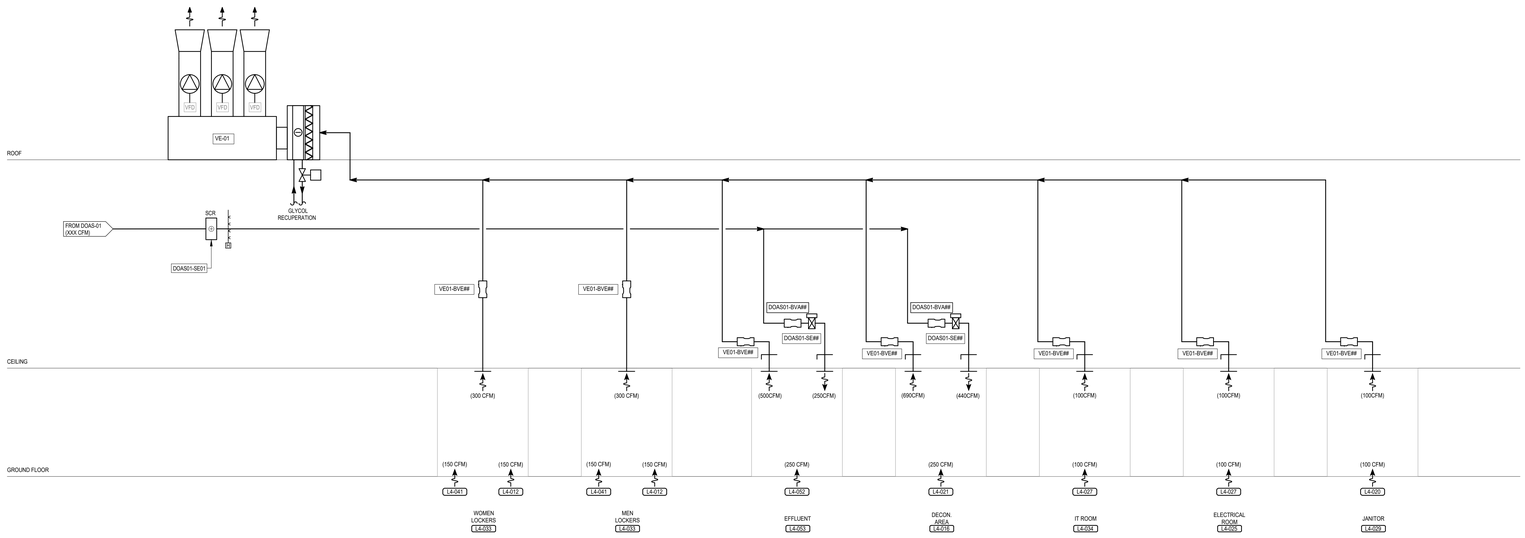
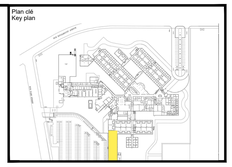


Plan clé
Key plan



Notes:

N°	Date	Par Drawn by	Révision Revision	Ver. par. Ch'kd by
00	2020-11-27	F.A.S.	ISSUED FOR FEASIBILITY STUDY	D.G.

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Sceaux
Seals

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NRC·CNRC

Projet
Project

FEASABILITY STUDY
FOR CLINICAL TRIAL
MATERIAL FACILITY

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Dessin
Drawing

VENTILATION
UTA-11 (DOAS01)
DIAGRAM

Date	2020-11-25	Échelle Scale	N.T.S.	Format Size	A0

Projet Project	NRC-14	Dessin Drawing	VEN-003	Rév. Rev.	00

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APPENDIX F: ELECTRICAL

APPENDIX G: BUDGET

Client: National Research Center
Project: CTMF
Description: Project Cost Estimate

Date: 2020-11-27

CTMF at NRC's facility cost estimate (+- 15%)

	Unit cost		Qty	Total cost
PROCESS EQUIPMENT, QC LABORATORY EQUIPMENT & AUTOMATION				
NEW QUALITY CONTROL LABORATORY				
QC Laboratory equipment (refer to Process equipment list for details)				972 000 $
Installation and rigging				49 000 $
Initial calibration (8% of laboratory equipment)				78 000 $
SUB-TOTAL - QUALITY CONTROL LABORATORY				1 099 000 $
NEW SUPPORTING EQUIPMENT				
Support Equipment (refer to Process equipment list for details)				4 363 000 $
Installation and rigging				218 000 $
SUB-TOTAL - NEW SUPPORTING EQUIPMENT				4 581 000 $
PROCESS EQUIPMENT				
Process equipment (refer to Process equipment list for details)				1 624 000 $
Installation and rigging of fixed process equipment				81 000 $
SUB-TOTAL - NEW SUPPORTING EQUIPMENT				1 705 000 $
AUTOMATION				
Manufacturing IT (3 x HPE DL360 servers, Centralized storage, 2 x Nexus Core Switches, 10 x Catalyst Dist. Switches, Firewall, Security appliances, Support contracts, Licensing, Software, Config & Installation) Wifi and Telephony system excluded.				615 000 $
Data historian (2 500 tags, EMS not included)				280 000 $
Environmental Monitoring System (ΔP, Tº, %RH, non viable particles counters)	4 200 $ /point		100	420 000 $
Quality System Software				80 000 $
Warehouse Management System				50 000 $
SUB-TOTAL - AUTOMATION				1 445 000 $
DIRECT COSTS - PROCESS EQUIPMENT, QC LABORATORY EQUIPMENT & AUTOMATION				**8 830 000 $**
MECHANICAL & ELECTRICAL				
CLEAN UTILITIES				
Purified water production system (pre-treatment, RO, EDI, TOC analyzer, 2000L storage tank, 35 gpm distribution pump, UV lamp, validation package)				Included in process
Purified water loop (Piping) (1 1/2'' 20 Ra SS, 12 point of uses with manual diaphragm valves)				186 000 $
Clean steam piping 1 1/2'' stainless steel, 4 point of uses, portable sample cooler				16 000 $
Biological effluent piping and accessories				16 000 $
Pure steam and Water for Injection production system				Included in process
Water for injection loop (Piping)				472 436 $
SUB-TOTAL - CLEAN UTILITIES				690 000 $
MECHANICAL				
Plumbing				650 500 $
Heating, Ventilation and air-conditioning (HVAC)				2 715 000 $
Instrumentation and control (BMS)				584 500 $
Fire protection				96 000 $
SUB-TOTAL - MECHANICAL SERVICES				4 046 000 $
ELECTRICAL SERVICES				
Electrical outlet				105 686 $
Services and lighting				151 586 $
Electrical distribution				391 279 $
Motor and equipment electrical hook-up				54 054 $
Telecommunication/computer network				8 518 $
Access control				56 780 $
Monitoring cameras				6 448 $
Fire alarm				30 419 $
SUB-TOTAL - ELECTRICAL SERVICES				804 769 $
DIRECT COSTS - MECHANICAL & ELECTRICAL				**5 540 769 $**
CONSTRUCTION				
ROOF				
Roof				72 000 $
SUB-TOTAL - ROOF				72 000 $
ARCHITECTURE				
Construction of new shell for extension	ft2	2 860		179 000 $
Construction of new GMP cleanrooms for production (prefab walls, ceiling, HEPA diffusers, lighting fixtures)	ft2	8 570		3 171 000 $
Construction of lockers, corridor 1st floor	ft2	599		56 000 $
Construction of new 2nd floor labs (prefab walls, ceiling, HEPA diffusers, lighting fixtures)	ft2	1 038		364 000 $
Construction of new warehouse	ft2	2 530		316 000 $
Construction of new interior for extension	ft2	2 860		179 000 $
Demolition of existing	Ft2	11 699		1 462 000 $
SUB-TOTAL - ARCHITECTURE				5 727 000 $
STRUCTURE				
Excavation, footing and slab for new extension				100 000 $
Steelwork				114 400 $
SUB-TOTAL - STRUCTURE				214 400 $
CIVIL				
Allocation for civil work				100 000 $
SUB-TOTAL - CIVIL				100 000 $
GENERAL EQUIPMENT AND FURNITURE				
Warehouse racking, quarantine cage, pedestrian barriers, mirrors, etc.				Included in process
Lift truck (electric forklift, charger and battery)				50 000 $
Elevator for samples (from warehouse to second floor)	200 000 $		1	200 000 $
Misc. Equipment and furniture (carts, inspection tables, PAL furniture for gowning, desks and chairs, etc.)				306 000 $
Cold rooms (1 in the warehouse)	40 000 $		1	40 000 $
Benches for the production area and QC Lab				Included in Misc. Equipement
SUB-TOTAL - GENERAL FURNITURE				596 000 $
DIRECT COSTS - CONSTRUCTION				**6 709 400 $**
DIRECT COSTS - PROCESS EQUIPMENT, QC LABORATORY EQUIPMENT & AUTOMATION				**8 830 000 $**
DIRECT COSTS - MECHANICAL & ELECTRICAL				**5 540 769 $**
DIRECT COSTS - ARCHITECTURE/CONSTRUCTION				**6 709 400 $**
SUB-TOTAL - DIRECT COST				**21 080 169 $**
General site conditions (Covid-19, assurances, trailer rental, toilets, fences, waste disposal, temporary services, etc.)				659 000 $
Construction Manager employees salary	16 000 $ /week		39	624 000 $
Construction Manager (management + administration + profits) (3,5%)				536 000 $
Detailed design and site support - architecture, structure, civil, electrical, mechanical, clean utilities (12%)				1 470 000 $
Validation (URS, VMP, Validation protocol, execution)				827 506 $
SUB-TOTAL - INDIRECT COST				**4 117 000 $**
SUB-TOTAL - GMP BIOMANUFACTURING AT NRC'S FACILITY (DIRECT + INDIRECT COSTS)				**25 197 000 $**
Miscellaneous/unforeseen (15%)				**3 780 000 $**
TOTAL - GMP BIOMANUFACTURING AT NRC'S FACILITY				**28 977 000 $**

Client: National Research Center
Project: CTMF
Description: Process Equipment Cost Estimate

Date: 2020-11-27

Rate 1 USD = 1,36 CAD

Process Equipment List

Room	Equipment	Model	Quantity	Existing	Cost/unit	Cost
Subculture	Large Stackable Incubated Orbital Shaker #1	Thermo Scientific™ MaxQ™ 8000 Incubated/Refrigerated Stackable Shakers	1	To be purchased	77 600,00 $	77 600,00 $
Subculture	Large Stackable Incubated Orbital Shaker #2	Thermo Scientific™ MaxQ™ 8000 Incubated/Refrigerated Stackable Shakers	1	To be purchased	77 600,00 $	77 600,00 $
Subculture	Large Stackable Incubated Orbital Shaker #3	Thermo Scientific™ MaxQ™ 8000 Incubated/Refrigerated Stackable Shakers	1	To be purchased	77 600,00 $	77 600,00 $
Subculture	Biosafetycabinet	ThermoFisher 6' (1300 A2)	1	To be purchased	14 111,00 $	14 111,00 $
Subculture	Media storage - fridge	Thermo Scientific™ TSX2305SA	1	To be purchased	7 760,00 $	7 760,00 $
Subculture	Cell counter Cedex	Cedex Hires	1	To be purchased	65 000,00 $	65 000,00 $
Subculture	Microscope	ZEISS Axio Vert.A1	1	To be purchased	5 000,00 $	5 000,00 $
Subculture	Pipetman	N/A	1	To be purchased	650,00 $	650,00 $
Subculture	Balance - under BSC	Sartorius Cubis-II TBench top balance	1	To be purchased	500,00 $	500,00 $
Subculture	Water Bath Flask culture	Fisherbrand™ Isotemp™ Shaking Water Baths	1	To be purchased	3 000,00 $	3 000,00 $
Subculture	Centrifuge for Cell thaw	Heraeus™ Megafuge™ 8 Small Benchtop Centrifuge Series	1	To be purchased	17 934,00 $	17 934,00 $
Upstream	Biosealer	Bioselect TC sartorius	1	To be purchased	20 000,00 $	20 000,00 $
Upstream	Bioreactor room BioWelder	Sartorius	1	To be purchased	56 000,00 $	56 000,00 $
Upstream	Biosafetycabinet for sample preparation	ThermoFisher 6' (1300 A2)	1	To be purchased	14 111,00 $	14 111,00 $
Upstream	Water Bath Flask culture	Fisherbrand™ Isotemp™ Shaking Water Baths	1	To be purchased	3 000,00 $	3 000,00 $
Upstream	Centrifuge for Cell thaw	Heraeus™ Megafuge™ 8 Small Benchtop Centrifuge Series	1	To be purchased	17 934,00 $	17 934,00 $
Upstream	Blood gas analyzer	Stat Profile Prime ES Plus analyzer	1	To be purchased	310 000,00 $	310 000,00 $
Upstream	Analyzer metabolite	Cedex Bio	1	To be purchased	68 700,00 $	68 700,00 $
Upstream	Jacketed 500L tank	Palletank® Jacketed	1	To be purchased	1 000,00 $	1 000,00 $
Downstream 1	Magnetic stirrer - intermediate product	20L carboy custom made	1	To be purchased	2 500,00 $	2 500,00 $
Downstream 1	Masterflex L/S Pump system	Masterflex L/S Digital Pump system	1	To be purchased	11 478,00 $	11 478,00 $
Downstream 1	Pipetman G P200G 1	N/A	1	To be purchased	650,00 $	650,00 $
Downstream 1	Pipetman G P200G 2	N/A	1	To be purchased	650,00 $	650,00 $
Downstream 1	Pipetman G P1000G 1	N/A	1	To be purchased	650,00 $	650,00 $
Downstream 1	Pipetman G P1000G 2	N/A	1	To be purchased	650,00 $	650,00 $
Downstream 1	Mixer 10/50L	Mobius mixer Millipore + load cell + 10L adaptator	1	To be purchased	50 000,00 $	50 000,00 $
Downstream 1	Floor scale	500kg scale	1	To be purchased	17 820,00 $	17 820,00 $
Downstream 2	Sartocheck plus - Filter integrity tester	Sartocheck 4 or 5 plus	1	To be purchased	45 000,00 $	45 000,00 $
Downstream 2	Magnetic stirrer - carboy product	20L carboy custom made	1	To be purchased	2 500,00 $	2 500,00 $
Downstream 2	Floor scale	500kg scale	1	To be purchased	17 820,00 $	17 820,00 $
Bulk filling	Floor scale	500kg scale	1	To be purchased	17 820,00 $	17 820,00 $
Bulk filling	Biosafetycabinet	ThermoFisher 6' (1300 A2)	1	To be purchased	14 111,00 $	14 111,00 $
Bulk filling	Biosealer	multisize sealer - sartorius	1	To be purchased	20 000,00 $	20 000,00 $
Bulk filling	BioWelder TC	Biowelder - diffrent adaptor for tube size	1	To be purchased	56 000,00 $	56 000,00 $
Bulk filling	Mixer 50L for stabilizer addition	Mobius mixer Millipore 50L + load cell + 10L adaptator	1	To be purchased	50 000,00 $	50 000,00 $
Bulk filling	Sartocheck plus - Filter integrity tester	Sartocheck 4 or 5 plus	1	To be purchased	45 000,00 $	45 000,00 $
Powder dispensing/ weighing	1 x weighing booth	TBD	1	To be purchased	161 559,00 $	161 559,00 $
Powder dispensing/ weighing	Solvent cabinet	TBD	1	To be purchased	1 500,00 $	1 500,00 $
Powder dispensing/ weighing	Balance 35kg max	Sartorius Cubis	1	To be purchased	8 145,00 $	8 145,00 $
Powder dispensing/ weighing	Balance 12kg max	Sartorius Cubis	1	To be purchased	2 400,00 $	2 400,00 $
Powder dispensing/ weighing	Analytical Balance	Sartorius Cubis	1	To be purchased	9 614,00 $	9 614,00 $
Buffer preparation	500L Mobius Power Mix with Load cell	500L Mobius Power Mix with Load cell	1	To be purchased	80 000,00 $	80 000,00 $
Buffer preparation	200L Mobius Power Mix with Load cell	200L Mobius Power Mix with Load cell	1	To be purchased	75 000,00 $	75 000,00 $
Buffer preparation	100L Mobius Power Mix with Load cell	100L Mobius Power Mix with Load cell	1	To be purchased	45 000,00 $	45 000,00 $
Buffer preparation	10/50L Mobius Power Mix with Load cell	10/50L Mobius Power Mix with Load cell	1	To be purchased	60 000,00 $	60 000,00 $
Buffer preparation	Floor balance	500kg scale	1	To be purchased	17 820,00 $	17 820,00 $
Buffer preparation	Balance 12kg max - for small volum	Sartorius	1	To be purchased	2 400,00 $	2 400,00 $
Buffer preparation	Magnetic stirrer plate	TBD	1	To be purchased	2 500,00 $	2 500,00 $
Buffer preparation	Pump Masterflex 77420-10	Masterflex 77420-10	1	To be purchased	11 478,00 $	11 478,00 $
Buffer preparation	Pump Masterflex 77602-10	Masterflex 77602-10	1	To be purchased	11 478,00 $	11 478,00 $
Buffer preparation	Pump Masterflex 07522-20	Masterflex 07522-20	1	To be purchased	11 478,00 $	11 478,00 $
Buffer preparation	Pump Masterflex 77800-60	Masterflex 77800-60	1	To be purchased	11 478,00 $	11 478,00 $
Buffer preparation	Orion star A215 pH and Conductivity meter (pH meter 2)	VSTAR-50	1	To be purchased	2 250,00 $	2 250,00 $
Buffer preparation	Laminar air flow	2' Purifier HEPA-Filtered Enclosure with Airflow Monitor	1	To be purchased	38 770,00 $	38 770,00 $
Buffer preparation	Sartocheck plus - Filter integrity tester	Sartocheck 4 or 5 plus	1	To be purchased	45 000,00 $	45 000,00 $
Buffer preparation	Extraction arm	FlexAct to be confirmed	1	To be purchased	56 223,00 $	56 223,00 $
Buffer preparation	Filter holder	N/A	1	To be purchased	300,00 $	300,00 $
Buffer preparation	Flexstation 100L x 6	N/A	1	To be purchased	35 088,00 $	35 088,00 $
Buffer preparation	Flexstation 200L x1	N/A	1	To be purchased	5 848,00 $	5 848,00 $
Buffer preparation	Flexstation 50L x 2	N/A	1	To be purchased	11 696,00 $	11 696,00 $
Staging 1 - solution/equipment	Flexstation 1000L	FlexStation 1000	1	To be purchased	6 000,00 $	6 000,00 $
Staging 1 - solution/equipment	Flexstation 1000L	FlexStation 1000	1	To be purchased	6 000,00 $	6 000,00 $
Staging 1 - solution/equipment	BioWelder TC	Biowelder - different adaptor for tube size	1	To be purchased	56 000,00 $	56 000,00 $
Staging 1 - solution/equipment	FS1000 SS Mobile cart	FlexStation 1000	1	To be purchased	6 000,00 $	6 000,00 $
Staging 1 - solution/equipment	FS1000 SS Mobile cart with load cells	FlexStation 1000	1	To be purchased	6 000,00 $	6 000,00 $
Staging 1 - solution/equipment	Flexstation 500L x 5	FlexStation 500	1	To be purchased	29 240,00 $	29 240,00 $
Staging 1 - solution/equipment	Flexstation 200L x 10	FlexStation 200	1	To be purchased	58 480,00 $	58 480,00 $
Staging 1 - solution/equipment	Flexstation 100L x 10	FlexStation 100	1	To be purchased	58 480,00 $	58 480,00 $
Staging 1 - solution/equipment	QuaDrum 50L with bottom drain x 10	Quadrum 50	1	To be purchased	2 500,00 $	2 500,00 $
Staging 1 - solution/equipment	Flex station SS Pallet Truck	N/A	1	To be purchased	2 500,00 $	2 500,00 $
Cleaning	Washer	Steris Reliance 480 PG	1	To be purchased	550 000,00 $	550 000,00 $
Sterilization	Sterilisation autoclave	FINN-AQUA BPS GMP STEAM STERILIZER 6915 WITH DOUBLE DOORS	1	To be purchased	530 000,00 $	530 000,00 $
Sterilization	Laminar air flow	2' Purifier HEPA-Filtered Enclosure with Airflow Monitor	1	To be purchased	38 770,00 $	38 770,00 $
Waste storage / outside	Decontamination autoclave	FINN-AQUA BPS GMP STEAM STERILIZER 91215 WITH DOUBLE DOORS	1	To be purchased	530 000,00 $	530 000,00 $
Cleaning/stérilization	Glass washer	Miele PG 8504	1	To be purchased	17 252,00 $	17 252,00 $
Cleaning/stérilization	Small sterilisation autoclave	Tuttnauer 5075 EL/ML	1	To be purchased	44 747,00 $	44 747,00 $
Janitor	Portable VHP biodecontamination system for cleanroom	N/A	1	To be purchased	288 000,00 $	288 000,00 $
CL2-lab	Biosafetycabinet	ThermoFisher 6' (1300 A2)	1	To be purchased	14 111,00 $	14 111,00 $
CL2-lab	Automatic pipette	N/A	1	To be purchased	650,00 $	650,00 $
CL2-lab	pH-Meter /conductivity meter	N/A	1	To be purchased	4 000,00 $	4 000,00 $
CL2-lab	HPLC /UPLC with fluorescence	Thermo Scientific™ Vanquish™ UHPLC system	1	To be purchased	309 222,00 $	309 222,00 $
CL2-lab	Automated Cell counter	Countess II	1	To be purchased	3 766,00 $	3 766,00 $
CL2-lab	Analytical Balance + printer (marbre plate)	TBD	1	To be purchased	9 614,00 $	9 614,00 $
CL2-lab	Top load Balance + printer	TBD	1	To be purchased	2 322,00 $	2 322,00 $
CL2-lab	Water bath	Fisherbrand™ Isotemp™ Shaking Water Baths	1	To be purchased	6 291,00 $	6 291,00 $
CL2-lab	TOC	QbD1200	1	To be purchased	20 360,00 $	20 360,00 $
CL2-lab	ELISA Plate reader with temperature control	MULTISKAN FC	1	To be purchased	59 900,00 $	59 900,00 $
CL2-lab	Microcentrifuge refrigerated	ROTANTA 460 R	1	To be purchased	17 934,00 $	17 934,00 $
CL2-lab	Conductivity meter for low conductivity water	TBD	1	To be purchased	2 250,00 $	2 250,00 $
CL2-lab	EndoSafe Nexgen-PTS	EndoSafe Nexgen-PTS	1	To be purchased	9 034,00 $	9 034,00 $
CL2-lab	Oven - furnace 25 or 100 - 400 °C - drying, depyrogenization	Heratherm™ General Protocol Ovens	1	To be purchased	2 000,00 $	2 000,00 $
CL2-lab	Large fridge - stability and retained	Thermo Scientific TSX Series Model TSX5005GA	1	To be purchased	10 546,00 $	10 546,00 $
CL2-lab	Large freezer - stability and retained	Thermo Scientific TSX Series High-Performance (TSX2320FA)	1	To be purchased	10 583,00 $	10 583,00 $
CL2-lab	Large ultralow freezer - stability and retained	Thermo Scientific TSX60086A 28.8 cu.ft. Ultra-Low	1	To be purchased	22 085,00 $	22 085,00 $
CL2-lab	incubator 25°C - stability and retained	TBD	1	To be purchased	20 686,00 $	20 686,00 $
CL2-lab	Medium Fridge 4°C - sampling	Thermo Scientific™ TSX2305SA	1	To be purchased	10 546,00 $	10 546,00 $
CL2-lab	Medium Freezer - sampling	Thermo Scientific TSX Series High-Performance (TSX2320FA)	1	To be purchased	10 583,00 $	10 583,00 $
CL2-lab	Ultralow freezer - sampling	Thermo Scientific TSX60086A 28.8 cu.ft. Ultra-Low	1	To be purchased	22 085,00 $	22 085,00 $
Microbiology (env.)	Biosafetycabinet	ThermoFisher 6' (1300 A2)	1	To be purchased	14 111,00 $	14 111,00 $
Microbiology (env.)	static incubator 35degC	Forma™ 3960 Series Environmental Chamber, 821.2 L, Stainless Steel	1	To be purchased	14 500,00 $	14 500,00 $
Microbiology (env.)	incubator 25degC	Forma™ 3960 Series Environmental Chamber, 821.2 L, Stainless Steel	1	To be purchased	14 500,00 $	14 500,00 $
Microbiology (env.)	Large fridge	Thermo Scientific TSX Series Model TSX5005GA	1	To be purchased	10 546,00 $	10 546,00 $
Warehouse	Palet racking (2 Level's)	N/A	1	To be purchased	60 000,00 $	60 000,00 $
Cryostorage	Liquid N2 Cell storage 797L	CryoExtra™ High-Efficiency Cryogenic Storage Systems	1	To be purchased	32 442,00 $	32 442,00 $
Cryostorage	Liquid N2 Cell storage - back up 797L	CryoExtra™ High-Efficiency Cryogenic Storage Systems	1	To be purchased	32 442,00 $	32 442,00 $
Cryostorage	Liquid nitrogen supply tank	CryoExtra™ High-Efficiency Cryogenic Storage Systems	1	To be purchased	32 442,00 $	32 442,00 $
Cryostorage	Large freezer - 20 back up	Thermo Scientific TSX Series High-Performance (TSX2320FA)	1	To be purchased	10 583,00 $	10 583,00 $
Clean utilities	WFI system / pure steam generator	Combi Stilmas	1	To be purchased	476 400,00 $	476 400,00 $
Clean utilities	WFI storage	Stilmas	1	To be purchased	90 000,00 $	90 000,00 $
Clean utilities	Purified water system Generation and storage	LSX	1	To be purchased	736 735,00 $	736 735,00 $

APPENDIX H: SCHEDULE

Client: National Research Center
Project: CTMF
Description: Project Schedule
Date: 2020-11-27

Task	End date	December	January	February	March	April	May	June	July	August	September	October	November	December	January 22	February 22
Contract awarding	31 DEC 2020															
Detailled design	27 OCT 2021															
Construction (phased)	27 OCT 2021															
Construction of extension shell and interior walls	02 JUL 2021															
Removal of tenants (progressive)	26 MAR 2021															
Removing of fermentation lab	26 MAR 2021															
Removing of fill and finish	30 APR 2021															
Demolition of existing	28 MAY 2021															
Qc lab revamping	02 JUL 2021															
Installation of drainage	30 JUL 2021															
Installation of cleanrooms and support rooms*	01 SEP 2021															
Introduction of equipment	26 NOV 2021															
Installation of racking and cold room	01 SEP 2021															
Validation of clean utilities	23 DEC 2021															
Validation of cleanrooms	26 NOV 2021															
Validation of equipment	25 FEB 2022														PQs	PQs
Validation of It systems	23 DEC 2021															

*Including mechanical, electrical, goods lift, piping, IT systems

PO suggested dates	Dates
Architects	18 JAN 2021
Engineering firm	18 JAN 2021
CM	18 JAN 2021
Mechanical contractor	07 MAR 2021
Electrical contractor	07 MAR 2021
Cleanrooms contractor	14 FEV 2021
Validation team	04 APR 2021
Equipments (first equipment - long lead items)	7 FEB 2021

APPENDIX I: CALCULATIONS

NRC-14 CTMF
Object: Human ressources
Date: 2020-11-27

Hypothesis: - no overlap between shifts except for DSP
-min 2 people per activity in production (double check requirement)
-closed office for the facility manager
-one shared office to support the facility day to day (mgt Project)
-HHT has as policy to give a closed office to team leads (TL) // possibility to share (2 in office)
-larger QA shared office to deal with the documents
-One open space with shared desk over shift for operator and production personnel

ROOM	pers/shift	nbr shift	Total	Comment
Production GMP				
Support leader	1	1	1	Desk required
Decontamination	1	1	1	
Cleaning	1	1	1	
Stérilisation	-	-	-	included in cleaning
Preparation	1	1	1	
Weighing	-	-	-	Included in preparation
Upstream leader	1	1	1	Desk required
Subculture	2	1	2	
Virus seed preparation	-	-	-	include in USP team
USP SS	2	1	2	
Downstream leader	1	1	1	Desk required
Chromatography support	0	2	0	include in DSP team
DSP 1 SS	4	2	8	
DSP 2 SS	4	2	8	
Bulk filling	-	2	-	Included in DSP team
Sous-total	**18**		**26**	
Zone entrepôt				
Warehouse	2	2	4	
Sous-total	**2**		**4**	
Autre que production				
Contrôle Qualité	4	1	4	3 technicians + 1 leader (dedicated office)
General & Admin. Usine	-	-	-	in HHT Research center
Assurance Qualité	2	1	2	large open space with documents storage
Réglementaires Usine	-	-	-	in HHT Research center
Mgt de Projets	2	1	2	in HHT Research center
Services Techniques/maintenance	2	1	2	1 open space for documentation
SSE	-	-	-	in HHT Research center
Sous-Total	**10**		**10**	
TOTAL (presence dans l'usine)	**30**	**TOTAL**	**40**	

Client: National Research Council

Date: 2020-11-04

Warehouse capacity requirement - Feasability Study Clinical Trial Material Facility

HYPOTHESIS

Product	Format	Vol. DS/Lot		Lot/month	Lot/year
Biomanufacturing- USP 500L		50	L	1,7	20,4
Total:					**20,4** **lots**

Storage duration:

Raw material	1	months
Consumables (filters, bags, tubing, gloves, hats, suits)	1	months

Other hypothesis

1) Minimum of one palet per item
2) Warehouse required surface area calculated for 2-high racking pallets
3) 882 lbs (400 kg) maximum allowable per pallet space — 400,0 kg
4) If many formulas require the same raw material, they will be packed on the same pallet if space is sufficient
5) Storage with pallets or cart (2 carts in 1 pallet space)
6) 3 pallet spaces for QC lab

CALCULATIONS

Raw materials

	Qty. Lot 500L		Qty. /month		Pallets /month	Required pallet space / month (min. 0,5)	Temperature (C)	Explosion Proof (Y/N)	
Viral vaccine (e.g. Client 62)									
Working cell bank	0,005	L/lot	0	L	0,0000	0,5	-193	N	Cryostorage
Virus cell bank (case of vector viral production)	0,005	L/lot	0	L	0,0000	**0,5**	**-60**	**N**	**Freezer**
Media ready to use	550	L/lot	935	L	2,3375	3,0	4	N	Cold room
Balance CD growth A	10	kg/lot	18	L	0,0438	0,5	4	N	Cold room
Sodium bicarbonate	3	kg/lot	5	mL	0,0128	0,5	RT	N	Warehouse
Cell Boost 7a	20	kg/lot	34	L	0,0846	0,5	4	N	Cold room
5N NaOH	4	kg/lot	6	L	0,0162	0,5	RT	N	Warehouse
Cell Boost 7b	1	kg/lot	2	kg	0,0044	0,5	4	N	Cold room
D-Glucose	10	kg/lot	17	kg	0,0421	0,5	RT	N	Warehouse
DPBS	303	L/lot	514	kg	1,2856	2,0	RT	N	Warehouse
Sodium chloride	306	kg/lot	521	kg	1,3025	2,0	RT	N	Warehouse
Sodium hydroxide	36	kg/lot	62	kg	0,1549	0,5	RT	N	Warehouse
EtOH 20%	166	L/lot	282	kg	0,7055	1,0	RT	Y	Warehouse Exproof cabinet
Tris	46	kg/lot	78	kg	0,1952	0,5	RT	N	Warehouse
Sodium formate	0,08	kg/lot	0	kg	0,0003	0,5	RT	N	Warehouse
L-Arginine	7	kg/lot	13	kg	0,0313	0,5	RT	N	Warehouse
Triton X100	12	L/lot	21	kg	0,0519	0,5	RT	N	Warehouse
Sodium acetate	6	kg/lot	10	kg	0,0247	0,5	RT	N	Warehouse
Sodium citrate	7	kg/lot	11	kg	0,0281	0,5	RT	N	Warehouse
Citric acid	1	kg/lot	1	kg	0,0031	0,5	RT	N	Warehouse
PS80	4	kg/lot	7	L	0,0185	0,5	4	N	Cold room
QC lab									
Various solutions, buffers …						2,0	RT	N	Warehouse
Various solutions, buffers …						0,5	4	N	Fridge
Various solutions, buffers …						0,5	-20	N	Freezer
						12,5	**pallets /month**		
								6	**Cold room**
					Total:	**12,5**	**pallets**	**1,1**	**Freezer**

Consumables

	Qty/ Lot 500L		Qty Unit / Carton	Volume / carton (m3)	Carton / pallet	Pallets / lot (500L)	Pallets /month	Required pallet space / month (min. 1)	
Biomanufacturing									
Sterilization wrap		units							
Powder transfer bag small volume		units	20	0,1584	6	0,00	0,00	0,5	Warehouse
Powder transfer bag large volume		units	10	0,1584	6	0,00	0,00	0,5	Warehouse
250mL flask	27	units	50	0,1584	6	0,09	0,15	0,5	Warehouse
750mL flask	4	units	25	0,1584	6	0,03	0,05	0,5	Warehouse
2000mL flask	4	units	6	0,1584	6	0,11	0,19	0,5	Warehouse
50L bioreactor bag	1	units	1	0,1433	6	0,17	0,28	0,5	Warehouse
500L bioreactor bag	1	units	1	1,6023	4	0,25	0,43	0,5	Warehouse
5L bag	3	units	20	0,1584	6	0,03	0,04	0,5	Warehouse
10L bag	3	units	10	0,1584	6	0,05	0,09	0,5	Warehouse
20L bag		units	10	0,1584	6	0,00	0,00	0,5	Warehouse
25L bag		units	10	0,1584	6	0,00	0,00	0,5	Warehouse
Mixers 50L	6	units	3	0,1584	6	0,33	0,57	1	Warehouse
Mixers 100L	7	units	2	0,1584	6	0,58	0,99	1	Warehouse
Mixers 200L	7	units	2	0,1584	6	0,58	0,99	1	Warehouse
Mixers 500L	25	units	2	0,1584	6	2,08	3,54	4	Warehouse
Mixers 2500L		units	1	0,1584	6	0,00	0,00	0,5	Warehouse
Tanks 50L	6	units	6	0,1584	6	0,17	0,28	0,5	Warehouse
Tanks 100L	7	units	4	0,1584	6	0,29	0,50	0,5	Warehouse
Tanks 200L	7	units	2	0,1584	6	0,58	0,99	1	Warehouse
Tanks 500L	10	units	2	0,1584	6	0,83	1,42	2	Warehouse
Tanks 1000L	8	units	2	0,1584	6	0,67	1,13	2	Warehouse
Filter 0,85 Maxi	1	units	1	-	8	0,13	0,21	0,5	Warehouse
Filter 0,45 Maxi	1	units	1	-	8	0,13	0,21	0,5	Warehouse
Filter 0,22 Maxi	1	units	1	-	8	0,13	0,21	0,5	Warehouse
Filter 0,22 Mini	3	units	4	-	8	0,09	0,16	0,5	Warehouse
Depth filration cartridge - clarification	6	units	40	1,056	1	0,14	0,23	0,5	Warehouse
UF/DF membrane large scale	1	units	20	1,056	1	0,05	0,09	0,5	Cold room
UF/DF membrane small scale	1	units	80	1,056	1	0,01	0,02	0,5	Cold room
Chromatography column large scale	2	units	1	-	1	2,00	5,00	5	Cold room
Chromatography membrane + nanofiltration	2	units	2	-	2	0,50	0,85	1	Cold room
Tubing and connectors	TBD	units	TBD	TBD	TBD			0,5	
General:									
Suit	0,125	m^3				0,3	1,0	1	
Gloves	0,05	m^3				0,3	1,0	1	
Hats	0,05	m^3				0,3	1,0	1	
Preventive maintenance	1	m^3				0,5	1,0	1	
Cleaning detergent	2	Units				1,0	1,0	1	
Quality control:									
Consumables									
							1,5		
						Total per month:	**34,0**	**pallets**	
						Total warehouse:	**34,0**	**pallets**	

RESULTS WAREHOUSE STORAGE SPACE

Number of pallets required according to storage duration			
Raw materials	13	pallets	
Consumables	34	pallets	
Total:	**47**	pallets	
Number of pallets required with turnover :	51	pallets	(hypothesis 1,1)
Number of pallets/ft^2 warehouse:			
Aisle width in module	9,00	ft	(varies according to lift type)
Pallet width (with racking)	4,10	ft	(varies according to racking type)
Pallet length (with racking)	4,01	ft	(varies according to racking type)
Area of module (two pallets with aisle)	68,97	ft^2	
Number of racking levels for pallets	2,00	pallets	maximum available in L4
Number of pallets per module	4,00	pallets	
Number of pallets per ft^2	0,06	pallets/ft^2	

Required pallets storage area:	**Approx:**	**882**	**ft^2**
		80	**m^2**

[NRC-14]
2020-11-27

Cooling water process requirements

Hypothesis:

- 1,1 kg of purified water is required to generate 1,00 kg of pure steam
- Hypothesis based on NRC-09/10

Calculation assumptions

Cp water =	kJ/kg*C	4,2	kJ/kg*C	
Heat of vaporization/latent heat (water to steam) =	KJ/KG	2057	kJ/kg	for 90 psig
Inox vessel mass estimation =		2	Kg/L	
Cp inox =		0,468	kJ/kg*C	

Cp chilled water	4,2	kJ/kg*C
masse volumique chilled water/water	1	kg/L
Delta T Chillled water (in: 6C / out: 12C)	6	deg C

Room/Equipment	Activity	Pressure required (psig)	Volume to cool (L)	Mass to cool (kg)	Start temp. (°C)	End temp. (°C)	Duration (minutes)	Energy $Q=mC_p(T_2-T_1)$ (kJ)	Nb of uses /week	Heat per week KJ/week	Cooling (kW)	Chilled water Temp in	Chilled water Temp out	Point of use flowrate (Lpm)	Point of use flowrate (gpm)	Simultaneous operation	Connection	Commentaires / Source
USP SU																		
Fermenter 50 TCU	Medium cooling		50	142	37	30	20	1935	<1	1935	1,6	6	12	3,8	1,0			
Fermenter 500 TCU	Medium cooling		500	445	37	30	75	16158	<1	16158	3,6	6	12	8,5	2,3			
Storage tank 500 TCU	Medium cooling		500	445	20	6	60	32316	<2	32316	9,0	6	12	21,4	5,6			
Connected load											**5**							
Mechanical room																		
Combi WFI&PS	Blowdown and effluent cooldown	30-45									242	6	71	53	14	X		Temp in: 15-20C, Temp out: 85C, deltaT=65degC Infos Stilmas
PW distribution	PW cooling after sanitization			115	22,4	20	1		1		21	6	12	50	13			Calcul (20% de 2000L de 85C à 20C en 120 min)
PW distribution	Maintain loop at 20C			115	20,9	20	1				7,5	6	12	18	5	X		Estimé - Charge thermique pompe EP
WFI distribution	Sub-loop cool-down at 20C for POUs			100	85,0	20	1				455	6	12	1083	286	X		Calcul
Thermal inactivation system	Cool-down effluents below 60C																	Outlet temperature max 60C selon soumission Actini
Neutralization system	Cool-down effluents below 60C										60	6	12	143	38	X		Estimé - non calculé
Connected load											**785**							
Supporting area																		
Sterilization autoclave	Drain + jacket cooling	44-87							21		44	6	16	63	17	X	1 1/4 male NPT	Steris data sheet - Finn Aqua BPS 6915
Decontamination autoclave	Drain + jacket cooling	44-87							21		44	6	16	63	17	X	1 1/4 male NPT	Steris data sheet - Finn Aqua BPS 91215
Part washer Steris 480 PG	Drain cooling	90 max							21		94	6	25	71	19	X	3/4"	Steris data sheet - 480 PG
Connected load											**183**							

	Peak load (kW)	Connected load (kW)	**Débit minimum (L/s)**
Cooling water requirement:	947	973	43,21
Design contingency (15%):	142	146	=PeakLoad/(Cp*μ*Tinit)
Total:	**1089**	**1119**	

[NRC-14]
2020-11-27

Plant steam process requirements

Hypothesis:
- 1,1 kg of purified water is required to generate 1,00 kg of pure steam - Hypothesis based on NRC-09/10

Calculation assumptions:

Cp water =	4,2	kJ/kg*C		
Heat of vaporization/latent heat =		kJ/kg	V=2.4QVs/A	
Inox vessel mass estimation =	2,5	Kg/L	V velocity	
CP inox =	0,468	kJ/kg*C	Q lbs/hrs	
Plant steam supply pressure	115	psig	Vs Sp.Vol.in cu.ft/lb at the following pressure	
Correction factor 100-115 psig	0,92		A internal area of the pipe sq.in	1 lbs = 0,453592 kg
masse volumique water	1	Kg/L		
Chaleur de vaporisation/chaleur latente (eau à vapeur) =	2057	kJ/kg	886 BTU/lbs	at 90 psig

Room/equipment	Activity	Pressure required (psig)	Volume (L)	Start temp. (°C)	End temp. (°C)	Duration (minutes)	Heat $Q=mC_p(T_2-T_1)$ (kJ)	Heat KW	Plant steam Flow (kg/h)	Plant steam Flow (lbs/h)	Steam/cycle (kg)	Nb.uses/week	Weekly consumption (kg)	Simultaneous operation	Connection	Comnentaires
Mechanical room																
Combi WFI&PS		6 barg							1687	3719				X		infos Stilmas
WFI distribution	Maintain main loop at 85C		100	82	85	1		21	37	81				X		Calcul
WFI distribution	Sub-loop heating after POUs demand		216	20	85	10		98	172	379						Calcul
Thermal inactivation system	Thermal inactivation at 135C								113	250				X		infos soumission Actini
Decontamination Finn Aqua BPS 91215						30			339		69	10	690	x		
Connected load																
Cleaning room																
Part washer		30-50							145	320	13	21	267	X	1/2'	infos data sheet Steris 480 PG
Connected load																
Total									**2154,20**	977			**956,70**	**2321**		

	Peak load (kg/h):	Peak load (lbs/h):
Plant steam requirement:	2321	5107
Design contingency (15%):	348	766
Total:	2669	**5873**

[NRC-14]
2020-11-27

Clean steam process requirements

Hypothesis:

- 1,1 kg of purified water is required to generate 1,00 kg of pure steam
- hypothesis based on NRC 09/10

Calculation assumptions:

Cp water =	4,186	kJ/kg*C	V=2.4QVs/A	
Heat of vaporization/latent heat (water to steam) =	2180	kJ/kg	V velocity	
Inox vessel mass estimation =	2	Kg/L	Q lbs/hrs	
Pipe mass estimation=	5,5	kg/m sch,40	Vs Sp.Vol.in cu.ft/lb at the following pressure	
Cp inox =	0,468	kJ/kg*C	A internal area of the pipe sq.in	
Pure steam supply pressure	50	psig		

1 lbs = 0,453592 kg

in general - 80 ft/sec (4800ft/min) is a recommended steam velocity

Room/equipment	Activity	Volume (L)	Pipe lenght (m)	Start temp. (°C)	End temp. (°C)	Duration (minutes)	Mass (kg)	Heat $Q=mC_p(T_2-T_1)$ (kJ)	Heat KW	Pure steam Flow (kg/h)	Pure steam Flow (lbs/h)	Steam/cycle (kg)	Nb.uses/week	Weekly consumpion (kg)	Simultaneous operation
Sterilisation in the CTMF															
Finn Aqua BPS 6915						30				250		50	15	750	x
Connected load										**250,00**					
Total										**250,00**		**50,00**		**750,00**	**750**

	Total connected load (kg/h):	Total connected load (lbs/h):	Peak load (kg/h):	Peak load (lbs/h):
Pure steam requirement:	250	550	250	550
Design contingency (25%):	63	138	63	138
Total:	**313**	688	313	688

Clean steam generator : PSG 1500 Siltmas Capacity: 862,5 lbs/hr

Consommation eau purifiée par semaine pour générateur : 863 Litres

[NRC-14]
2020-11-27

TCU heating process requirements
Hypothesis:

hypothesis based on NRC 09/10

Calculation assumptions

Cp water =	kJ/kg*C	4,186	kJ/kg*C
Inox vessel mass estimation =		2	Kg/L
Cp inox =		0,468	kJ/kg*C
masse volumique water		1	Kg/L

Room/Equipment	Activity	Volume to heat (L)	Mass stainless steel to heat kg	Start temp. (°C)	End temp. (°C)	Duration (minutes)	Energy $Q=mC_p(T_2-T_1)$ (kJ)	Nb of uses /week	Heat per week KJ/week	Heating (kW)	Simultaneous operation	Comments
USP SU												
Fermenter 50	Medium heating	20	142	20	37	15	2553	<1	2553	3		
Fermenter 500	Medium heating	200	445	20	37	45	17773	<1	17773	7		
Storage tank 500 TCU	Medium Heating	500	445	6	20	60	32218	<2	32218	9		
Mechanical Room												
PW system	Thermal sanitization (Prod)									20	x	20 kW selon Stilmas
PW system	Thermal sanitization (Distr.)		115	20	22,4	1				21		Calcul (20% de 3000L de 20C à 85C en 120 min)
Connected load										**59**		
Total										**59**	**20**	

	Peak load (kW)	Connected load (kW)
Electrical requirement:	20	59
Design contingency (15%)	3	9
Total:	**23**	**68**

Date: 2020-11-19

Water for Injection process requirements

Hypothesis	V	min working V
Water for injection requirement based NRC-14-NDC-03 (Mass Balance mAb)		
Clarification skid 109LMH	50	12,5
15L/min 50L mixer	200	50
35L/min large mixer	500	125
11,4 L/min sink Based on Code de Plomberie du QC (Évier de service = 0,19 L/s)	1000	250
Affinity chromatography skid : 45cm diam colonne - 200cm/h flowrate	250	62,5
Cation exchange chromatography skid : 35,9diam column - 200cm/h flowrate	100	25
Anion exchange chromatography skid : 5L membrane - 1MV/min flowrate		
Nanofiltration skid : 1sqm membrane - 90LMH flowrate		
UDF/DF skid : 9sqm filtration - 240LMH		
Maximum working volum for Mixer system could be 105% of working volume specification		
Mixer 50L includes 10L adaptor as minimal working volum		
Media/Buffer preparation follows Campaign mode _ one preparation at the same time		

Room/equipment	Activity	Pressure required (psig)	Flow (L/min)	Diameter	Duration (min)	Volume / use (L)	Worst case	Total WC (L)
Equipment preparation								
Sink	Washing small equipment		11,4		10	114	1	114
Sink	Washing small equipment		11,4		10	114	1	114
Glass washer	Final rinse	90 max	75	1"		130	21	2730
Total								**2958**
Media/Buffer preparation								
Small volum system	10L Media for Subculture		11,4		0,9	10		0
	6L 7.5% Sodium Bicarbonate - Cell amplification		11,4		0,5	6		0
	1L 1,0M NaCl - Affinity Chromatography		11,4		0,1	1		0
	1L 1,0M NaCL- Cation exchange chromatography		11,4		0,1	1		0
	7L 30mM trisodium citrate, 122mM NaCl, pH6,0		11,4		0,6	7		0
	1L 10g/L PS80 - Adjustment 4		11,4		0,1	1		0
Mixer 50L	50L BalanCD CHO Growth A Medium D-01 - Cell amplification		15		3,3	50		0
	11L Cell boost b - mAb production		15		0,7	11		0
	22L Glucose 450 g/L - mAb production		15		1,5	22		0
	22L 7.5% Sodium Bicarbonate - mAB production		15		1,5	22		0
	11L 2M acetic acid - Adjustment 1		15		0,7	11		0
	13L 30mM trisodium citrate/122mM NaCl/400 mg/L polysorbate 80, pH 6.0, - Adjustment 4		15		0,9	13		0
Mixer 100L	105L 2,0M NaCL - Affinity Chromatography stripping run 1		15		7,0	105		0
	105L 2,0M NaCL - Affinity Chromatography stripping run 2		15		7,0	105		0
	61L 20% Octoxynol-100 - Viral Inactivation		15		4,1	61		0
	61L 1M Tris pH9 - Viral Inactivation		15		4,1	61		0
	66L 20mM Tris, 160mM NaCl, pH7,0 - Cation exchange chromatography		15		4,4	66		0
	68L 20mM Tris, 160mM NaCl, pH 7,0 - Adjustument 3		15		4,5	68		0
	55L - 30mM trisodium citrate, 122mM NaCl, pH6.0 - Nanofiltration		15		3,7	55		0
Mixer 200L	110L Cell boost a - mAb production		35		3,1	110		0
	211L 25mM Tris, 1,2M NaCl, pH 7,1 - Affinity Chromatography run 1 +2		35		6,0	211		0
	211L 5mM Sodium formate, 0.2M Arginine, pH3.1 - Affinity Chromatography run 1 +2		35		6,0	211		0
	211L 1M Tris pH 9 - Affinity Chromatography run 1 +2		35		6,0	211		0
	211L 25mM Tris, 25mM NaCl, pH 5.0 - Affinity Chromatography run 1 +2		35		6,0	211		0
	132L 0,2M Sodium Acetate / 20 %Ethanol - Cation exchange chromatography		35		3,8	132		0
	115L 50mM Tris, pH 8,15 - Adjustment 3		35		3,3	115		0
Mixer 500L	385L BalanCD CHO Growth A Medium - mAb production		35		11,0	385		0
	300L DPBS - Harvest and clarification		35		8,6	300		0
	351L 0,4M NaCl - Affinity Chromatography		35		10,0	351		0
	351L 0,5M NaOH - Affinity Chromatography prep		35		10,0	351		0
	351L 0,5M NaOH - Affinity Chromatography sanit run 1		35		10,0	351		0
	351L 0,5M NaOH - Affinity Chromatography sanit run 2		35		10,0	351		0
	351L 2,0M NaCL - Affinity Chromatography prep		35		10,0	351		0
	351L 2,0M NaCL - Affinity Chromatography sanit run 1		35		10,0	351		0
	351L 2,0M NaCL - Affinity Chromatography sanit run 2		35		10,0	351		0
	457L 25mM Tris, 25mM NaCl, pH 7.1 - Affinity chromatography run 1		35		13,1	457		0
	457L 25mM Tris, 25mM NaCl, pH 7.1 - Affinity chromatography run 2		35		13,1	457		0
	308L 20mM Sodium Acetate, 30 mM NaCl, pH6,0 - adjustment 2		35		8,8	308		0
	219L 0,4M NaCl - Cation exchange chromatography		35		6,3	219		0
	438L 0,5M NaOH - Cation exchange chromatography		35		12,5	438		0
	504L 20mM Sodium Acetate, 30mM NaCl, pH 6.0 - Cation exchange chromatography		35		14,4	504	1	504
	504L 2,0M NaCl - Cation exchange chromatography		35		14,4	504		0
	275L 0,5M NaOH - Anion exchange chromatography		35		7,9	275		0
	275L 2,0M NaCl - Anion exchange chromatography		35		7,9	275		0
	330L 20mM Tris/83mM NaCl, pH 8,0 - Anion exchange chromatography		35		9,4	330		0
	495L 0,5M NaOH - UF/DF		35		14,1	495		0
	396L 0,1M NaOh - UF/DF		35		11,3	396		0
	396L 0,1M NaOh - UF/DF		35		11,3	396		0
	396L 30mN trisodium citrate, 122mM NaCl, pH6 - UF/DF		35		11,3	396		0
	396L 30mN trisodium citrate, 122mM NaCl, pH6 - UF/DF		35		11,3	396		0
Total								**504,0**
Upstream								
Clarification skid	Sanitization		5,5		133,2	726	1	726
Total								**726**
Downstream 1								
Affinity chromatography skid	Preparation - Rinse 1		5,3		60,2	319		0
	Preparation - Rinse 2		5,3		60,2	319		0
	Preparation - Rinse 3		5,3		60,2	319		0
	Run 1 - Rinse 1		5,3		60,2	319		0
	Sanitization 1 - Rinse 1		5,3		60,2	319		0
	Sanitization 1 - Rinse 2		5,3		60,2	319		0
	Sanitization 1 - Rinse 3		5,3		60,2	319	1	319
	Run 2 - Rinse 1		5,3		60,2	319		0
	Sanitization 2 - Rinse 1		5,3		60,2	319		0
	Sanitization 2 - Rinse 2		5,3		60,2	319		0
	Sanitization 2 - Rinse 3		5,3		60,2	319		0
Total								**319**
Downstream 2								
Cation exchange chromatography skid	Preparation rinse 1		3,4		58,5	199		0
	Preparation rinse 2		3,4		58,5	199		0
	Preparation rinse 3		3,4		58,5	199		0
	Run rinse		3,4		58,5	199		0
	Sanitization rinse 1		3,4		58,5	199		0
	Sanitization rinse 2		3,4		58,5	199		0
	Sanitization rinse 3		3,4		58,5	199	1	199
Anion exchange chromatography skid	Preparation rinse 1		5		50,0	250	1	250
	Preparation rinse 2		5		50,0	250		0
	Preparation rinse 3		5		50,0	250		0
Nanofiltration	Rinse		1,6		62,5	100		0
Total								**449**
Bulk Filling								
UD/DFskid	Preparation rinse 1		26,7		33,7	900	1	900
	Preparation rinse 2		26,7		33,7	900		0
	Preparation rinse 3		26,7		33,7	900		0
	Run rinse		26,7		33,7	900		0
	Sanitization - rinse 1		26,7		33,7	900		0
	Sanitization - rinse 2		26,7		33,7	900		0
Total								**900**
Total requirement per week (L)								**5407**

Client : Canadian National Research Council
Date : 2020-11-18

Water for Injection consumption simulation

System parameters		
WFI Storage tank total volume:	2600 (L)	
WFI Storage tank:	2000 (L)	
WFI Production flow rate :	20 (LPM)	1200 Liters/hour produce by the reserve osmosis system

Points of use - Water for injection						D8								D9										D10										D11										D12									
					Consumption over a one week production (Liters)																																																
Room	**Equipment**	**Activity**	**Vol. per week**	**00:00**	**02:00**	**04:00**	**06:00**	**08:00**	**10:00**	**12:00**	**14:00**	**16:00**	**18:00**	**20:00**	**22:00**	**00:00**	**02:00**	**04:00**	**06:00**	**08:00**	**10:00**	**12:00**	**14:00**	**16:00**	**18:00**	**20:00**	**22:00**	**00:00**	**02:00**	**04:00**	**06:00**	**08:00**	**10:00**	**12:00**	**14:00**	**16:00**	**18:00**	**20:00**	**22:00**	**00:00**	**02:00**	**04:00**	**06:00**	**08:00**	**10:00**	**12:00**	**14:00**	**16:00**	**18:00**	**20:00**	**22:00**
Cleaning	Glass washer	Final rinse	2090		130				130			130					130				130				130										130										130									
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114	
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114		114	
Preparation 1	Take-off point	Solution preparation	7																												1												6									
	50L Mixer	Solution preparation	897																11																											50									
	500L Mixer	Solution preparation	6256						351	351	457	457									308	219	438	504	504									275	275										330	495	396	396							
	200L Mixer	Solution preparation	458					211																																													
	100L Mixer	Solution preparation	68																														68																				
Upstream	Clarification	Rinse	726									484	242																																								
Downstream 1	Affinity chromatography skid	Rinse	3509						319		319	319							319		319	319	319								319		319	319	319																			
Downstream 2	Cation exchange Chromatography skid	Rinse	1393																																												199	199	199					199			199	199	199			
	Anion exchange Chromatography skid	Rinse	750																																																	250	250	250			
	Nanofiltration	Wetting	0																																																		
Bulk filling	UD/DF skid	Rinse	120																																																	120					
			26067																																																			
Volume of water for injection at the begining of the period (L) :				2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000
Consumption in two hour (L):				228	130	228	0	439	800	579	776	1618	242	228	0	228	130	228	319	239	757	766	757	732	634	228	0	228	130	228	319	229	517	679	434	503	405	228	0	228	358	228	0	234	50	558	824	823	725	228	0	228	130	228	199	359	152	449	834	1073	380	228	0
Water for injection storage tank filling (L):				228	130	228	0	439	800	579	776	1618	242	228	0	228	130	228	319	239	757	766	757	732	634	228	0	228	130	228	319	229	517	679	434	503	405	228	0	228	358	228	0	234	50	558	824	823	725	228	0	228	130	228	199	359	152	449	834	1073	380	228	0
Volume of water for injection at the begining of the period with 15% contingency (L) :				2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000	2000
Consumption in two hour with 30% contingency (L):				296,4	169	296,4	0	570,7	1040	752,7	1008,8	2103,4	314,6	296,4	0	296,4	169	296,4	414,7	310,7	984,1	995,8	984,1	951,6	824,2	296,4	0	296,4	169	296,4	414,7	297,7	672,1	882,7	564,2	653,9	526,5	296,4	0	296,4	465,4	296,4	0	304,2	65	725,4	1071,2	1069,9	942,5	296,4	0	296,4	169	296,4	258,7	466,7	197,6	583,7	1084,2	1394,9	494	296,4	0
Water for injection storage tank filling (L):				296,4	169	296,4	0	570,7	1040	752,7	1008,8	2103,4	314,6	296,4	0	296,4	169	296,4	414,7	310,7	984,1	995,8	984,1	951,6	824,2	296,4	0	296,4	169	296,4	414,7	297,7	672,1	882,7	564,2	653,9	526,5	296,4	0	296,4	465,4	296,4	0	304,2	65	725,4	1071,2	1069,9	942,5	296,4	0	296,4	169	296,4	258,7	466,7	197,6	583,7	1084,2	1394,9	494	296,4	0

Peak in two hours (L): 2103
Average peak in one hour (L): 1052
Distribution loop flow: 17,528333

SCENARIO 1

loop no.1 sizing: production	Flow	
Clarification		lpm
Affinity chromatography skid		lpm
Cation exchange Chromatography skid		lpm
Anion exchange Chromatography skid		lpm
Nanofiltration	1,6	lpm
UD/DF skid	26,7	lpm

Client: NRC
Project no.: NRC-14

Vessel Sizing Calculations
Date : 2020-11-20

Volume- Cylindre avec bouts arrondis

WFI TANK

WFI tank	
Diam: pouces	
84	
Diam: pieds	
7,0	
Aire: po^2	
5542	

Volume tête	**221**	**gal**
Volume tête	837	L
IDD	1,229	ft
	14,75	**in**
	0,375	m
Surface	3,575	m2
Nominal volume	**2000**	**L**
Volume total	2600	L
Volume cylindre	926,85	L
Longueur cylindre	0,26	m
	0,85	ft
	10,21	in
TOTAL LENGTH	**1,01**	**m**
	3,3	**ft**

2,1336 m
TOTAL HEIGHT

isolation

50,8 mm
0,0508 m

L/D - shell lenght 0,1

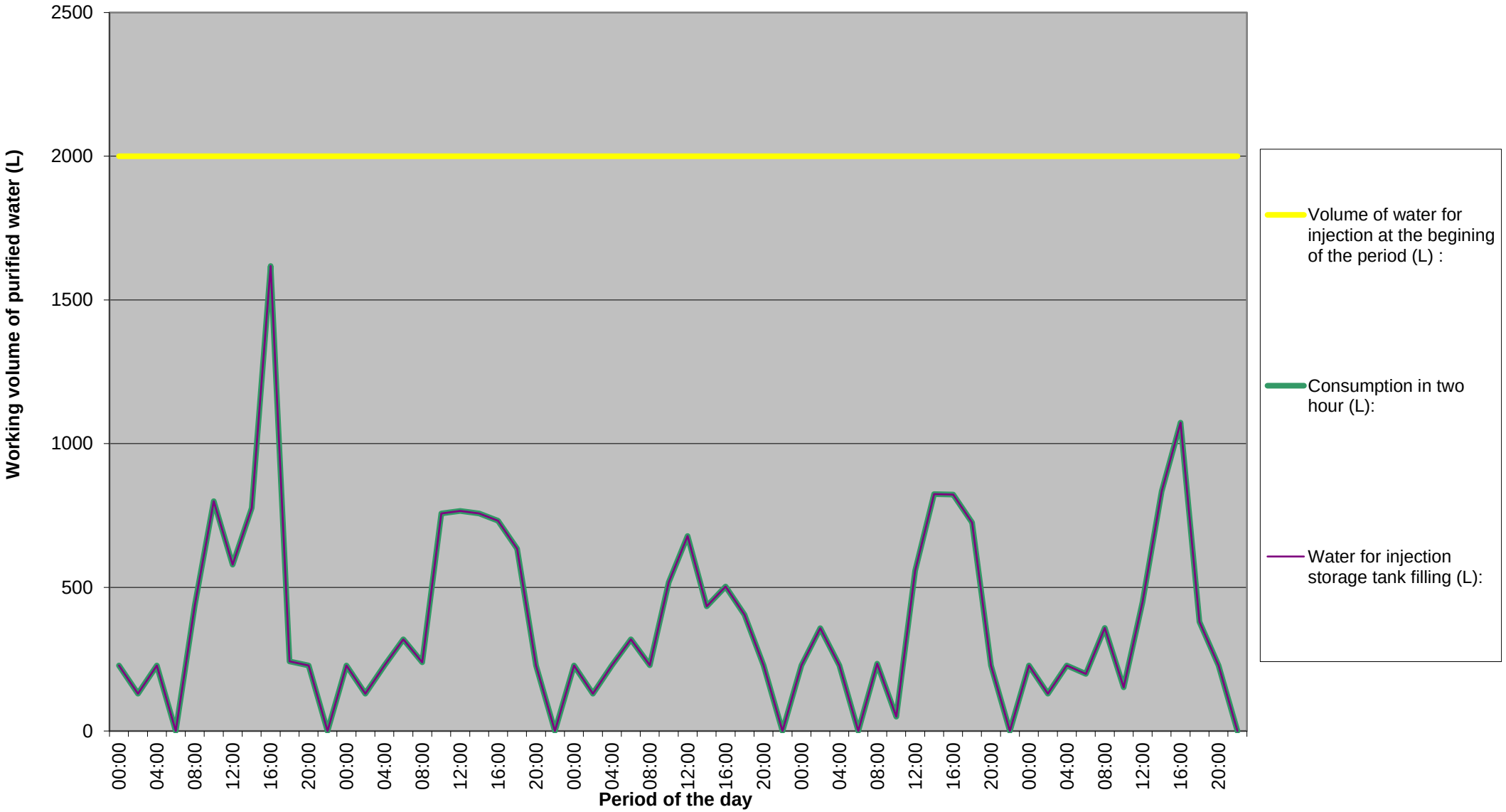
+ legs (3 feet) 6,3 ft

2,7 1,9 m

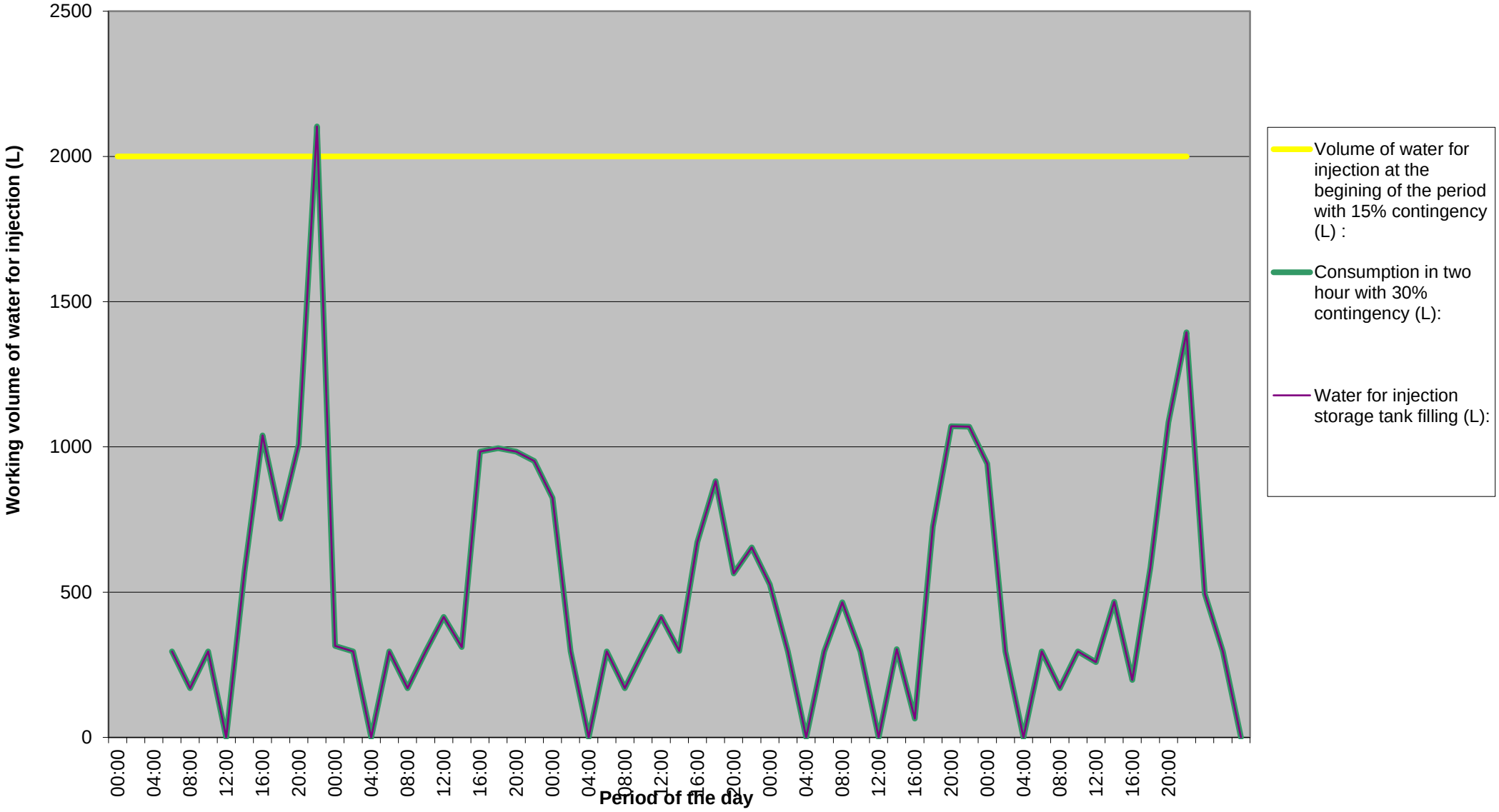
reste 0,8 m en haut pour composantes au-dessus

OK

Simulation of purified water working volume in storage tank



Simulation of Water For Injection working volume in storage tank with 30% contingency



NRC-14-NDC-06

[NRC-14]
Biological wasterwater simulation
Modified by :
Date : 2020-11-04

Effluent type:

Effluents contaminés biologiques (ECB)

Connections:
Direct (D)
Indirect (I)

Drain:
DPD-01 Drain au plancher – Direct
+ECH Point d'échantillonnage EPU ou EPPI
SPH-01 SPH-01 : Siphon de sol – Fermé
SPH-02 SPH-02 : Siphon de sol – Ouvert
EVR-01 EVR-01 : Évier
EVR-02 EVR-02 : Évier de plancher

Hypothesis: To be confimed
Ref.NRC-14-NDC-03 (Mass Blance mAb)
Solution using for step preparation are not concidering as biological contaminated liquid waste

No.	Zone	Local name	Local	Grade	Equipment	Effluent	Connection	Drain:	Solution description	pH	Temperature description	Temperature	WC qty (Volume en L)	Flowrate (LPM)	Diameter (mm)	Simultaneous hypothesis	Frequency	Source	Connection decontamination requirement (yes/No)	Comment
1	Production	Upstream	TBD	C	Depth filtration /Bioreactor	ECB	D	DPD-01 +ECH	ph neutre (6,8-7,2)	7	max 37°C	37°C	0	17	DN50	x	une fois par lot	waorst case scenario : 500L media additional as worst case scenario ; will be collected manually and transfer to another drain	Non	
2	Production	Downstream 1	TBD	C	Chromatography system_Affinity	ECB	D	DPD-01	Produit - pH neutre Solutions tampons - pH variés (grande majorité à pH neutre, peu à pH basique)	7	20±5°C	20°C	2924	5,3	DN25	x	une fois par lot	AktaReady_Cytiva NDC-03 (mass balance) max flowarate Worst case - time porcess reduce in 10hrs	Non	
3	Production	Downstream 2	TBD	C	Chromatography system_Capto core 700	ECB	D	DPD-01 +ECH	Produit - pH neutre Solutions tampons - pH variés (grande majorité pH neutre, peu pH basique)	7	20±5°C	20°C	2153	3,4	DN80		une fois par lot	AktaReady_Cytiva NDC-03 (mass balance) max flowarate	Non	
4	Production	Downstream 2	TBD	C	Chromatography system_AEX	ECB	D	DPD-01	Produit - pH neutre Solutions tampons - pH variés (grande majorité à pH neutre, peu à pH basique)	7	20±5°C	20°C	25	5	DN25	x	une fois par lot	AktaReady_Cytiva NDC-03 (mass balance) max flowarate	Non	
5	Production	Bulk filling	TBD	C	TFF	ECB	D	DPD-01 +ECH	Produit - pH neutre Solutions tampons - pH variés (grande majorité pH neutre, peu pH basique)	7	20±5°C	20°C	2953	1,6	DN80		une fois par lot	mAb process Model skid : Akta ready flux feed flow : 18LPM permeate: 1,6LPM	Non	
6	Warehouse	Decontamination	TBD	D	Autoclave de decontamination	ECB	D	DPD-01 +ECH	Condensat vapeur pure (pH 7)	7	max 60°C	60°C	720	0,5	1 1/2	x	fréquent	source: Sterinova/Getinge [20201120] [JDE] validated by Teffanie Le François	Non	
7	Bio-Prod.	Corridor support	TBD	D	Douche d'urgence	ECB	I	SPH-01	ph neutre	7	20±5°C	20°C	114	11,4	DN50		excessivement rare	11.4 LPM * 10 min (code plomberie)	Oui	
8	QC	QC lab CL2	TBD	CNC	Évier	ECB	I	EVR-01	ph eau domestique (7) + savon	7	4-40°C	30°C	114	11,4	DN50	x	fréquent	11.4 LPM * 10 min (code plomberie)	Oui	
9	QC	QC lab CL2	TBD	CNC	Douche d'urgence	ECB	I	SPH-01	ph neutre	7	20±5°C	20°C	114	11,4	DN50		excessivement rare	11.4 LPM * 10 min (code plomberie)	Oui	
10	QC	Janitor	TBD	CNC	Évier de plancher	ECB	I	EVR-02	ph eau domestique (7) + savon	7	4-40°C	30°C	57	11,4	DN50		fréquent - ménage	11.4 LPM * 5 min (code plomberie)	Oui	

Jour 17

No.		7h00	7h30	8h00	8h30	9h00	9h30	10h00	10h30	11h00	11h30	12h00	12h30	13h00	13h30	14h00	14h30	15h00	15h30	16h00	16h30	17h00	17h30	18h00
1									125	125	125	125												
2			159,5	159,5	159,5	159,5	152,5	152,5	152,5	152,5	144	144	144			159,5	159,5	159,5	159,5	159,5	159,5	159,5	159,5	
3																								
4																								
5																								
6																					360	360		
7																								
8				114			114			114						114				114		114		
9																								
10																								57

No.	18h30	19h00	19h30	20h00	20h30	21h00	21h30	22h00	22h30	23h00	23h30	00h00	00h30	1h00	1h30	2h00	2h30	3h00	3h30	4h00	4h30	5h00	5h30	6h00	6h30
1																									
2																									
3																									
4																									
5																									
6																									
7																									
8																									
9																									
10																									

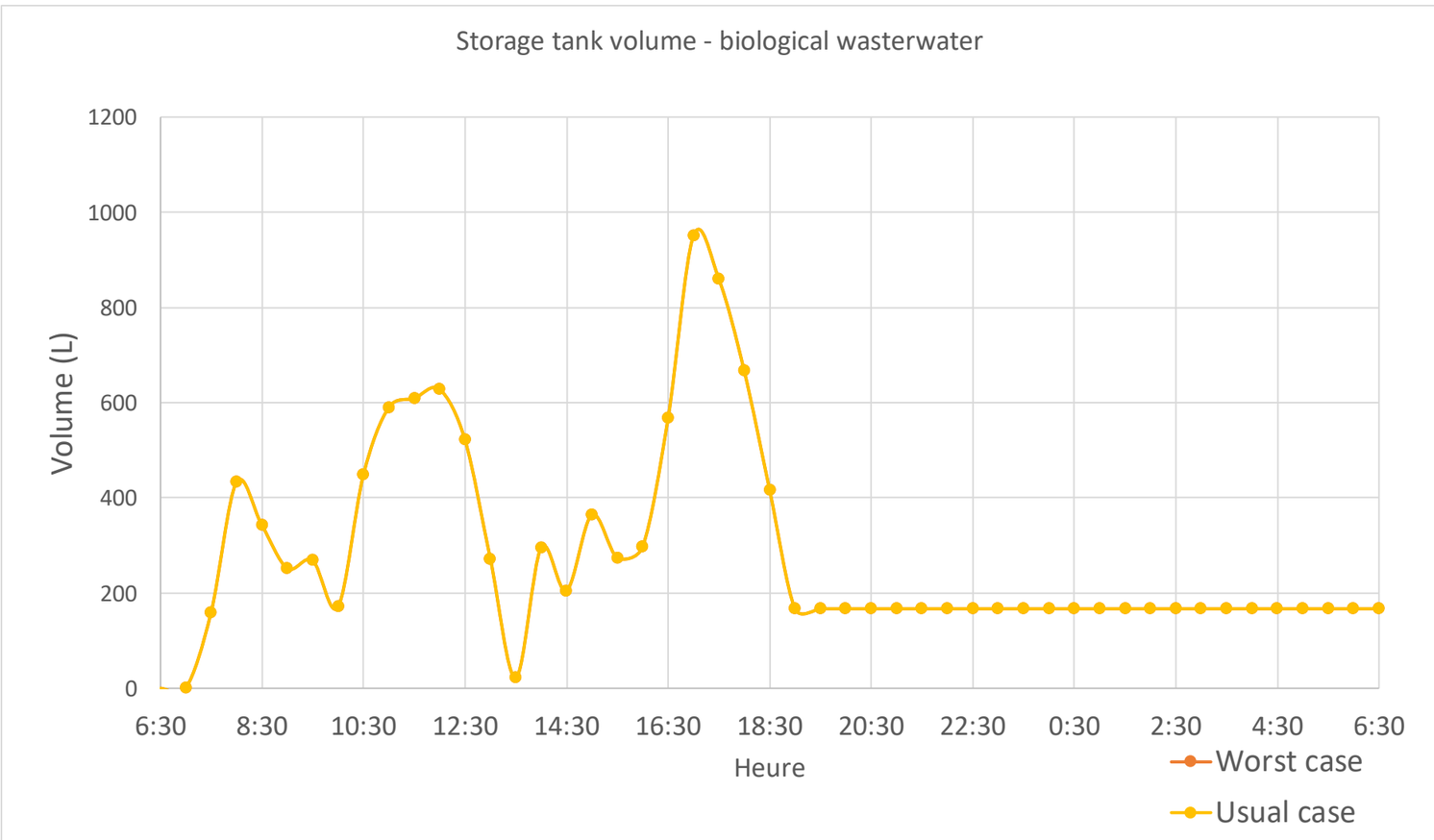
Contaminated effluent total volume for the waorst case day	4,9 m³
Contingency	10%
Working volum of the storage tank for 24hrs holding	5,4 m³	10m3 ou 7.5m3
Treatment capacity	500 LPH
Tank volume	8,0 m³	deux jours de stockage (supplier recommandation)

Average pH
7,0
Worst case

Average Temperature (degC)
28,2
Worst case

Heure (Day 17)	6:30	7:00	7:30	8:00	8:30	9:00	9:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00	15:30	16:00	16:30	17:00	17:30	18:00
Worst case	0	0	160	433	343	252	269	171	449	590	609	628	522	272	22	296	205	365	274	298	567	951	860	667
Usual case	0	0	160	433	343	252	269	171	449	590	609	628	522	272	22	296	205	365	274	298	567	951	860	667
				0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Heure (Day 17)	18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	0:00	0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00	6:30
Worst case	417	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167
Usual case	417	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167
	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0



Working volum	8,0 m³	
Overhead	15%	
Total volume	9,20 m³	Actini: 1500Gal
Tank	Horizontale	
Quantity	1	
Working volume per tank	8,0 m³	
Total volum per tank	9,2 m³	
Tank diameter	2,3 m	cf. Actini
Tank lenght	2,5 m	cf. Actini

Holding goal	8,0 m³	
L footprint	3,5 m	
D footprint	3,0 m	
Height	0,76 m	
	2,19	ft
Holding capacity volum	**8,0 m³**	

Canadian Biosafety Standard (CBS) – 2nd Edition

3.8	Effluent Decontamination Systems	CL2	CL2-Ag	CL3	CL3-Ag	CL4
3.8.5	Rooms housing an effluent decontamination system serving as a primary **decontamination technology** to: • have lockable doors; • have doors with biohazard warning signage; • have sealed floor surfaces; • have floor drains that are sealed or re-routed to the effluent decontamination system; and • have suitable **personal protective equipment** (PPE) and a spill kit available for emergency response.		P		■	
3.8.6	Rooms housing an effluent decontamination system serving as a primary decontamination technology to: • have lockable doors; • have doors with biohazard warning signage; • contain the release of the full volume of the largest holding tank operating capacity of the effluent decontamination system; • have sealed floor surfaces; • have floor drains that are sealed or re-routed to the effluent decontamination system; • maintain **inward directional airflow** (IDA); • have an **anteroom** for entry/exit; • have **high efficiency particulate air (HEPA) filtration** on exhaust air; and • have suitable PPE and a spill kit available for emergency response.					■

NRC-14-NDC-06

[NRC-14]

Bilan des effluents contaminés biologiques

Date : 2020-09-04
Révision : 0A

Type effluent:

Effluents contaminés biologiques (ECB)

Réseaux connexion:
Direct (D)
Indirect (I)

Hypothesis: A vérifier
Ref.NRC-14-NDC-03 (Mass Blance mAb)
Solution using for step preparation are not concidering as biological contaminated liquid waste

Type drain:
DPD-01 Drain au plancher – Direct
+ECH Point d'échantillonnage EPU ou EPPI
SPH-01 SPH-01 : Siphon de sol – Fermé
SPH-02 SPH-02 : Siphon de sol – Ouvert
EVR-01 EVR-01 : Évier
EVR-02 EVR-02 : Évier de plancher

à basé sur sortie du skid (voir fournisseur)
A VALIDER

No.	Zone	Nom du local	Local	Classe	Équipement associé	Type effluent	Réseaux connection	Type de drain	pH	Pour calcul pH	Température	Pour calcul Température	Quantité - pire cas (Volume en L)	Débit (L/PM)	Durée(hr) exposé (max)	Simultanéité par salle	Fréquence	Source	Décontamination du / accès à	Commentaires
1	Production	Upstream	TBD	C	Depth filtration /Bioreactor	ECB	D	DPD-01 +ECH	ph neutre (6,8-7,2)	?	max 37°C	37°C	0	17	DN50	x	une fois par lot	worst case scenario : 500L media additional as worst case scenario ; will be collected manually and transfer to another drain	Non	
2	Production	Downstream 1	TBD	C	Chromatography system_Affinity	ECB	D	DPD-01	Produit - pH neutre Solutions tampons - pH variés (grande majorité à pH neutre, peu à pH basique)	?	20±5°C	20°C	2924	5,3	DN25	x	une fois par lot	AktaReady_Cytiva NDC-03 (mass balance) max flowarate Worst case - time porcess reduce in 10hrs	Non	
3	Production	Downstream 2	TBD	C	Chromatography system_Capto core 700	ECB	D	DPD-01 +ECH	Produit - pH neutre Solutions tampons - pH variés (grande majorité pH neutre, peu pH basique)	?	20±5°C	20°C	2153	3,4	DN80		une fois par lot	AktaReady_Cytiva NDC-03 (mass balance) max flowarate	Non	
4	Production	Downstream 2	TBD	C	Chromatography system_AEX	ECB	D	DPD-01	Produit - pH neutre Solutions tampons - pH variés (grande majorité à pH neutre, peu à pH basique)	?	20±5°C	20°C	25	5	DN25	x	une fois par lot	AktaReady_Cytiva NDC-03 (mass balance) max flowarate	Non	
5	Production	Bulk filling	TBD	C	TFF	ECB	D	DPD-01 +ECH	Produit - pH neutre Solutions tampons - pH variés (grande majorité pH neutre, peu pH basique)	?	20±5°C	20°C	2953	1,6	DN80		une fois par lot	mAb process Model skid : Akta ready flux feed flow : 1,8L/PM permeate: 1,6LPM	Non	
6	Warehouse	Decontamination	TBD	D	Autoclave de decontamination	ECB	D	DPD-01 +ECH	Condensat vapeur pure (pH ?)	?	max 60°C	60°C	720	0,5	1 1/2	x	fréquent	source: Sterinova/Getinge [20201120] [IDR] validated by Teffanie Le François	Non	
7	Bio-Prod.	Corridor support	TBD	D	Douche d'urgence	ECB	I	SPH-01	ph neutre	?	20±5°C	20°C	114	11,4	DN50		excessivement rare	11.4 LPM * 10 min (code plomberie)	Oui	
8	QC	QC lab CL2	TBD	CNC	Évier	ECB	I	EVR-01	ph eau domestique (7) + savon	?	4-40°C	30°C	114	11,4	DN50	x	fréquent	11.4 LPM * 10 min (code plomberie)	Oui	
9	QC	QC lab CL2	TBD	CNC	Douche d'urgence	ECB	I	SPH-01	ph neutre	?	20±5°C	20°C	114	11,4	DN50		excessivement rare	11.4 LPM * 10 min (code plomberie)	Oui	
10	QC	lamitor	TBD	CNC	Évier de plancher	ECB	I	EVR-02	ph eau domestique (7) + savon	?	4-40°C	30°C	57	11,4	DN50		fréquent - ménage	11.4 LPM * 5 min (code plomberie)	Oui	

No.	Commentaires
1	
2	
3	
4	
5	
6	
7	
8	
9	
10	

Jour 17	7h00	7h30	8h00	8h30	9h00	9h30	10h00	10h30	11h00	11h30	12h00	12h30	13h00	13h30	14h00	14h30	15h00	15h30	16h00	16h30	17h00	17h30	18h00	18h30	19h00	19h30	20h00	20h30	21h00	21h30	22h00	22h30	23h00	23h30	00h00	00h30	1h00	1h30	2h00	2h30	3h00	3h30	4h00	4h30	5h00	5h30	6h00	6h30
1								125	125	125	125																																				
2		159,5	159,5	159,5	159,5	152,5	152,5	152,5	152,5	144	144	144			159,5	159,5	159,5	159,5	159,5	159,5	159,5	159,5																								
3																																															
4																																															
5																																															
6																				360	360																											
7																																															
8			114			114			114						114				114		114																										
9																																															
10																							57																								

Heure (Jour 17)	6:30	7:00	7:30	8:00	8:30	9:00	9:30	10:00	10:30	11:00	11:30	12:00	12:30	13:00	13:30	14:00	14:30	15:00	15:30	16:00	16:30	17:00	17:30	18:00	18:30	19:00	19:30	20:00	20:30	21:00	21:30	22:00	22:30	23:00	23:30	0:00	0:30	1:00	1:30	2:00	2:30	3:00	3:30	4:00	4:30	5:00	5:30	6:00	6:30
Pire cas	0	0	166	433	343	252	269	171	446	590	609	628	522	272	22	296	205	365	274	298	367	951	866	667	417	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167
Cas usuel	0	0	166	433	343	252	269	171	446	590	609	628	522	272	22	296	205	365	274	298	367	951	866	667	417	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167	167
			0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Total effluents contaminés biologiques sur pire journée	4,9 m³
Contingence	10%
Volume utile de cuve requis pour rétention 24h	5,4 m³
Débit de traitement	50m3/jou 7.5m3/h
Volume de cuve	8,0 m³
	Deux jours de stockage (supplier recommandation)

pH moyen dans le réservoir d'effluents
7,0
(Pire cas)

Température moyenne dans le réservoir d'effluents
28,2
(Pire cas)

Volume utile	8,0 m³
Overhead	15%
Volume total	9,20 m³ Actini: 1500Gal
Cuve	Horizontale
Nombre de cuve	1
Volume utile par cuve	8,0 m³
Volume total par cuve	9,2 m³
Diamètre de cuve	2,1 m cf. Actini
Longueur de cuve	2,5 m cf. Actini

Rétention cible dans la salle	8,0 m³
Longueur de la zone	3,5 m
Largeur de la zone	3,0 m
Profeur de la zone	0,76 m
	2,33 ft
Volume retenu	**8,0 m³**

Canadian Biosafety Standard (CBS) – 2nd Edition

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3.8.5	Rooms housing an effluent decontamination system serving as a primary decontamination technology to: • have lockable doors; • have doors with biohazard warning signage; • have sealed floor surfaces; • have floor drains that are sealed or rerouted to the effluent decontamination system; and • have suitable personal protective equipment (PPE) and a spill kit available for emergency response.			P		■
3.8.6	Rooms housing an effluent decontamination system serving as a primary decontamination technology to: • have lockable doors; • have doors with biohazard warning signage; • contain the release of the full volume of the largest holding tank operating capacity of the effluent decontamination system; • have sealed floor surfaces; • have floor drains that are sealed or rerouted to the effluent decontamination system; • maintain inward directional airflow (IDA); • have an anteroom for entry/exit; • have high efficiency particulate air (HEPA) filtration on exhaust air; and • have suitable PPE and a spill kit available for emergency response.					■

[NRC-14] National Research Council

Object: Solid waste volum estimation

Date: 2020-11-20

Hypothesis:

1 Contaminated wastes Usptream/Downstream1/Downstream2/Bulkfilling/QC lab
2 Wastewater to be treated in specific way
3 All solid waste volum are estimated or based on technical specification from random suppliers
4 Waste from toilet, janitor and office are not included
5 Quantities of items are based on Warehouse estimation NRC-14-NDC-02

legende: **biowaste** **potential biowaste**

Activity/waste items	Items quantity		Volum per item		Total volum		Comment
Biomanufacturing							
Sterilization wrap	100	units	-	m^3	1,812	m^3	1,2192m x 1,2192m x 1,2192m
Powder transfer bag small volume	88	units	0,005	m^3	0,440	m^3	5L en m3
Powder transfer bag large volume	44	units	0,025	m^3	1,100	m^3	25L en m3
250mL flask	15	units	0,00025	m^3	0,004	m^3	250mL flask en m3
750mL flask	8	units	0,00075	m^3	0,006	m^3	750mL flask en m3
2000mL flask	12	units	0,002	m^3	0,024	m^3	2000mL flask en m3
50L bioreactor bag	1	units	0,0375	m^3	0,020	m^3	0,75 of bag volum (flexible line included)
500L bioreactor bag	1	units	0,375	m^3	0,297	m^3	0,75 of bag volum (flexible line included)
5L bag	3	units	0,00375	m^3	0,011	m^3	0,75 of bag volum (flexible line included) - biowaste if contact with product
10L bag	5	units	0,0075	m^3	0,038	m^3	0,75 of bag volum (flexible line included)- biowaste if contact with product
20L bag	2	units	0,015	m^3	0,030	m^3	0,75 of bag volum (flexible line included)- biowaste if contact with product
25L bag	6	units	0,01875	m^3	0,113	m^3	0,75 of bag volum (flexible line included)- biowaste if contact with product
Mixers 50L	25	units	0,0375	m^3	0,938	m^3	0,75 of bag volum (flexible line included)
Mixers 100L	32	units	0,075	m^3	2,400	m^3	0,75 of bag volum (flexible line included)
Mixers 200L	22	units	0,15	m^3	3,300	m^3	0,75 of bag volum (flexible line included)
Mixers 500L	10	units	0,375	m^3	3,750	m^3	0,75 of bag volum (flexible line included)
Tanks 50L	8	units	0,0375	m^3	0,300	m^3	0,75 of bag volum (flexible line included)
Tanks 100L	32	units	0,075	m^3	2,400	m^3	0,75 of bag volum (flexible line included)
Tanks 200L	22	units	0,15	m^3	3,300	m^3	0,75 of bag volum (flexible line included)
Tanks 500L	10	units	0,375	m^3	3,750	m^3	0,75 of bag volum (flexible line included)
Tanks 1000L	2	units	0,75	m^3	1,500	m^3	0,75 of bag volum (flexible line included)
Filter 0,85 Maxi	10	units	0,000978	m^3	0,010	m^3	filter 10 in: 254mm height x 70mm D - biowaste if contact with product
Filter 0,45 Maxi	10	units	0,000978	m^3	0,010	m^3	filter 10 in: 254mm height x 70mm D
Filter 0,22 Maxi	3	units	0,000978	m^3	0,003	m^3	filter 10 in: 254mm height x 70mm D
Filter 0,22 Mini	1	units	0,000827	m^3	0,001	m^3	filter 5 in: 125mm height x 70mm D
Depth filration cartridge - clarification	2	units	0,002841	m^3	0,006	m^3	cassette 2.5m2: 178mm long x 210mm largeur x 76mm hauteur
UF/DF membrane large scale	3	units	0,025517	m^3	0,077	m^3	cassette 0.8m2: 634mm long x 387mm largeur x 104mm hauteur
UF/DF membrane small scale	5	units	0,012759	m^3	0,064	m^3	0,5 x cassette 0.8m2: 634mm long x 387mm largeur x 104mm hauteur
Chromatography column large scale	5	units	0,079522	m^3	0,398	m^3	30L resin: 500mm L x 450mm D
Chromatography membrane	5	units	0,115021	m^3	0,575	m^3	4x capsule 5L: 605mm L x 246mm D
Filling buffer bag 50L	5	units	0,0375	m^3	0,188	m^3	0,75 of bag volum (flexible line included)
Cleaning/Sterilization							
Empty bag	40	units	-	m^3	0,2265348	m^3	0,6096m x 0,6096m x 0,6096m
QC lab							
Large sample	300	units	5,3E-05	m^3	0,016	m^3	vial 30ml Schott: 75 mm H x 30mm D
Small sample	20	units	7,04E-06	m^3	0,0001	m^3	vial 2ml Schott: 35mm H x 16mm D
Warehouse							
Overwrap	77	units	0,226535	m^3	17,443	m^3	100 palets- 0,6096m x 0,6096m x 0,6096m
Gowning							
Gowning disposable bag	15	units	0,5	m^3	7,500	m^3	estimation
Subtotal					52,0	m^3	
Contengency (15%)					7,8	m^3	
TOTAL					**60**	**m3**	

Date: 2020-11-18
[NRC-14]

Purified Water process requirements

Hypothesis

Ref NRC-10

ref. NRC-14-NDC-05 (WFI simulation)

Room/equipment	Activity	Pressure required	Flow	Diameter	Duration	Volume / use	Worst case	Total WC
		(psig)	(L/min)		(min)	(L)		(L)
Cleaning								
Sink	Washing small equipment		11,4		10	114	42	4788
Sink	Washing small equipment		11,4		10	114	42	4788
Glass washer	Rinces	90 max	75	1"		260	21	5460
Total								**15036**

Client : Canadian National Research Council
Project : Royalmount Viral Vaccine Facility
Project NRC-14

Date : 2020-11-18

Purified water consumption simulation

System parameters				
PW Storage tank total volume:	3900	(L)		
PW Storage tank:	3000	(L)		
PW Production flow rate :	25,3	(LPM)	1518,4025	Liters/hour produce by the reserve osmosis system

LSX15 flowrate 26,5-56,7 LPM

D8

Points of use - Purified water

Room	Equipment	Activity	Vol. per week	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00	18:00	20:00	22:00
Cleaning	Sink	Cleaning	4902		114		114		114		114	114	114		114
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114	
Cleaning	Glass washer	Cleaning	5460		260				260			260			
Mechanical room	Multiple-effect still	Produce WFI	22071	0,0	169,0	0,0	0,0	274,3	1040,0	456,3	1008,8	1955,2	314,6	0,0	0,0
Labo QC-cleaning	Sink	Cleaning	114									114,0			
	Glass washer	Cleaning	26									26,0			
Sterilization	Clean steam generator	Produce pure steam	1208		57,5				57,5			57,5			
			38682												
Volume of purified water at the begining of the period (L) :			**484**	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour (L):				114	600,5	114	114	388,3	1471,5	570,3	1122,8	2640,7	428,6	114	114
Purified water storage tank filling (L):				114	600,5	114	114	388,3	1471,5	570,3	1122,8	2640,7	428,6	114	114
Volume of purified water at the begining of the period with 15% contingency (L) :				7605	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour with 15% contingency (L):				131,1	690,58	131,1	131,1	446,55	1692,2	655,85	1291,2	3036,8	492,89	131,1	131,1
Purified water storage tank filling (L):				0	690,58	131,1	131,1	446,55	1692,2	655,85	1291,2	3036,8	492,89	131,1	131,1

Peak in two hours (L): 3037
Peak in one hours (L): 1518

Distribution loop flow:	**Points of use**	**Flow**		**Diameter**
	Sink	11,4	lpm	
	Sink	11,4	lpm	
	Glass washer	75	lpm	1" TC
	Clean steam generator	20	lpm	3/4" TC
		118	**lpm**	
		153		
	Flow	0,002552333	m3/s	
	Piping	**2**	**inches**	
	Internal diameter	47,5	mm	
	Internal diameter	0,0475	m	
	Area	0,002	m2	
	Velocity	1,44	m/s	
	Velocity	**4,73**	**ft/s**	

TECHNICAL DATA

Product Specifications					
BioPure LSX USP Purified Water System					
Part Number	LSX6.5	LSX15	LSX20	LSX30	LSX40
Product Flow Rate at 77°F (25°C)	2.5 to 6.5 US gpm 9.5 to 24.6 lpm	7.0 to 15.0 US gpm 26.5 to 56.7 lpm	14.0 to 20.0 US gpm 53.0 to 75.7 lpm	16.0 to 30.0 US gpm 60.6 to 113.6 lpm	26.0 to 40.0 US gpm 98.4 to 115.4 lpm
Dry Weight	4,000 lbs (1814 kg)	5,500 lbs (2495 kg)	6,000 lbs (2722 kg)	6,800 lbs (3084 kg)	7,300 lbs (3311 kg)
Dimensions - Inches (mm)	124" L x 66" W x 93" H (3150mm x 1676mm x 2362mm)		124" L x 66" W x 82" H (3150mm x 1676mm x 2083mm)	143" L x 87" W x 86" H (3632mm x 2210mm x 2184mm)	
Power	460,575VAC / 3PH / 60HZ. Power selected at time of order.				

Client : Canadian National Research Council
Project : Royalmount Viral Vaccine Facility
Project NRC-14

Date : 2020-11-18

Purified water consumption simulation

System parameters			
PW Storage tank total volume:	3900	(L)	
PW Storage tank:	3000	(L)	
PW Production flow rate :	25,3	(LPM)	1518,4025

LSX15 flowrate 26,5-56,7 LPM

D9

Points of use - Purified water

Room	Equipment	Activity	Vol. per week	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00	18:00	20:00	22:00
Cleaning	Sink	Cleaning	4902		114		114		114		114		114		114
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114	
Cleaning	Glass washer	Cleaning	5460		260				260				260		
Mechanical room	Multiple-effect still	Produce WFI	22071	0,0	169,0	0,0	414,7	14,3	984,1	699,4	984,1	655,2	824,2	0,0	0,0
Labo QC-cleaning	Sink	Cleaning	114												
	Glass washer	Cleaning	26												
Sterilization	Clean steam generator	Produce pure steam	1208		57,5				57,5				57,5		
			38682												
Volume of purified water at the begining of the period (L) :			**484**	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour (L):				114	600,5	114	528,7	128,3	1415,6	813,4	1098,1	769,2	1255,7	114	114
Purified water storage tank filling (L):				114	600,5	114	528,7	128,3	1415,6	813,4	1098,1	769,2	1255,7	114	114
Volume of purified water at the begining of the period with 15% contingency (L) :				3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour with 15% contingency (L):				131,1	690,58	131,1	608,01	147,55	1627,9	935,41	1262,8	884,58	1444,1	131,1	131,1
Purified water storage tank filling (L):				131,1	690,58	131,1	608,01	147,55	1627,9	935,41	1262,8	884,58	1444,1	131,1	131,1

Peak in two hours (L): 3037
Peak in one hours (L): 1518

Distribution loop flow:

Points of use	**Flow**	
Sink	11,4	lpm
Sink	11,4	lpm
Glass washer	75	lpm
Clean steam generator	20	lpm
	118	**lpm**
	153	
Flow	0,002552333	m3/s
Piping	**2**	**inches**
Internal diameter	47,5	mm
Internal diameter	0,0475	m
Area	0,002	m2
Velocity	1,44	m/s
Velocity	**4,73**	**ft/s**

TECHNICAL DATA

Product Specifications					
BioPure LSX USP Purified Water System					
Part Number	LSX6.5	LSX15	LSX20	LSX30	LSX40
Product Flow Rate at 77°F (25°C)	2.5 to 6.5 US gpm 9.5 to 24.6 lpm	7.0 to 15.0 US gpm 26.5 to 56.7 lpm	14.0 to 20.0 US gpm 53.0 to 75.7 lpm	16.0 to 30.0 US gpm 60.6 to 113.6 lpm	26.0 to 40.0 US gpm 98.4 to 115.4 lpm
Dry Weight	4,000 lbs (1814 kg)	5,500 lbs (2495 kg)	6,000 lbs (2722 kg)	6,800 lbs (3084 kg)	7,300 lbs (3311 kg)
Dimensions - Inches (mm)	124" L x 66" W x 93" H (3150mm x 1676mm x 2362mm)		124" L x 66" W x 82" H (3150mm x 1676mm x 2083mm)	143" L x 87" W x 86" H (3632mm x 2210mm x 2184mm)	
Power	460,575VAC / 3PH / 60HZ. Power selected at time of order.				

Client : Canadian National Research Council
Project : Royalmount Viral Vaccine Facility
Project NRC-14
Date : 2020-11-18

Purified water consumption simulation

System parameters			
PW Storage tank total volume:	3900	(L)	
PW Storage tank:	3000	(L)	
PW Production flow rate :	25,3	(LPM)	1518,4025

LSX15 flowrate 26,5-56,7 LPM

D10

Points of use - Purified water													
Room	**Equipment**	**Activity**	**Vol. per week**	**00:00**	**02:00**	**04:00**	**06:00**	**08:00**	**10:00**	**12:00**	**14:00**	**16:00**	**18:00**	**20:00**	**22:00**
Cleaning	Sink	Cleaning	4902		114		114		114		114		114		114
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114	
Cleaning	Glass washer	Cleaning	5460		260				260				260		
Mechanical room	Multiple-effect still	Produce WFI	22071	0,0	169,0	0,0	414,7	1,3	672,1	586,3	564,2	357,5	526,5	0,0	0,0
Labo QC-cleaning	Sink	Cleaning	114												
	Glass washer	Cleaning	26												
Sterilization	Clean steam generator	Produce pure steam	1208		57,5				57,5				57,5		
			38682												
Volume of purified water at the begining of the period (L) :			**484**	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour (L):				114	600,5	114	528,7	115,3	1103,6	700,3	678,2	471,5	958	114	114
Purified water storage tank filling (L):				114	600,5	114	528,7	115,3	1103,6	700,3	678,2	471,5	958	114	114
Volume of purified water at the begining of the period with 15% contingency (L) :				3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour with 15% contingency (L):				131,1	690,58	131,1	608,01	132,6	1269,1	805,35	779,93	542,23	1101,7	131,1	131,1
Purified water storage tank filling (L):				131,1	690,58	131,1	608,01	132,6	1269,1	805,35	779,93	542,23	1101,7	131,1	131,1

Peak in two hours (L): 3037
Peak in one hours (L): 1518

Distribution loop flow:

Points of use	**Flow**	
Sink	11,4	lpm
Sink	11,4	lpm
Glass washer	75	lpm
Clean steam generator	20	lpm
	118	**lpm**
	153	
Flow	0,002552333	m3/s
Piping	**2**	**inches**
Internal diameter	47,5	mm
Internal diameter	0,0475	m
Area	0,002	m2
Velocity	1,44	m/s
Velocity	**4,73**	**ft/s**

TECHNICAL DATA

Product Specifications					
BioPure LSX USP Purified Water System					
Part Number	LSX6.5	LSX15	LSX20	LSX30	LSX40
Product Flow Rate at 77°F (25°C)	2.5 to 6.5 US gpm 9.5 to 24.6 lpm	7.0 to 15.0 US gpm 26.5 to 56.7 lpm	14.0 to 20.0 US gpm 53.0 to 75.7 lpm	16.0 to 30.0 US gpm 60.6 to 113.6 lpm	26.0 to 40.0 US gpm 98.4 to 115.4 lpm
Dry Weight	4,000 lbs (1814 kg)	5,500 lbs (2495 kg)	6,000 lbs (2722 kg)	6,800 lbs (3084 kg)	7,300 lbs (3311 kg)
Dimensions - Inches (mm)	124" L x 66" W x 93" H (3150mm x 1676mm x 2362mm)		124" L x 66" W x 82" H (3150mm x 1676mm x 2083mm)	143" L x 87" W x 86" H (3632mm x 2210mm x 2184mm)	
Power	460,575VAC / 3PH / 60HZ. Power selected at time of order.				

Client : Canadian National Research Council
Project : Royalmount Viral Vaccine Facility
Project NRC-14

Date : 2020-11-18

Purified water consumption simulation

System parameters			
PW Storage tank total volume:	3900	(L)	
PW Storage tank:	3000	(L)	
PW Production flow rate :	25,3	(LPM)	1518,4025

LSX15 flowrate 26,5-56,7 LPM

D11

Points of use - Purified water				**Consumption over a one week production (Liters)**												
Room	**Equipment**	**Activity**	**Vol. per week**	**00:00**	**02:00**	**04:00**	**06:00**	**08:00**	**10:00**	**12:00**	**14:00**	**16:00**	**18:00**	**20:00**	**22:00**
Cleaning	Sink	Cleaning	4902		114		114		114		114		114		114
Cleaning	Sink	Cleaning	4902	114	114	114		114		114		114		114	
Cleaning	Glass washer	Cleaning	5460		260				260				260		
Mechanical room	Multiple-effect still	Produce WFI	22071	0,0	169,0	0,0	0,0	7,8	65,0	429,0	1071,2	773,5	942,5	0,0	0,0
Labo QC-cleaning	Sink	Cleaning	114												
	Glass washer	Cleaning	26												
Sterilization	Clean steam generator	Produce pure steam	1208		57,5				57,5					57,5	
			38682												
Volume of purified water at the begining of the period (L) :			**484**	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour (L):				114	714,5	114	114	121,8	496,5	543	1185,2	887,5	1316,5	171,5	114
Purified water storage tank filling (L):				114	714,5	114	114	121,8	496,5	543	1185,2	887,5	1316,5	171,5	114
Volume of purified water at the begining of the period with 15% contingency (L) :				3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour with 15% contingency (L):				131,1	821,68	131,1	131,1	140,07	570,98	624,45	1363	1020,6	1514	197,23	131,1
Purified water storage tank filling (L):				131,1	821,68	131,1	131,1	140,07	570,98	624,45	1363	1020,6	1514	197,23	131,1

Peak in two hours (L): 3037
Peak in one hours (L): 1518

Distribution loop flow:	**Points of use**	**Flow**	
	Sink	11,4	lpm
	Sink	11,4	lpm
	Glass washer	75	lpm
	Clean steam generator	20	lpm
		118	**lpm**
		153	
	Flow	0,002552333	m3/s
	Piping	**2**	**inches**
	Internal diameter	47,5	mm
	Internal diameter	0,0475	m
	Area	0,002	m2
	Velocity	1,44	m/s
	Velocity	**4,73**	**ft/s**

TECHNICAL DATA

Product Specifications					
BioPure LSX USP Purified Water System					
Part Number	LSX6.5	LSX15	LSX20	LSX30	LSX40
Product Flow Rate at 77°F (25°C)	2.5 to 6.5 US gpm 9.5 to 24.6 lpm	7.0 to 15.0 US gpm 26.5 to 56.7 lpm	14.0 to 20.0 US gpm 53.0 to 75.7 lpm	16.0 to 30.0 US gpm 60.6 to 113.6 lpm	26.0 to 40.0 US gpm 98.4 to 115.4 lpm
Dry Weight	4,000 lbs (1814 kg)	5,500 lbs (2495 kg)	6,000 lbs (2722 kg)	6,800 lbs (3084 kg)	7,300 lbs (3311 kg)
Dimensions - Inches (mm)	124" L x 66" W x 93" H (3150mm x 1676mm x 2362mm)		124" L x 66" W x 82" H (3150mm x 1676mm x 2083mm)	143" L x 87" W x 86" H (3632mm x 2210mm x 2184mm)	
Power	460,575VAC / 3PH / 60HZ. Power selected at time of order.				

Client : Canadian National Research Council
Project : Royalmount Viral Vaccine Facility
Project NRC-14

Purified water consumption simulation

System parameters		
PW Storage tank total volume:	3900	(L)
PW Storage tank:	3000	(L)
PW Production flow rate :	25,3	(LPM)

1518,4025

LSX15 flowrate 26,5-56,7 LPM

D12

Points of use - Purified water

Room	Equipment	Activity	Vol. per week	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00	18:00	20:00	22:00
Cleaning	Sink	Cleaning	4902		114		114		114		114		114		114
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114	
Cleaning	Glass washer	Cleaning	5460		260				260				260		
Mechanical room	Multiple-effect still	Produce WFI	22071	0,0	169,0	0,0	258,7	170,3	197,6	287,3	1084,2	1098,2	1098,5	494,0	0,0
Labo QC-cleaning	Sink	Cleaning	114												
	Glass washer	Cleaning	26												
Sterilization	Clean steam generator	Produce pure steam	1208		57,5				57,5				57,5		
			38682												
Volume of purified water at the begining of the period (L) :			**484**	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour (L):				114	600,5	114	372,7	284,3	629,1	401,3	1198,2	1212,2	1530	608	114
Purified water storage tank filling (L):				114	600,5	114	372,7	284,3	629,1	401,3	1198,2	1212,2	1530	608	114
Volume of purified water at the begining of the period with 15% contingency (L) :				3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour with 15% contingency (L):				131,1	690,58	131,1	428,61	326,95	723,47	461,5	1377,9	1394	1759,5	699,2	131,1
Purified water storage tank filling (L):				131,1	690,58	131,1	428,61	326,95	723,47	461,5	1377,9	1394	1759,5	699,2	131,1

Peak in two hours (L): 3037
Peak in one hours (L): 1518

Distribution loop flow:

Points of use	**Flow**	
Sink	11,4	lpm
Sink	11,4	lpm
Glass washer	75	lpm
Clean steam generator	20	lpm
	118	**lpm**
	153	
Flow	0,002552333	m3/s
Piping	**2**	**inches**
Internal diameter	47,5	mm
Internal diameter	0,0475	m
Area	0,002	m2
Velocity	1,44	m/s
Velocity	**4,73**	**ft/s**

TECHNICAL DATA

Product Specifications					
BioPure LSX USP Purified Water System					
Part Number	LSX6.5	LSX15	LSX20	LSX30	LSX40
Product Flow Rate at 77°F (25°C)	2.5 to 6.5 US gpm 9.5 to 24.6 lpm	7.0 to 15.0 US gpm 26.5 to 56.7 lpm	14.0 to 20.0 US gpm 53.0 to 75.7 lpm	16.0 to 30.0 US gpm 60.6 to 113.6 lpm	26.0 to 40.0 US gpm 98.4 to 115.4 lpm
Dry Weight	4,000 lbs (1814 kg)	5,500 lbs (2495 kg)	6,000 lbs (2722 kg)	6,800 lbs (3084 kg)	7,300 lbs (3311 kg)
Dimensions - Inches (mm)	124" L x 66" W x 93" H (3150mm x 1676mm x 2362mm)		124" L x 66" W x 82" H (3150mm x 1676mm x 2083mm)	143" L x 87" W x 86" H (3632mm x 2210mm x 2184mm)	
Power	460,575VAC / 3PH / 60HZ. Power selected at time of order.				

Client : Canadian National Research Council
Project : Royalmount Viral Vaccine Facility
Project NRC-14
Date : 2020-11-18

Purified water consumption simulation

System parameters			
PW Storage tank total volume:	3900	(L)	
PW Storage tank:	3000	(L)	
PW Production flow rate :	25,3	(LPM)	1518,4025

LSX15 flowrate 26,5-56,7 LPM D13

Points of use - Purified water

Room	Equipment	Activity	Vol. per week	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00	18:00	20:00	22:00
Cleaning	Sink	Cleaning	4902		114		114		114		114		114		114
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114	
Cleaning	Glass washer	Cleaning	5460		260				260				260		
Mechanical room	Multiple-effect still	Produce WFI	22071	0,0	0,0	0,0	0,0	0,0	0,0	500,0	0,0	0,0	0,0	0,0	0,0
Labo QC-cleaning	Sink	Cleaning	114												
	Glass washer	Cleaning	26												
Sterilization	Clean steam generator	Produce pure steam	1208		57,5				57,5				57,5		
			38682												
Volume of purified water at the begining of the period (L) :			**484**	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour (L):				114	431,5	114	114	114	431,5	614	114	114	431,5	114	114
Purified water storage tank filling (L):				114	431,5	114	114	114	431,5	614	114	114	431,5	114	114
Volume of purified water at the begining of the period with 15% contingency (L) :				3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour with 15% contingency (L):				131,1	496,23	131,1	131,1	131,1	496,23	706,1	131,1	131,1	496,23	131,1	131,1
Purified water storage tank filling (L):				131,1	496,23	131,1	131,1	131,1	496,23	706,1	131,1	131,1	496,23	131,1	131,1

Peak in two hours (L): 3037
Peak in one hours (L): 1518

Distribution loop flow:

Points of use	**Flow**	
Sink	11,4	lpm
Sink	11,4	lpm
Glass washer	75	lpm
Clean steam generator	20	lpm
	118	**lpm**
	153	
Flow	0,002552333	m3/s
Piping	**2**	**inches**
Internal diameter	47,5	mm
Internal diameter	0,0475	m
Area	0,002	m2
Velocity	1,44	m/s
Velocity	**4,73**	**ft/s**

TECHNICAL DATA

Product Specifications					
BioPure LSX USP Purified Water System					
Part Number	LSX6.5	LSX15	LSX20	LSX30	LSX40
Product Flow Rate at 77°F (25°C)	2.5 to 6.5 US gpm 9.5 to 24.6 lpm	7.0 to 15.0 US gpm 26.5 to 56.7 lpm	14.0 to 20.0 US gpm 53.0 to 75.7 lpm	16.0 to 30.0 US gpm 60.6 to 113.6 lpm	26.0 to 40.0 US gpm 98.4 to 115.4 lpm
Dry Weight	4,000 lbs (1814 kg)	5,500 lbs (2495 kg)	6,000 lbs (2722 kg)	6,800 lbs (3084 kg)	7,300 lbs (3311 kg)
Dimensions - Inches (mm)	124" L x 66" W x 93" H (3150mm x 1676mm x 2362mm)		124" L x 66" W x 82" H (3150mm x 1676mm x 2083mm)	143" L x 87" W x 86" H (3632mm x 2210mm x 2184mm)	
Power	460,575VAC / 3PH / 60HZ. Power selected at time of order.				

Client : Canadian National Research Council
Project : Royalmount Viral Vaccine Facility
Project NRC-14

Date : 2020-11-18

Purified water consumption simulation

System parameters			
PW Storage tank total volume:	3900	(L)	
PW Storage tank:	3000	(L)	
PW Production flow rate :	25,3	(LPM)	1518,4025

LSX15 flowrate 26,5-56,7 LPM D14

Points of use - Purified water

Room	Equipment	Activity	Vol. per week	00:00	02:00	04:00	06:00	08:00	10:00	12:00	14:00	16:00	18:00	20:00	22:00
Cleaning	Sink	Cleaning	4902		114		114		114		114		114		114
Cleaning	Sink	Cleaning	4902	114		114		114		114		114		114	
Cleaning	Glass washer	Cleaning	5460		260				260				260		
Mechanical room	Multiple-effect still	Produce WFI	22071	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0
Labo QC-cleaning	Sink	Cleaning	114												
	Glass washer	Cleaning	26												
Sterilization	Clean steam generator	Produce pure steam	1208		57,5				57,5				57,5		
			38682												
Volume of purified water at the begining of the period (L) :			**484**	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour (L):				114	431,5	114	114	114	431,5	114	114	114	431,5	114	114
Purified water storage tank filling (L):				114	431,5	114	114	114	431,5	114	114	114	431,5	114	114
Volume of purified water at the begining of the period with 15% contingency (L) :				3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000	3000
Consumption in two hour with 15% contingency (L):				131,1	496,23	131,1	131,1	131,1	496,23	131,1	131,1	131,1	496,23	131,1	131,1
Purified water storage tank filling (L):				131,1	496,23	131,1	131,1	131,1	496,23	131,1	131,1	131,1	496,23	131,1	131,1

Peak in two hours (L): 3037
Peak in one hours (L): 1518

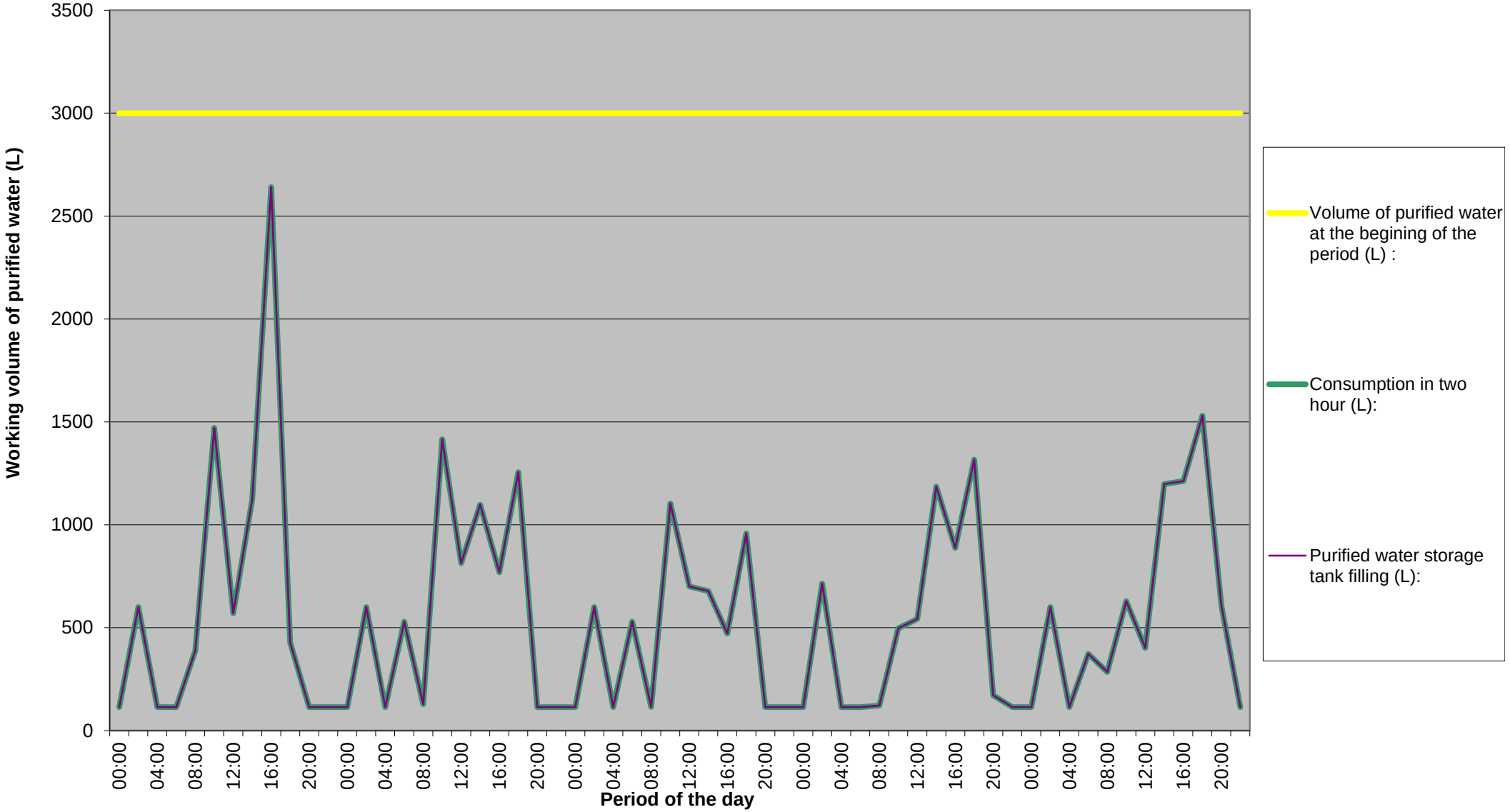
Distribution loop flow:

Points of use	**Flow**	
Sink	11,4	lpm
Sink	11,4	lpm
Glass washer	75	lpm
Clean steam generator	20	lpm
	118	**lpm**
	153	
Flow	0,002552333	m3/s
Piping	**2**	**inches**
Internal diameter	47,5	mm
Internal diameter	0,0475	m
Area	0,002	m2
Velocity	1,44	m/s
Velocity	**4,73**	**ft/s**

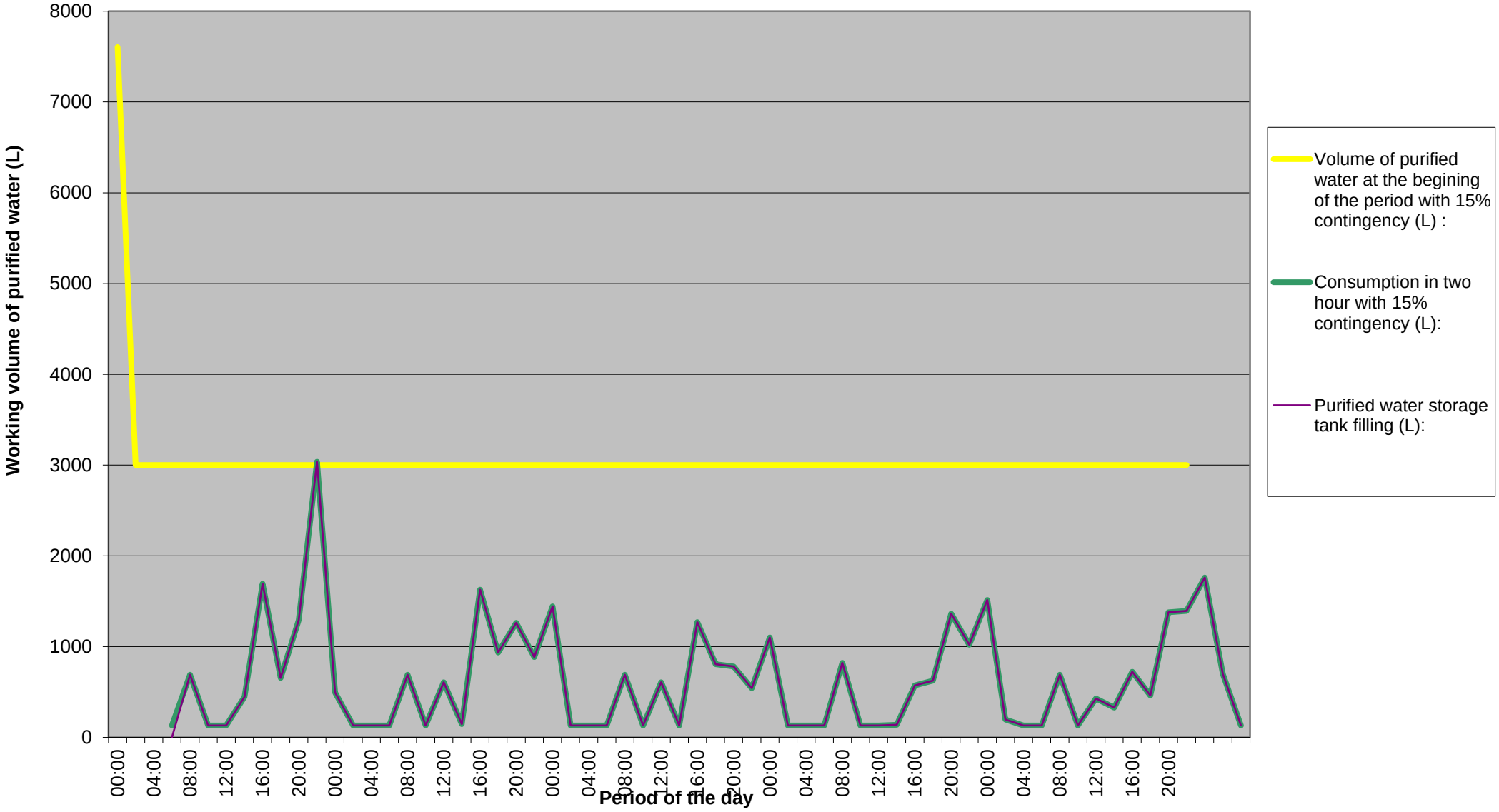
TECHNICAL DATA

Product Specifications					
BioPure LSX USP Purified Water System					
Part Number	LSX6.5	LSX15	LSX20	LSX30	LSX40
Product Flow Rate at 77°F (25°C)	2.5 to 6.5 US gpm 9.5 to 24.6 lpm	7.0 to 15.0 US gpm 26.5 to 56.7 lpm	14.0 to 20.0 US gpm 53.0 to 75.7 lpm	16.0 to 30.0 US gpm 60.6 to 113.6 lpm	26.0 to 40.0 US gpm 98.4 to 115.4 lpm
Dry Weight	4,000 lbs (1814 kg)	5,500 lbs (2495 kg)	6,000 lbs (2722 kg)	6,800 lbs (3084 kg)	7,300 lbs (3311 kg)
Dimensions - Inches (mm)	124" L x 66" W x 93" H (3150mm x 1676mm x 2362mm)		124" L x 66" W x 82" H (3150mm x 1676mm x 2083mm)	143" L x 87" W x 86" H (3632mm x 2210mm x 2184mm)	
Power	460,575VAC / 3PH / 60HZ. Power selected at time of order.				

Simulation of purified water working volume in storage tank



Simulation of purified water working volume in storage tank with 15% contingency



APPENDIX J: FEASIBILITY STUDY – MOVING MICROBIAL SUITE

For this project, the fermentation laboratory must be relocated to another area. The H3 is currently the chosen area for relocation. The new area will also need storage spaces as indicated by NRC. A layout was drawn to meet two goals (See Appendix B):

- Verify if the available space in H3 is sufficient.
- Estimate the required space

The following equipment will be moved and installed in H3:

- One (1) Refrigerator
- Two (2) Freezers (-20 ºC and -80ºC)
- Multiples cabinets for storage
- Two (2) Ovens
- One (1) Gas analyzer
- One (1) Kill Tank
- One (1) Control unit
- Two (2) DASGIP system
- Multiples tables and furniture
- One (1) Toolbox
- One (1) Garbage
- One (1) Biological safety cabinet
- Two (2) Bioreactors (20 L and 150 L)
- One (1) TOC Cart
- One (1) Autoclave
- One (1) Centrifuge
- Three incubators (Two statics and one shaker incubators)
- One (1) oxygen distribution system with a switch over valve
- One (1) Autoclave with capacity for autoclaving 8 X 2 L glass
- One (1) Ceiling lifting equipment (not represented on the layout, hung to the ceiling)
- One (1) Sink
- One (1) bench (with bench equipment: Spectrophotometer, microscope, microfuge, pH meter, computer for data analysis)

Two storage rooms (Storage 1 and Storage 2) are needed for the fermentation laboratory. Both rooms will be tempered, and Storage 1 will be vented. The storage area in H3 will be 1.5 times larger than the storage area for the current fermentation laboratory storage. The layout is only a preliminary drawing. Material and personal flows shall be evaluated in a future report/project. Moving costs are not included in this feasibility study. Also, we assumed all equipment currently in H3 is removable and walls can be moved to accommodate the new laboratory.