D3.4 FINAL DESIGN OF THE FACILITIES AND INFRASTRUCTURE

WP3 – FACILITIES AND INFRASTRUCTURE

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I. Introduction

EURO-CARES (European Curation of Astromaterials Returned from Exploration of Space) is a three year, multinational project, funded under the European Commission's Horizon2020 research programme to create a roadmap for the implementation of a European Extra-terrestrial Sample Curation Facility (ESCF). EURO-CARES team work is organized around five technical Work Packages (WP), led by scientists and engineers representing institutions from all over Europe.

The ESCF must be designed to curate and characterize samples returned from space, from different types of bodies. COSPAR defines the terms "Unrestricted" for sample return missions from locations judged by scientific opinion to have no indigenous lifeforms, such as the Moon or asteroids, and "Restricted" for sample return missions where scientific opinion is unsure regarding indigenous lifeforms, such as Mars. In our study, we use these terms for the samples themselves. The infrastructure should be designed and constructed to prevent sample contamination and alteration on one hand, and to prevent release of potential biohazards from the facility on the other hand (in the case of restricted samples).

The objective of the WP3 "Facilities and Infrastructures" is to define the state-of-the-art facilities required to receive, contain, and curate extra-terrestrial samples whilst guaranteeing terrestrial planetary protection. All the aspects of building design, ranging from sample reception to their storage/curation are covered by this work package. The curation facility should enable long-term, high quality research, either by providing pristine samples to the science community, or by planning fully functional laboratories within the facility.

The first task of this Work Package was to conduct an extensive literature review in year 1 (2015; see D1.3). Then, as with the other WPs, an international meeting was organised gathering experts to present the work completed by the WP3 team and to identify the way to progress. This workshop was organized by L. Ferrière and A. Hutzler at the Natural History Museum Vienna (NHMV), Austria, in year 2 (2016; http://www.euro-cares.eu/wp3_vienna_home and proceedings). The meeting report was published in the deliverable D3.2. The WP3 team produced a Preliminary Design (D3.1) then an Advanced Design (D3.3) for the ESCF with inputs from the workshop, experts and visits of various facilities around the world.

To summarize, here are the identified main activities to be conducted in the ESCF:

- to receive the return capsule,
- to extract the sealed sample container(s) from the spacecraft,
- to open and to recover the sample(s) from the sample container(s),
- to store the sample(s),
- to curate and characterize the sample(s), as to allow further science activities,
- for restricted samples, to conduct life detection tests,
- to allocate samples for research, in the case of unrestricted samples; in the case of restricted samples after biohazard assessment and sterilisation.

The current report focuses on a comprehensive study of the architectural requirements, with interpretation of these requirements, for restricted and unrestricted samples, respectively.

Curation and storage aspects are then discussed separately for unrestricted and restricted samples.

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II. Acronyms

AMUF: Analogue/Mock-Up Facility

ASRS: Automated Storage and Retrieval System

BAP: Biohazard Assessment Protocol

BSL: Biosafety Level

COSPAR: COmmittee on SPAce Research

DWI: Double-Walled Isolator

ERC: Earth Return Capsule

ESCF: Extra-terrestrial Sample Curation Facility

EURO-CARES: EUROpean Curation of Astromaterials Returned from Exploration of Space

FFI: Flexible Film Isolators

FU: Functional Unit

HAZOP: HAZard and OPerability study

HEPA: High-Efficiency Particulate Air

HSE: Health and Safety Executive

HVAC: Heating, ventilation and air conditioning

IPA: IsoPropyl Alcohol

JAXA: Japan Aerospace eXploration Agency

LPF: Laboratory Protection Factor

LD: Life Detection

LOPA: Layer Of Protection Analysis

LSPET: Lunar Sample Preliminary Examination Team

MSC: Microbiological Safety Cabinets

NASA: National Aeronautics and Space Administration

NIH: National Institutes of Health

PE: Preliminary Examination

PHE: Public Health England

PMSCF: Planetary Material Sample Curation Facility

PP: Planetary Protection

PPE: Personal Protective Equipment

PPL: Planetary Protection Level

PRF: Portable Receiving Facility

PTFE: PolyTetraFluoroEthylene

SCF: Sample Curation Facility

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SEC: Sample Early Characterisation

SRF: Sample Receiving Facility

STIFF-FLOP: STIFFness controllable Flexible and Learnable manipulator for surgical Operations

SWIFT: Structured What IF Technique

TBD: To Be Decided

ULPA: Ultra Low Penetration Air

UP: Utility Plant

UPS: Uninterruptible Power Supply

URS: User Requirements Specification

WP: Work Package

WHO: World Health Organisation

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III. Design theoretical approach

This section was elaborated from the previous deliverables, and from a collaboration with the Canadian Branch of Merrick and Company (a company focused on designing, implementing and commissioning highly technical facilities, such as containment laboratories; http://www.merrick.com/). An intensive workshop was conducted at their offices in Kanata (Ontario, Canada) from the 6th to the 17th of March 2017, period during which Aurore Hutzler and Emre Kilic (architecture student from the Vienna University of Technology, Austria) visited Merrick and Company.

In this document the requirements and assumptions for building an ESCF are summarised, the design process is explained, and the different solutions that can fulfil those requirements are described. Finally, functional layouts for the scientific laboratories as well as the general design and siting considerations are presented.

1. Design requirements

The "design requirements" used here were derived from scientific requirements and on a study of the evolution of similar facilities (i.e. in term of complexity) all over the world.

The ESCF is designed to curate precious samples returned from Solar System exploration missions to asteroids, Mars and the Moon.

COSPAR (https://planetaryprotection.nasa.gov/categories) has defined several categories regarding sample missions return, depending on the type of mission (orbiter, lander, etc.) and the type of body. For Earth-Sample return, they defined the subcategory unrestricted, for bodies deemed by scientific opinion to have no indigenous life form, and the subcategory restricted, for bodies potentially bearing life. In this report, we adopted the term "Restricted" (typically for samples returned from Mars) for potentially biohazardous samples, and "Unrestricted" (typically for samples returned from the Moon and asteroids) for non-biohazardous samples.

For restricted samples, the facility should be designed so that an unsterilized particle >0.1µm should have a probability $P<1x10^{-6}$ of release (Ammann et al., 2012).

Several locations could be envisioned for the ESCF, such as a "remote location" (i.e. relatively far from uninhabited area), an existing research centre, an existing governmental (or non-governmental) facility, etc. Not having constraints on this aspect, we made the assumption that the ESCF is a stand-alone facility which will not use any remodelled building(s).

Flexibility is seen as one of the most important concept to be considered for such a project. We developed this concept at several levels, with the requirement of future extensions and expansion. Each core function of the ESCF is linked to a Functional Unit (FU). FUs are developed below (figure 1).

- "Campus" scale: units should be linked in a way that allows the efficient flow of personnel and materials. Any meaningful combination of units, at any time, should make sense structurally, technically and architecturally. *This flexibility is important as long as the funding and building status is not better defined, to allow for different working scenarios. It can also be a way to (quickly) adapt to a change of mission politics, or to the failure of a mission.*

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- "FU" scale: one unit should be easily adaptable for future developments and expansion of activities and utilities (mechanical, electrical, etc.). *In most of the similar facilities (such as at NASA JSC and JAXA), non-scientific rooms (usually work spaces or public outreach spaces) are retrofitted after some time to accommodate new missions or science goals. It usually results in "not so functional" (i.e. not as much functionality as if they would have been planned from the beginning) laboratories, and it reduces the well-being of workers.*
- "Room" scale: some rooms should allow for easy restructuring or change of the activity to be conducted inside. *It should be stated here that a given laboratory will need to be completed years before the return of the samples. Consequently, without knowledge of the exact nature of the samples or of the condition of the sample inside the containers (see NASA's Genesis sample-return mission), the laboratory should be easily adaptable (i.e. by adding new instruments that were not originally planned for).*

The architectural layout shall encourage meetings and communication between personnel to increase working efficiency and cooperation.

The architectural layout shall encourage a pleasant work environment. This aspect is rarely considered in similar facilities (NASA JSC and JAXA) from; lack of interest, lack of funds, or not collaborating with an architect during the pre-design phase. Since cleanroom workers show significantly higher sick leave statistics (i.e. based on discussions with a number of different persons using cleanrooms; Sullivan and Krieger 2001) than other personnel, this requirement should not been overlooked.

Security should be layered according to risk associated with samples/personnel/building in general.

Scientific units should be protected from a range of natural (such as seismic hazard) and non-natural hazards.

As stated clearly in the proposal, the ESCF should be built in Europe. European and local (when a country is chosen) legislation should then prevail for the design and building.

The human/restricted samples interaction should be eliminated, for safety and security reasons.

Additionally, the facility shall be designed in order to avoid unnecessary resource or energy use, both in the building and operational phase (material selection, energy efficiency, etc.).

The facility shall be cost-effective by considering the whole life cycle, including the initial design and construction costs, operations and maintenance as well as disposal.

2. Architectural and building objectives

Functional Units

The ESCF will have a number of diverse functions, and is designed to be able to host various types of samples. For the sake of clarity, we break down the ESCF concept to several areas linked with specific functions (figure 1).

Portable Receiving Facility (PRF) is not to be considered in the ESCF building design.

Remote Storage is neither physically linked to the ESCF and is not discussed in the present report.

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All the other FUs, Sample Receiving Facility (SRF), Sample Curation Facility (SCF), Analogue/Mock-Up Facility (AMUF), Work Space, and Public Outreach are units to be co-located on a single campus.

PRF Unrestricted	PRF Restricted	Assessing, cleaning and packaging the spacecraft on the landing site. Delivery of the spacecraft to SRF.
SRF Unrestricted	SRF Restricted	Receiving the sample container, cleaning and opening of the outer layers and delivery of the unopened sample canisters to the curation facility. Clean environment. For restricted samples, containment environment required.
SCF Unrestricted	SCF Restricted	Receiving of the sample canister, accessing the samples. Preliminary Examination (sample and hardware) and Sample Early Characterisation, Curation and Dissemination. For restricted samples, Life Detection and Biohazard Assessment Protocol. Ultra-clean environment. For restricted samples, high containment environment required.
Work Space		Support space for workers (offices, meeting rooms, social rooms, restaurant, etc.).
Public Outreach		Space accessible to the public (different categories of public, TBD) to promote the activities of the ESCF.
AMUF		Personnel training, instruments and protocols testing on analogue samples. Material testing for cleanliness and containment suitability.
Remote Storage Unrestricted	Remote Storage Restricted	Storage under dead-mode of a TBD part of the samples. Clean environment. For restricted samples, contained environment.

Figure 1. FU for the ESCF. *The color red is used for scientific FUs dealing with potentially biohazardous samples. The color blue is used for scientific FUs dealing with unrestricted samples. The color yellow is used for the last scientific FU, which will host only terrestrial samples. The color green is used for accommodation of people.*

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We examine below (table 1) the relationships between FUs, in term of circulation of staff.

Table 1. Links matrix for onsite FUs. *Physical links to allow for transfer of personnel were taken into account. + indicates a necessary link; - indicates a necessary absence of link; () indicates a possible link, if it is deemed beneficial for scientific goals; no marker indicates that the presence or absence of link is scenario dependent.*

FUs	SRF Restricted	SCF Restricted	SRF Unrestricted	SCF Unrestricted	Work Space	Public Outreach	AMUF
SRF Restricted		+	()	-	+		
SCF Restricted	+		-	-	+		
SRF Unrestricted	()	-		+	+		
SCF Unrestricted	-	-	+		+		
Work Space	+	+	+	+			+
Public Outreach							+
AMUF					+	+	

Siting considerations and trade-offs

We deliver here a theoretical project, since there is no plan and funding yet to build an ESCF - hence, there is no chosen site. This section aims at summarizing the characteristics to take into account when choosing a building site for the ESCF.

The siting of the facility is in relation and dependence to the following main factors:

- Site constraints
  - Topographical
  - National regulations
- Possibility of international/European/multinational politics
- Funding phases

Because the ESCF will have to receive the Earth Return Capsule (ERC), and will be visited by external researchers and officials (and potentially by a wider audience in case of a strong Public Outreach program), it is recommended that the facility be easily accessible. It involves choosing a site with existing transportations networks (roads, airport, train station), or to create the necessary infrastructure (in the second case, associated costs can be a major issue).

In the case of the restricted samples, it is recommended to have a medical facility nearby trained to handle patients infected with unknown biohazards.

Although the design is a multinational effort, the building itself is usually constructed by local contractors. A country for the ESCF should be chosen on several criteria, including the quality

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and efficiency of the available contractors. In case the quality is not deemed high enough, it is possible to adapt the design of the ESCF to build these specific parts in another country with trusted contractors and to ship these parts to the site, but this would greatly increase the cost of the facility.

Natural and manmade hazards for a specific site are to be considered (see the section "Safety and Risk Assessment").

Although we recognised the impact of politics on the project, we have not conducted a full trade-off to compare the impact of having the ESCF built entirely in one site, or with FUs separated over several sites/countries. Scenarios were presented in D3.1.

ESCF phasing

The combination of FUs should be considered to present the most efficient use of resources and space, whilst providing the necessary scientific benefit to the projects handled within the facility. The facility should also be built with the idea of future proofing to ensure the minimum amount of work is required in the future. Although any meaningful combination of units, at any time, should make sense structurally, technically and architecturally, some scenarios are more likely than others and are discussed below.

The most probable phasing is:

- Step 1/ AMUF laboratory with enough offices, in order to test protocols and building and to train staff.
- Step 2/ Either Restricted Laboratories or Unrestricted Laboratories, with extension of offices unit (if necessary).
- Step 3/ The other scientific laboratories, with extension of offices unit.

Public Outreach should be considered from the beginning.

Extension of scientific FUs is not considered here.

We identify the main steps of the project, with an estimated time required for each step (Space Studies Board, 2002; NIH, 2016; personal communication Merrick and Co.). In between each step, there will certainly be added time for reviews by external experts or by the funding agency. Since it is not clear at the moment where and how the ESCF will be built, these in-between steps might vary.

Development of new technologies: for the restricted sample facility there will be requirements for the development of new technologies in order to produce a facility that meets the cleanliness and containment requirements while allowing scientific objectives. These development may include double-walled isolators (DWI) and novel methods of incorporating scientific equipment into DWI.

Pre design phase: this phase is to identify and document factors that will impact the project. We recommend an integrated pre-design phase, with an assembly of all the stakeholders involved in the project: users (PIs, technical staff, etc.), architects and engineers, safety officers, commissioning agents and an executive committee. Depending on the mission planned, this phase should focus on protocols for the AMUF, and for one of the scientific laboratories (12-24 months). The outputs of this design phase should be white papers regarding:

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- Scientific objectives
- Ergonomics and staff well-being
- Staffing
- Budget
- Master planning
- Biocontainment strategy
- Safety and security
- Sample Early Characterisation Protocols
- Life Detection Protocols

Out of this process should come a user requirements specification document (URS) which can be provided to designers and architects in order for them to provide detailed designs.

Design phase: incorporating the requirements defined earlier room by room (with technical information), the design aims at delivering plans that can be used for building the facility. This phase is composed of the Concept Designed Phase, and of the Detailed Design Phase. Based on the detailed design, contractors can be contacted for price estimations (up to 24 months).

Construction phase: the construction phase will be dependent on the type of facility i.e. restricted or unrestricted. The possible timelines for this are +12 months depending on the construction materials to be used and the complexity of the design.

Certification and Commissioning: this phase aims at troubleshooting and testing all building parts and laboratory mechanisms: Heating, ventilation and air conditioning (HVAC), pumps, redundancy systems, etc. (12-24 months depending on complexity).

Procedures and protocols testing phase: all procedures should be rehearsed with a trained staff. If required mock ups can be constructed to assess the practicalities of the procedures. If deemed necessary, procedures will be adapted (6-12 months).

The minimum time required to build the first steps of the ESCF would then require around 7 years, before the return of the samples.

3. Safety and risk assessment

Hazards in the case of the ESCF can be classified in three different categories:

- External hazards (natural and non-natural)
- Infrastructure hazards (failure of pumps, filters, etc.)
- Protocol and Human-related hazards

These hazards must be listed, with worst-case scenarios associated. Each hazard must then be weighted by Severity of Impact, and by Likelihood, to assess the risk behind a hazard. Table 2 below shows then the case where the risk is acceptable (green), where the risk is acceptable with mitigation (yellow), and where the risk is not acceptable (orange and red).

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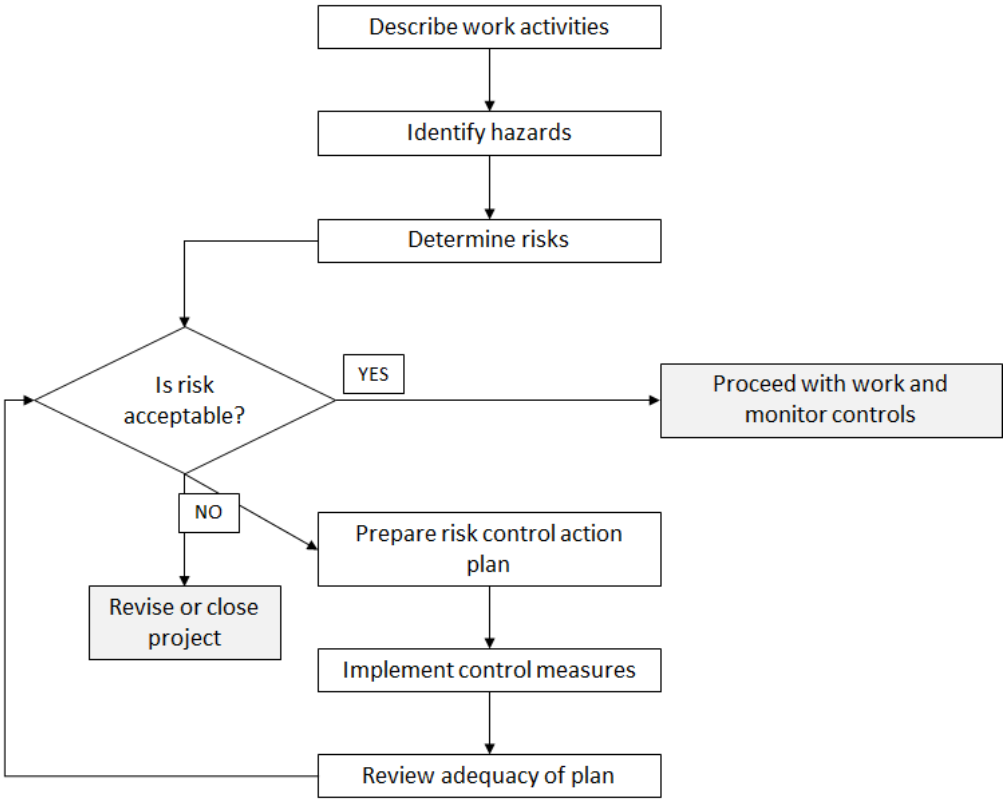
Table 2. Risk matrix. *(adapted from http://euro-cares.eu/files/WP3_Vienna/Presentations/Mueller-Doblies_EUROCARES_WP3_2016_PRESENTATION.pdf)*

		Likelihood				
		Rare	Unlikely	Possible	Likely	Certain
Impact	Severe	Medium	Medium	High	Extreme	Extreme
	Major	Low	Medium	Medium	High	Extreme
	Moderate	Low	Low	Medium	Medium	High
	Minor	Low	Low	Low	Medium	Medium
	Minimal	Low	Low	Low	Low	Low



The following strategy should be followed (figure 2):

Figure 2. Risk assessment strategy and mitigation. *Figure modified from http://www.dartmouth.edu/~ehs/biological/risk.html.*

Accidents in a facility such as the ESCF can impact a number of different targets, including: the staff themselves, the environment and public, and the samples themselves. The Risk Matrix above should be considered for each category of targets. Where hazards to health may not be the only risk but failure in the facility can lead to the loss of scientific importance of the mission, impacting on the financial and reputation aspects of the facility and project staff. Table 3 shows a non-exhaustive list of potential hazards for the ESCF.

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Table 3. Potential hazards for the ESCF. Modified after presentation by U. Müller-Doblies, EURO-CARES WP3 Workshop, Vienna, Austria, 2016.
www.euro-cares.eu/files/WP3_Vienna/Presentations/Mueller-Doblies_EUROCARES_WP3_2016_PRESENTATION.pdf

	Category	Hazard	***Example***
Infrastructure Hazards	**Building**	Sealability	*Leak tightness less than that specified*
		Surfaces	*Outgassing*
		Doors	*Leak tightness less than that specified*
		Penetrations	*Leak through poorly designed penetrations*
	Laboratories	Emergency procedures	*Faulty alarm*
		Equipment	*Outgassing*
		Furniture	*Furniture broken*
	Air	Air Handling Units (AHU)	*Failure of AHU*
		Ventilation controls	*Failure of pressure sensors*
		Air filtration	*Failure of filters leading to contamination of the samples*
	Liquid	Effluent treatment	*Inefficient decontamination protocol*
		Effluent piping	*Leakage of pipes*
		Flood detection	*Failure of flood sensors*
	Solid	Waste treatment	*Inefficient decontamination protocol*
		Autoclaves	*Fails certification testing; autoclave seals fail.*
		Dunk tank	*Leakage of tank*
		Incinerator	*Failure of incinerator*
	Services	Electricity	*Low continuity of power*
		Generators	*Failure*
		Water	*Flood*
		IT & Telecom	*Leak of data*
		Gasses	*Unclean gas*
Protocol and Staff related hazards	**Processes**	Documentation	*Wrong sample code*
		Entry/exit of laboratories	*Wrong exit process*
		Human factors	*Loss of a sample*
		Maintenance	*Infrequent maintenance*
		Change management	*Loss of information*
		Competency management and Training	*Untrained staff*
External Hazards	**Natural**	Earthquake	*Barrier break*
		Tsunami	*Flood*
		Tornados	*Air flux disrupted*
		Wild fire	*Contamination by particles*
		Floods	*Water contaminated*
		Air pollution	*Risk to samples integrity*
		Water pollution	*Risk to staff*
		Solar storm	*Power outage*
	Non-natural threats	Terrorism	*Barrier break*

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A full risk analysis of the facility will be required using one or more of the following methodologies HAZOP, SWIFT, LOPA, etc. This will require input from the architects, designers, scientists, biosafety and safety professionals from the project and from external organisations.

The risk analysis will inform the design of the ESCF and will specify requirements for redundancy such as:

- having dual HVAC systems operating at less than full capacity so that if one fails the other can take the full load
- the use of back-up generators or uninterruptible power supply (UPS) to prevent loss of power
- Back up storage vault

The facility shall be designed to minimize risks related to natural disasters (such as earthquakes, floods, etc.), man-made disasters (such as terrorism, etc.) and other external hazards, such as a fire (topic developed in D3.1).

Security processes will be designed according to the risks associated with the samples, personnel and building (human errors, technical failures, etc.). The indirect interaction between humans and samples (especially for restricted samples) shall be kept minimal, for safety and security reasons.

Restriction of access

A constant concern for sample and personnel protection is to define levels of authorization amongst people in the facility (and even more if there is a strong public outreach activity). To do so, three types of identification tools can be used:

- **What you have**, such as an identification badge
- **What you know**, such as a code
- **Who you are**, by using biometric identification (for example fingerprints, facial or retinal recognition, etc.)

For a low level of security (entering an office, for example), a personal badge should suffice. For higher security parts, one or two other types of identification should be added, such as a code to enter a cleanroom, and a biometric identification reader to access the sample storage room (a "robot-only" option may also be considered). This type of system is very flexible, and can fine tune the access of the various rooms.

Examples of well-designed security levels can be found at most high containment facilities. for example the PHO facility in Toronto (Canada), or the UN/IAEA Seibersdorf laboratories (Austria).

The ESCF must be designed to be able to curate both restricted and unrestricted samples. These two types of samples require different environmental considerations, which is the reason why we have decided to separate our report in two distinct sections for restricted and for unrestricted samples, respectively.

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Unrestricted Laboratories

Laboratories for unrestricted samples are cleanrooms designed to eliminate contamination from the sample (particulate, organic, microbiological etc.). The approach here is to start with the ISO norm for particulate contamination (relying on filtering the incoming air with high-efficiency filters and keeping the room under positive pressure), and to restrict as much as possible other types of contamination from the materials and instruments used in the cleanroom. Any personnel accessing the facility will need to change into cleanroom clothing so change areas will need to be included in design including lockers for storage of outer clothing and belongings.

Buffer corridors and increasing levels of cleanliness are used to go step by step up to the cleanest part of the laboratory. This is typically what is done at NASA JSC and JAXA (Yada et al., 2013).

Restricted Laboratories

Laboratories for restricted samples have to address two big challenges: on one hand, keep the precious samples as pristine as possible (in the same way as for unrestricted samples), and on the other hand, avoid any release of a potential biological agent to the environment.

Containment of biological agents is a well-known process, with levels of containment adapted to known pathogens (WHO, 2004). The concept of a containment laboratory is to use successive layers of protection, safe practices of work and engineering controls (primary, secondary and tertiary) to ensure that aerosols of agents are not released to the environment and the workers.

Containment is provided by a high level of redundancy, by access control, barrier minimization and by an approved decontamination methodology, safe practices of work are also required to ensure these measures are used correctly and the worker reduces any possible contamination to start with. For unknown pathogens, it is recommended to adopt the highest level of containment, Biosafety Level (BSL) 4, and to keep this level until the samples can be proven devoid of biohazard, or sterilised using a validated method (Rummel et al., 2002).

Rummel et al. (2002) proposes four planetary protection levels (PPL), combinations of containment and cleanliness conditions (table 4).

Table 4. Anticipated laboratory conditions and PPL categories. Note: levels of cleanliness associated with each PPL are TBD and should be defined explicitely well in advance of sample return.

PPL-type	Biocontainment	Cleanliness	"Ambient" conditions	Used for
PPL-α	Max. (BSL-4)	Maximum	1atm, inert gas	Incoming container and materials; some preliminary tests; sample bank/storage; some LD
PPL-β	Max. (BSL-4)	Maximum	Earth-like	LD; some physical/chemical; TBD
PPL-γ	Max. (BSL-4)	Moderate	Earth-like	Some BAP testing, some physical/chemical processing and animal testing
PPL-δ	Strict BSL-3-Ag	Ambient	Earth-like	Some BAP; post-release tests TBD

We used this classification as a starting point for defining different areas in the SRF and SRC. As a result, we consider a hybrid of a BSL-4, with different ways to handle samples.

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Levels of containment

Primary containment

At the highest level of biological containment, BSL-4, there are two engineering approaches that are generally used for the safe handling of the high consequence pathogens (WHO, 2004). These are either:

- Cabinet Line Laboratory. Work is carried out within a series of interconnected class 3 Microbiological Safety Cabinets (MSC) where the worker uses gauntlets on the side of the cabinets to manipulate the infectious materials. Samples enter through disinfectant baths (dunk tanks) and waste leave through double door autoclave.
- Suited Laboratory. Workers wear a positive pressure suit supplied with breathing air by umbilicals, linked to compressors in the service floor. Within a suited laboratory class 2 MSC are normally used to confer extra protection to the worker and the samples from contamination during manipulation.

In the case of the ESCF, another engineering approach is being considered: a Double-Walled Isolator (DWI), being the primary and secondary containment (see section VII.4). This isolator is operated at negative pressure with all penetrations or seals being surrounded by an outer compartment at positive pressure. If there is a leak from the DWI operating area it will be from the positive pressure compartment which will be filled with filtered gas and so will not contaminate the sample. If there is a leak in the outside of the positive pressure compartment it will just be filtered gas without any biohazard. Choking hazards should be kept minimal, with enough sensors and emergency procedures to avoid a depletion of oxygen around the DWIs.

These three different approaches have huge impact on the design of the laboratory.

Secondary containment

The next level is the secondary containment of the laboratory (room, systems, etc.), some aspects of which are the negative pressure, directional airflow, sealability and filtration of extracted air.

Negative pressure

Each high containment laboratory has a set of design requirements and these will vary greatly between the different laboratories. Negative pressure is stated as a requirement in a number of guidance documents that have been produced by regulators around the world (WHO, EUI Directive), but no specific international recommendations are made on the magnitude of the differentials (e.g. Rogers et al., 2007; Ide, 1979).

For example, in the UK, the Health and Safety Executive requires a BSL-4 facility to have a minimum pressure differential of at least -75 Pascals between the laboratory and the ambient environment when handling specified animal pathogens, where the Advisory Committee for Dangerous Pathogens state there should be a pressure cascade of -30 Pascals for each containment layer (HSE, 2009). Other regulations around the world recommend different figures and this can be seen by the pressures used in those facilities:

- The BSL-4 laboratories built and used by Public Health Canada use a series of four airlocks with a difference of 50 Pascals between each one (Crane et al., 1999).

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- In the high containment facility in Geelong, Australia, increments of 100 Pascals are used between facility sections (Crane et al., 1999).
- The National Institute of Health, USA, employs a negative pressure of 50 Pascals in the facility shell, with a further reduction of 12 Pascals for the suit entry and laboratories (Crane et al., 1999).
- The P4 facility in Lyon, France, uses final pressures of -40 Pascals in the entry room, decreasing to -90 Pascals in the animal facility autoclave room (ABSA, 2002).

The use of high pressures within a facility needs to be balanced with the operation and functionality of the facility. The facility will need to be built to withstand high pressure differentials and this can add cost to that facility in terms of building quality and in the energy consumption of the facility when in operation. Achieving the desired pressure differentials can be challenging and can be the cause of delays caused by lengthy commissioning periods. However, there is little evidence for the use of complex pressure cascades or high pressure differentials increase aerosol containment (Bennett et al., 2005).

Air change rates

Air change rates are calculated to remove the laboratory heat load and to reduce the concentration of contaminants within the laboratory. It is often thought that a high air change rate in the containment laboratory is a sign of good performance, but there is little evidence as to what level of air change rates is required. Air changes inside DWI could be effective at removing contaminants produced by off-gassing, however, high air changes could lead to turbulence which could aerosolise dust samples.

Pressure tightness of the laboratory

Testing the leak tightness of the laboratory is important to define the build quality of the facility and to define a standard value that can be used for regular testing. Pressure testing of the facility can be carried out by pressurising the required area to a set point and measuring the rate of decay over a defined period of time. This can be done at positive or negative pressure.

Laboratory filtration

A major requirement of the restricted SCF is its ability to contain particles of 0.1 microns. To achieve this there will be an extensive use of High-Efficiency Particulate Air (HEPA) filtration. HEPA filters are used in different laboratory types to prevent the release of particulate matter from containment. HEPA filters were originally designed for use in the nuclear industry (Abraham et al., 1999). HEPA filters are produced from one continuous sheet of filter medium that is then folded, with the folds being separated to avoid them touching each other. This folded filter medium is then bonded into a filter housing which has a gas tight seal running around the outer edges (First 1998). Usually the HEPA filter is sealed in place using clamps and this requires compression of the seal to about 80% for a leak proof finish. HEPA filters capture airborne particles in one of three ways:

- Impaction (particles >1 μm), larger particles will impact onto the filter fibres as opposed to following the air currents around the fibres. The impaction factor will decrease with increasing airflow or greater distance between fibres.

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- Interception (<1 μm), small particles are drawn along the air flow path and contact the outer surface of the fibres and captured.
- Diffusion (<0.1 μm), the smallest particles that are under the influence of Brownian motion will contact the fibre and adhere to it. The diffusion capture process increases with low flow rates through the filter.

As a general rule once a particle has contacted a fibre, it is attached via van der Waals forces and is not released (First, 1998). The size of the particle most likely to penetrate through the filter is approximately 0.3 μm, but this will be dependent on the velocity of the air passing through the filter.

Filters are rated on their performance to stop particles of 0.3 μm passing through them. In Europe there are 7 classes of HEPA filters according to the European standard EN 1822. The qualifying standards for HEPA filter testing were developed when HEPA filters were first produced and modern production means that the majority of the filters exhibit greater performance, providing a buffer for the filter to the expected standard. Newer designs of HEPA filters are being developed, using PolyTetraFluoroEthylene (PTFE) membranes, and this may be an advantage for the ESCF as it would reduce the possibility of fibre shedding into the working area.

The EU Directive 2000/54 requires the air supplying a BSL4 facility to pass through at least one HEPA filter, and two HEPA filters in series on the extract, mounted separately. This allows the independent testing and replacement of each filter (HSE, 2009). Once a filter is installed it still requires *in situ* testing to ensure it is operating correctly and identify if there have been any issues in the transport of installation of the filter. To make the testing and replacement of the extract HEPA filters easier they are usually located in the plant room outside of the laboratory. HEPA filters installed should be regularly tested to ensure they are continuing to operate correctly, presently, for example in the UK, the regulators require testing to be performed every 6 months (HSE, 2009), other rules applies in other countries.

The use of double HEPA filters is designed to provide protection if one of the filters ever failed. The guidance for this was written over 30 years ago when the filter production techniques were not as good as the current methods. A review of the reasons for HEPA filter replacement in the Australian Animal Health Laboratory (Geelong, 1999) found that the reasons for replacement changed over the course of 13 years. From a mixture of defects in the filter medium, failures of the gaskets, and blockage of the filter material at the beginning of the study and in conjunction with the methodology for producing HEPA filters improving the major reason at the end of the study was due to blockages of the filters (Abraham et al., 1999).

The use of double HEPA filtration for the extract of BSL-4 laboratories can be seen as above what is necessary. All aerosol generating procedures are undertaken within safety cabinets that themselves are double HEPA filtered. Therefore it is difficult to envisage any procedure that, barring intentional aerosol generation, will produce enough particles to penetrate one, let alone two HEPA filters. Within an ESCF this would also be the case and an argument could be made to decide on the number of HEPA filters on a risk assessment basis for each of the laboratories, depending on the procedures that will be undertaken in them and the likely challenge to the filters.

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Required height for the laboratories

The height between floors in laboratory areas is determined by the space required for working within the laboratory itself, and for the servicing areas (in addition, the minimum height of a given instrument could also influence the minimum height of a laboratory but none of the ones to be used in the ESCF (Franchi et al., 2016) seems to be problematic in that respect). Each FU has different requirements, hence different heights (figure 3). A comprehensive design of the ESCF must take into account these space requirements.

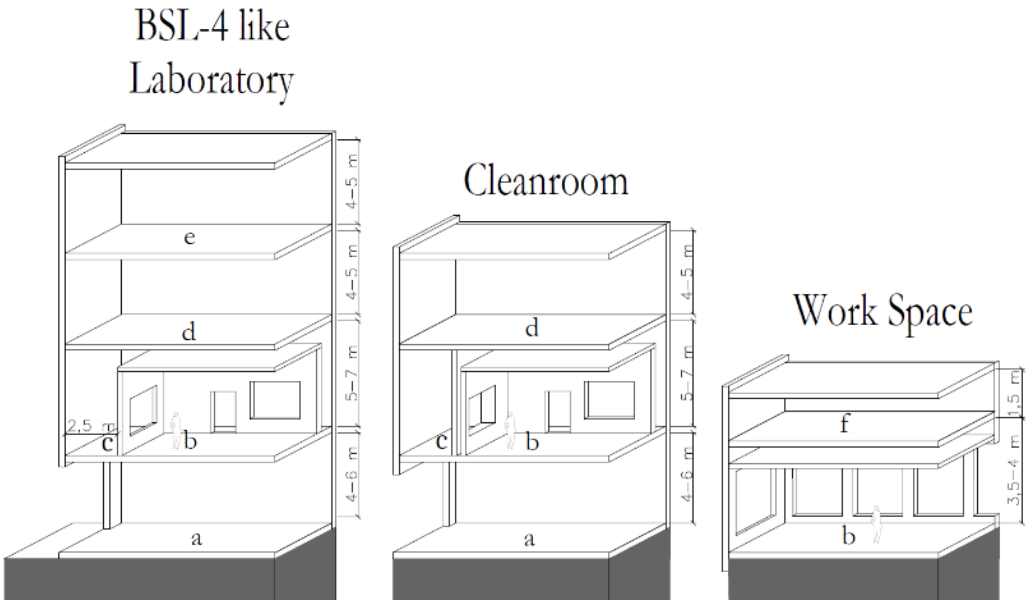

Figure 3. Required heights for FUs. *A BSL-4 like laboratory will be used for all restricted FUs. Cleanroom design will be used for all unrestricted FUs. (a) Effluent systems and waste treatment; (b) Working space; (c) Buffer corridor; (d) Air filtering systems I; (e) Air filtering systems II (if necessary); (f) Ventilation systems.*

Restricted (BSL-4 like) laboratories require the most space above and below, usually two floors above and one floor below large enough to accommodate waste treatment (waste tanks). In general, liquids are kept below the laboratory floor, while air handling systems are kept above it. The machinery itself typically does not require a height of several meters, but it will impact the maintenance and servicing if staff cannot easily access this floor.

Unrestricted Laboratories have less need regarding waste and effluent treatment systems, and have also a more limited heating, ventilation and air conditioning (HVAC) system. All the different cleanrooms can be located on one floor, with a system of "grey area" surrounding these, hosting the machinery. However, a dedicated floor for the machinery will help with the maintenance and servicing. Leaving the outside walls of the cleanrooms "free" would also allow space for better integration of the instruments and possibilities for public outreach, by using see-through windows.

The third block shows a standard office level with a false ceiling for comparison purposes to the scientific FUs.

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4. Position of ground

Each floor, most importantly for the scientific FUs, must be easily accessible to accommodate ingress of new equipment, egress of decommissioned instruments and of waste. Figure 4 shows several possibilities, by using good lifts and by using the position of the ground relatively to the building. We use in this example a BSL-4 like configuration.

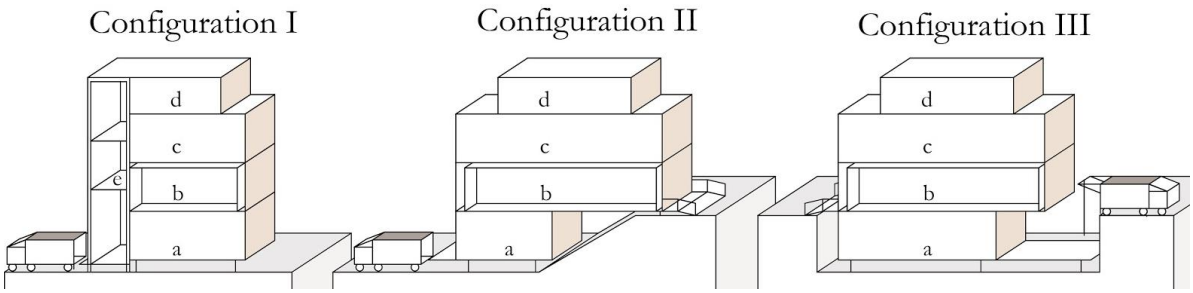

Figure 4. Placement of ground level. *(a) Effluent systems and waste treatment; (b) Laboratory level; (c) Air filters and machinery I; (d) Air filters and machinery II; (e) Good lift.*

In configuration I, the entire building is above ground level, and a goods lift is used to service each floors. The lift must be robust enough to carry heavy machinery. Movement of such a big lift should be accounted for, since the air circulation of the building could be affected as it moves. In this configuration, the laboratory itself is on the second floor, hence being less easily accessible in case of an attempt of break-in.

In configuration II, a sloped terrain is used (or built) to allow an access to different floors from ground level. The concept could be artificially generated by building a ramp around the building, allowing a road access to each of the main levels. It is an interesting solution, but it would increase the cost of the infrastructure and may also generate for example unwanted vibrations.

In configuration III, the effluent systems and waste treatment floor is below ground and can be reached through an opening on the side while offering ground floor access for the laboratory level. Access to the lower level is somewhat more complex than in the other two configurations, and a goods lift is still required for upper levels.

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IV. Design decisions and rationale

Here we show how the requirements and assumptions presented above were interpreted.

1. Site planning

Although the site is unknown at the moment, we are proposing different possible approaches for building the entire ESCF to fulfil the "Campus" scale flexibility requirement. We then reflect on each approach regarding flexibility, security, costs and other parameters as summarized in table 5.

These approaches are all generated over a unique site, however, the entire concept is made so that if one FU is not built, it does not impact on the other FUs. Each different approach is presented with a conceptual diagram and a schematic interpretation (to allow better visualisation).

To accommodate such a campus a dedicated Utility Plant (UP) must be planned, providing power, water, steam and anything necessary to the operation of the FUs. In emergency cases, single functions should be able to work independently. It is also imperative to allow shut down protocols to be effective in certain time frames. UP is not shown in the diagrams below, for clarity reasons.

Orientation to the surroundings is also important as to how to connect the functions to each other and to the outside world, be it roads for transportation or blocked directions for security reasons (against man-made disasters). The terrain itself and the degree of elevation and slope might require some changes depending of the design.

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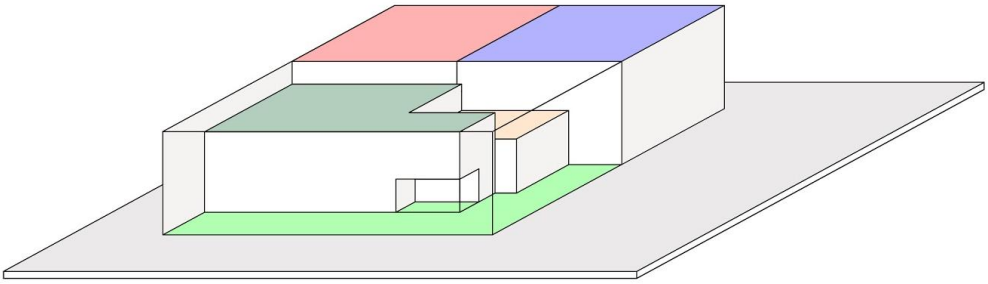
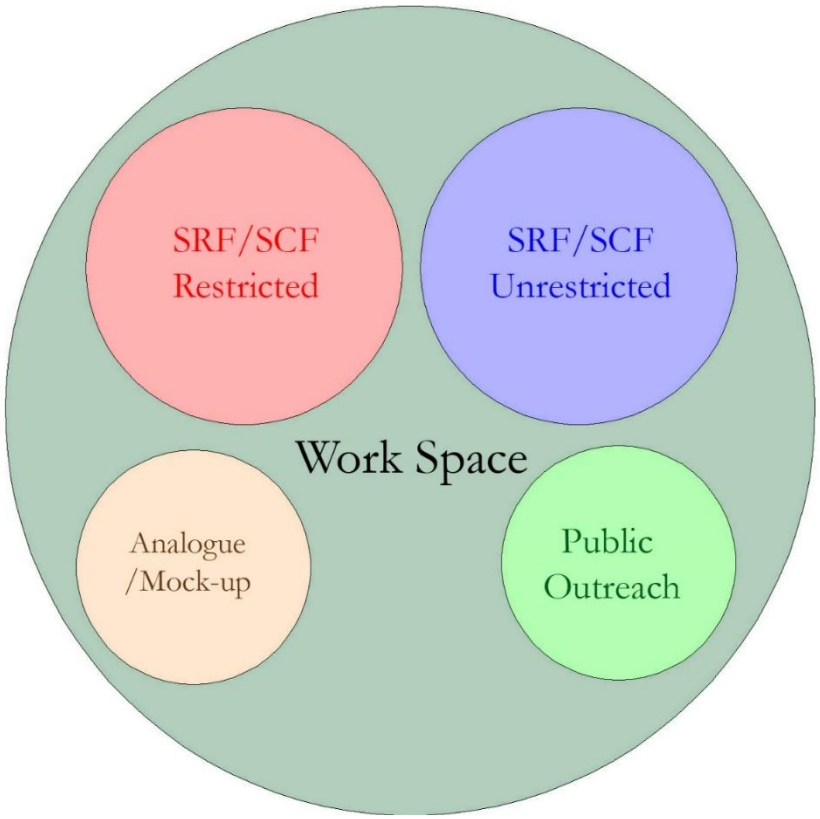
Approach 1 - Unique building

The FUs are stacked next to one another in a very classical way and hidden under a regular facade.

This method does not allow any easy expansion and the entire complex should be planned at the same time. This might allow, however, for certain plumbing and effluent systems to be shared (if there is no containment requirements, hence reducing the total costs. Outer walls are kept to a minimum, reducing the costs as well. Scientific FUs are better protected from outer threats.

Public and office spaces are close and they allow for visitors to have a very close view at the researcher's activities, which may be good for the complex if a public outreach program is a heavy focus point.





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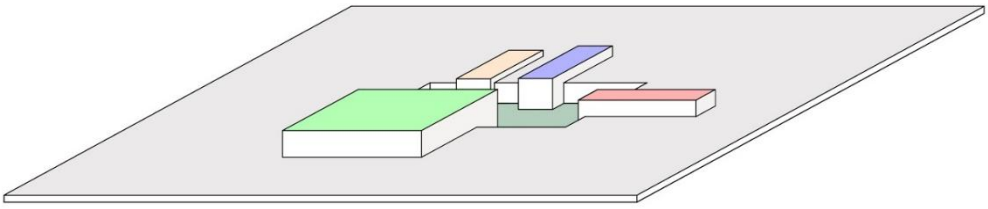
Approach 2 - Puzzle

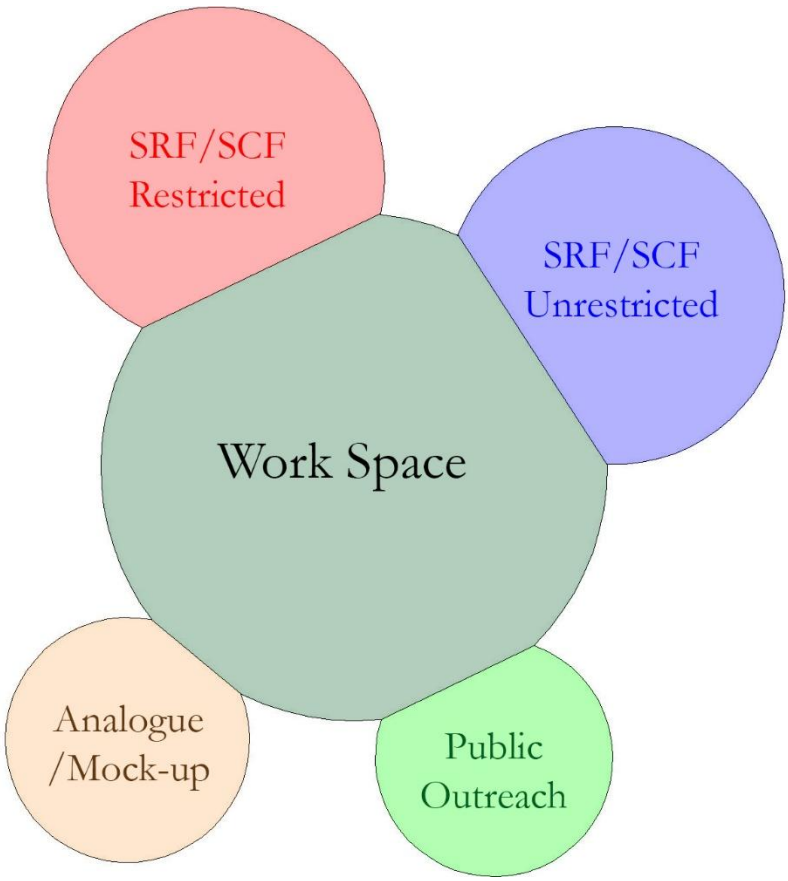
Functions are partially separated and one FU (in this instance the work space for the staff) connects the separated functions with each other. The shape of this central FU can take is highly flexible.

Flexibility and adaptability are high for the entire complex, as well as for each FU, with a number of outward and vertical expansion possibilities.

Scientific FUs can be placed away from the entrance of the site (for example to lower the risk of terrestrial attacks).

Because of the expanse of external walls, the construction costs will be high. The restricted facility will not be as secure.





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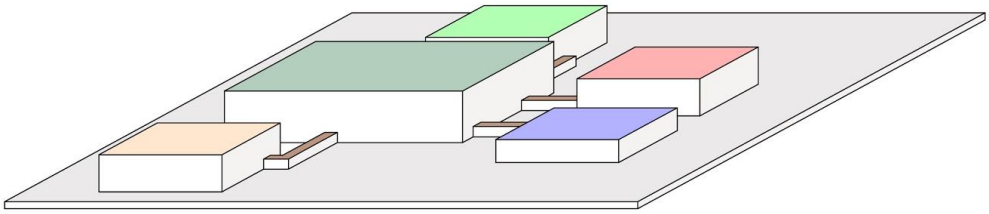
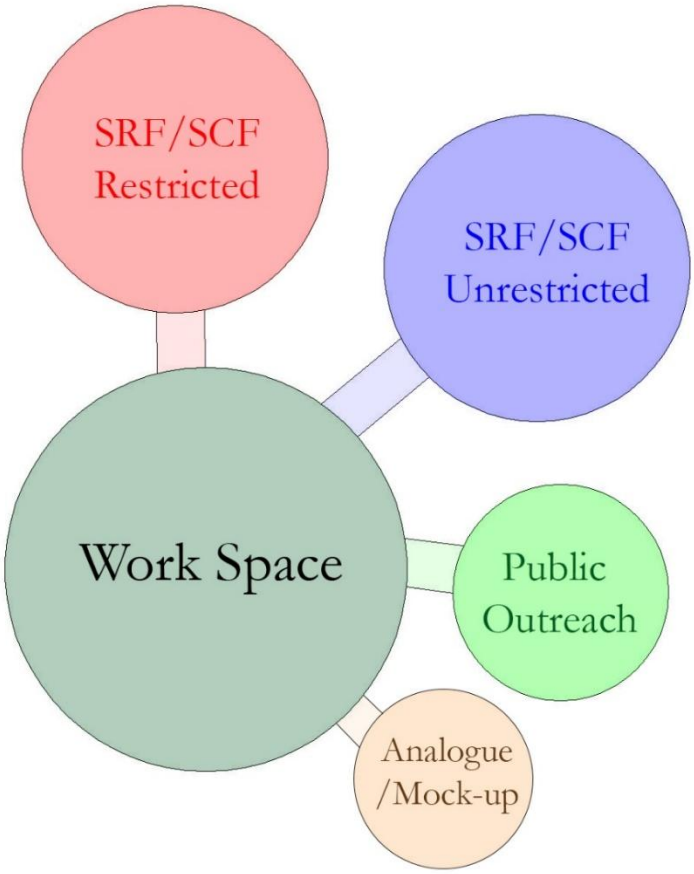
Approach 3 - Bridges

The FUs are independent blocks that are positioned to allow for future expansion.

A number of bridges/corridors are used to connect the FUs together. This configuration allows for great independence of each unit but puts them farther away from each other which results in greater distance for the staff to move around. The cost of such a configuration would be relatively high compared to other approaches as each FU would effectively be a single unit in regards to security and utility.

This approach has the advantage to be highly flexible and great for modular design for an incremental build of the complex. Again a costly design with security implications.





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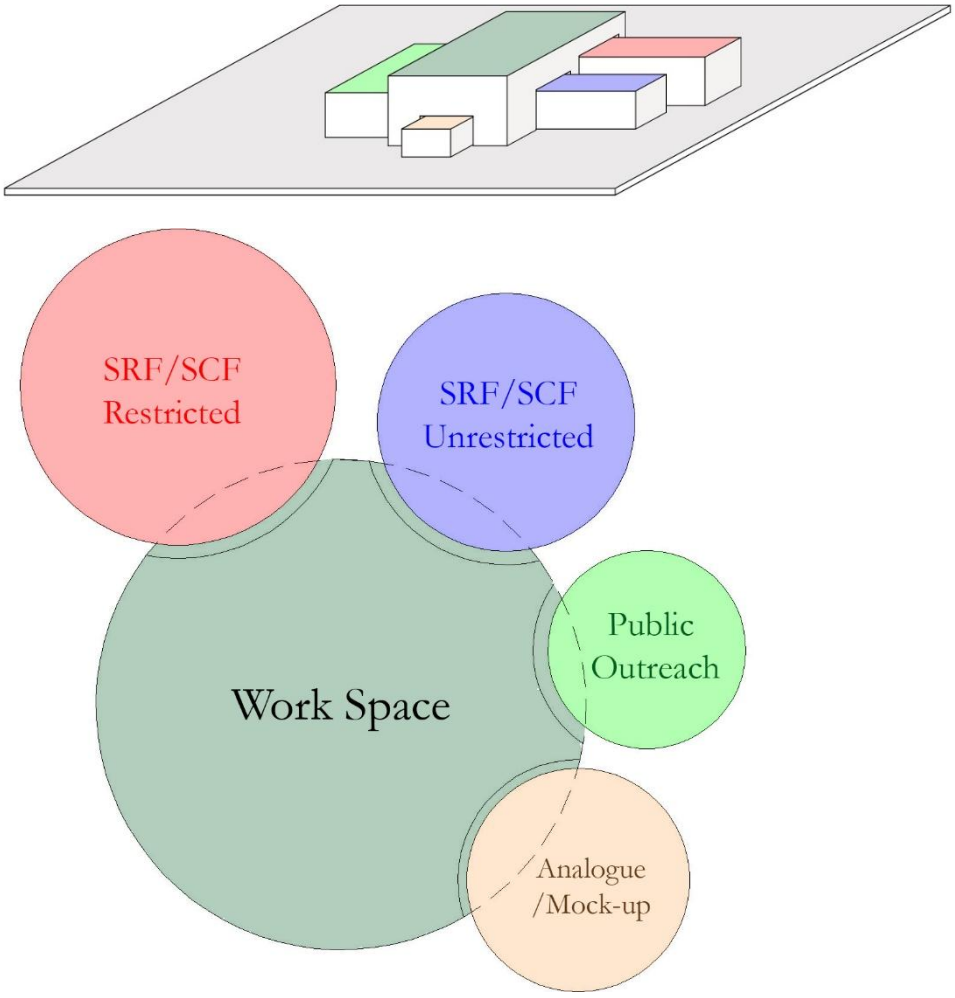
Approach 4 - Docking station

In this configuration the central work space overhangs the other FUs. This allows for researcher flow to be seamless from office space to laboratory area while allowing expansion to the sides. External sides of the labs are reserved for transportation and stores purposes. Please note that on the diagram that the functions not only border each other but intersect, unlike in the "Unique Building" approach.

This particular configuration offers great versatility whilst offering a small footprint of the campus.

The laboratories are partially exposed (to aerial threats), but the more restricted parts could be flipped to the side where they are merging with the office portion, to offer an extra level of security concerning non-natural threats.



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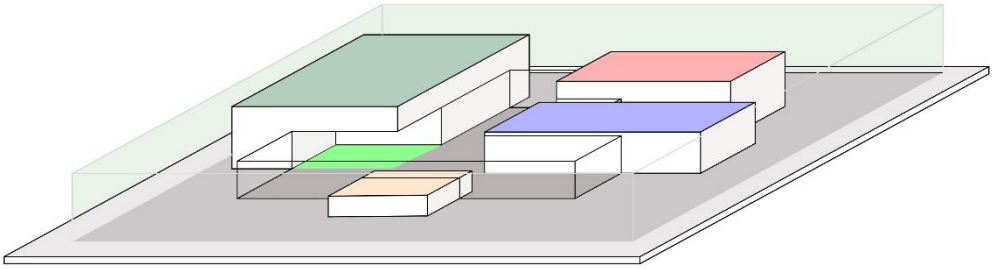
Approach 5 - Shell

Each function is laid on the site and the entire site is covered with a shell. FUs are placed far from each other so they can be expanded as needed in the future. This configuration offers the most versatility as the shell protects the whole complex despite everything being separated.

The downside of this approach would be the initial cost and estimation of the covered site portion with the shell. A certain margin would have to be calculated and the blocks would be placed giving them enough room to expand in future. In a different scenario (shell I) this shell could be between the functions instead of covering the entire site.



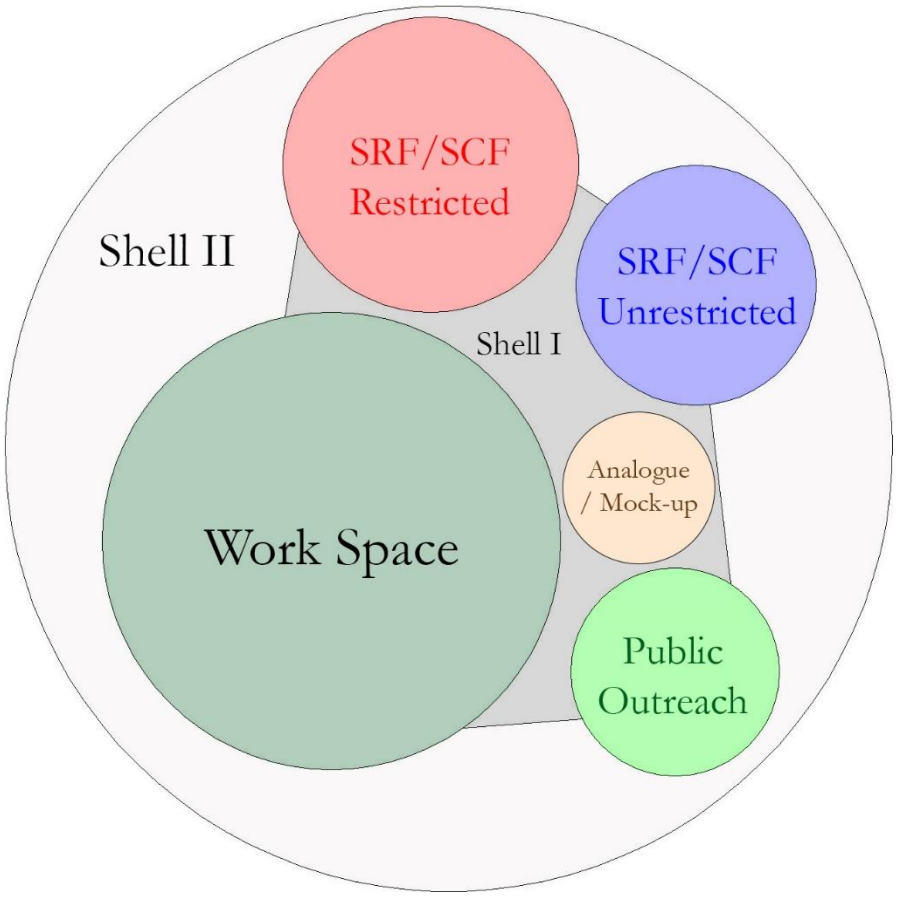


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Table 5. Trade-off between the different siting approaches. *"+" indicates that the approach ranks positively for the criterion, "=" indicates that the approach is neutral, and "-"indicates that the approach is at a disadvantage for the criterion.*

Approach	"Campus" flexibility	Security	Economics	"FU" flexibility
1 - Single building	-	=	+	-
2 - Puzzle	=	-	=	=
3 - Bridges	+	-	=	+
4 - Docking station	=	+	+	=
5 - Shell	+	+	-	+

2. Flexibility on FU scale

While designing the functional layouts for scientific FUs, we tried to follow three requirements: allow easy and efficient staff flow, allow access by truck (with an access ideally far from the staff entrance) and keep expansion possibilities for the future.

The staff flow was mostly enabled by a buffer corridor surrounding the laboratories - and incidentally fulfilling the requirements on cleanliness and containment successive layers. The staff entrance to the buffer corridor should be kept close to the office portion of the complex, in order not to increase the route to the laboratories.

The future expansion was enabled by dedicating one or two sides of the unit for the said expansion. These fixed sides are adding more constraints on the siting plans.

The laboratories have at least one side reserved for the sample transportation (with a high bay) which should have a road leading to the outside of the complex.

Given all these considerations, adjacency or not of FUs might be heavily constrained, and it will at the end largely influence the final design of the ESCF in its entirety. Below (figure 5) is a schematic representation of these three requirements.

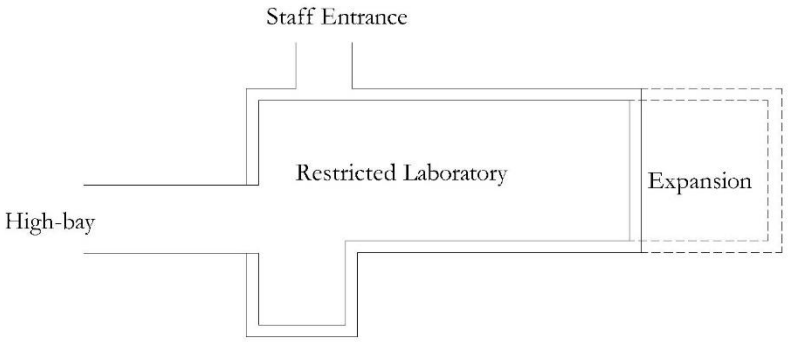

Figure 5. Schematic representation of access and expansion possibilities for a laboratory, in the case of the restricted SRF/SCF.

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Security aspects also factor in the consideration of the design of the ESCF. Higher security risk units/buildings can be covered physically by larger, less security demanding units/buildings. The connections will need to reflect these considerations. Restricted FUs for example should not have direct connections with the public outreach program.

3. Workflows

The activities undertaken within the facilities have been defined and translated into workflows, for samples, operations and workers. These are workflows based on the current requirements and assumptions as defined in the present report.

Samples

Figure 6 shows the splitting sequence of samples in the SCFs for restricted and unrestricted samples. Operations to be conducted on the samples are indicated as well, without a specific location for these operations.

Operations

Figure 7 aims at showing the operations to be conducted in the Unrestricted SCF, with the specific area in which they should be conducted. Cleanliness levels have been indicated, so we can discuss the physical connections between areas, the flow of workers and samples.

We have differentiated operations where the sample can be left inside the container (yellow boxes) and the operations where the sample will need to be taken out of the container (orange boxes).

Figure 8 aims at showing the operations to be conducted in the Restricted SCF.

Workers

Figure 9 (for unrestricted facilities only) aims at showing which physical links should exist between different areas, to allow a smooth path of the human workers. It can be modified depending on the future reviews investigating the use of robotics in the ESCF (see specific discussion on the use of robotics).

Maintenance staff comprises three categories of workers, with different security clearance and different frequencies of frequentation:

- Cleanroom technicians, mostly for cleanroom instruments, on a daily basis.
- Facility engineers, for technical areas (power supply, air filtration, etc.), on a daily basis.
- External companies, in both technical and curation areas, for periodic service and maintenance.

Cleaning staff will not access clean room and other controlled areas. Cleaning of sensitive areas (such as clean rooms, containment rooms, etc.) will be performed by the appropriate Curators/Technicians.

Security staff should be granted access in unclean/unrestricted areas and in viewing corridors.

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Workflows have been developed mainly for curators and technicians, considering that they will access the facility on a daily basis. Mapping their activities is of the utmost importance to define the adjacencies for the facility.

Some rooms should be visible through viewing corridors (solution allowing visitors to see what is done inside without having to enter the "confined area"). This can be adapted to the requirements of the facility.

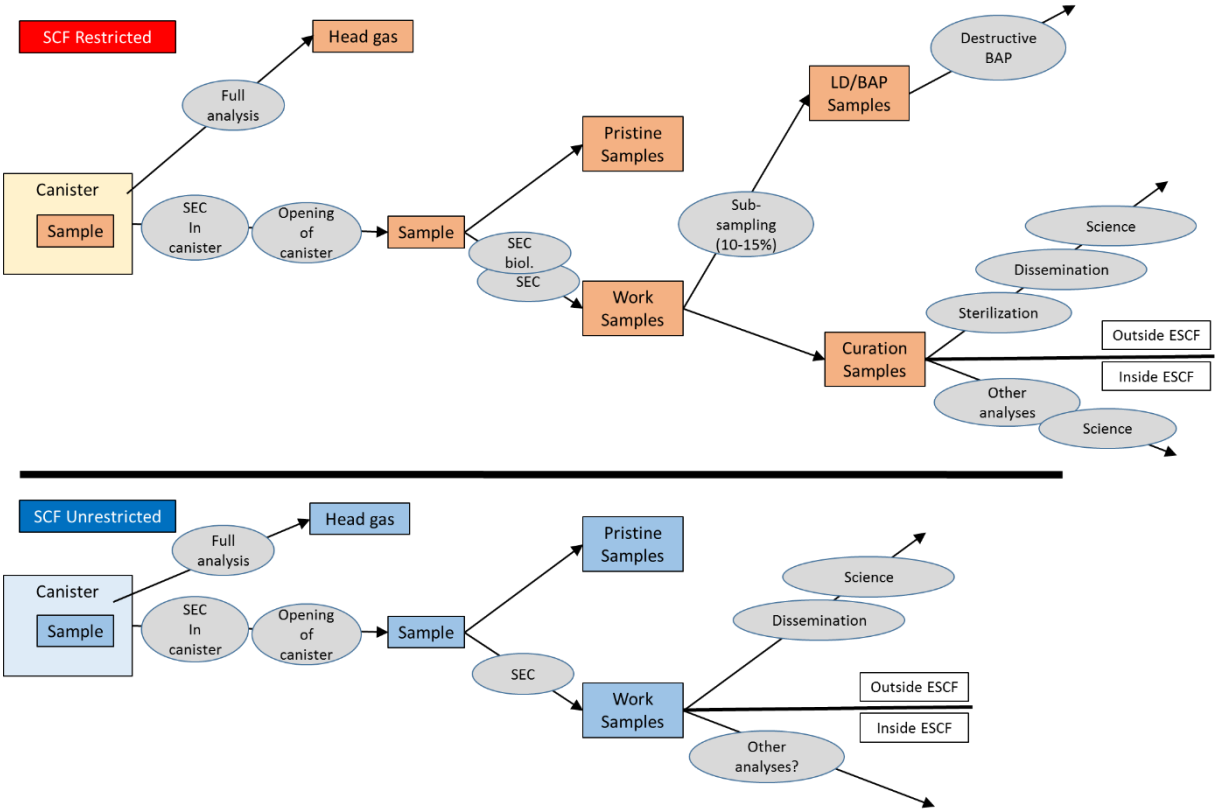

Figure 6. Splitting of samples, for restricted and unrestricted samples, alongside the procedures in the SCFs.

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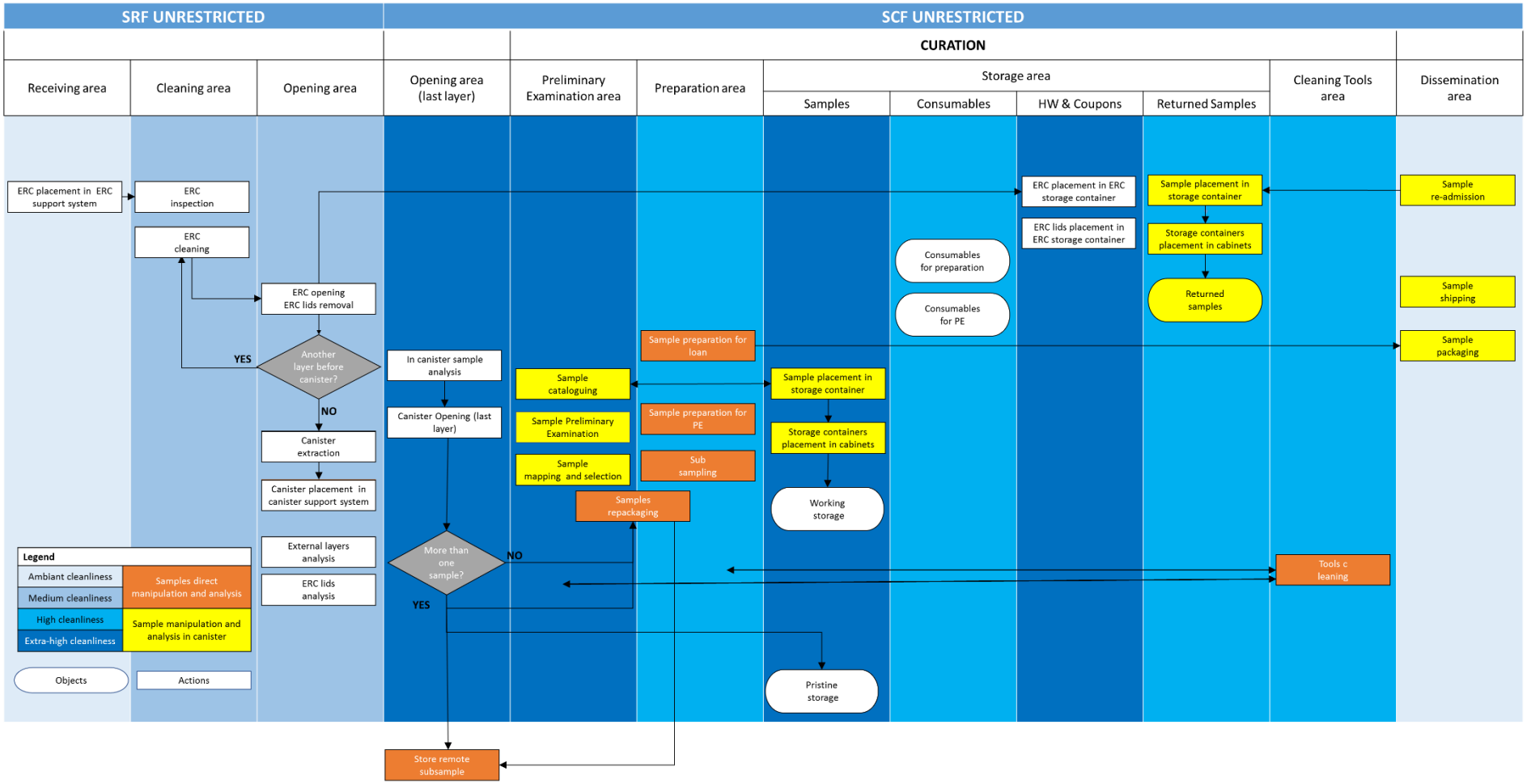

Figure 7. Flow of operations for unrestricted science areas.

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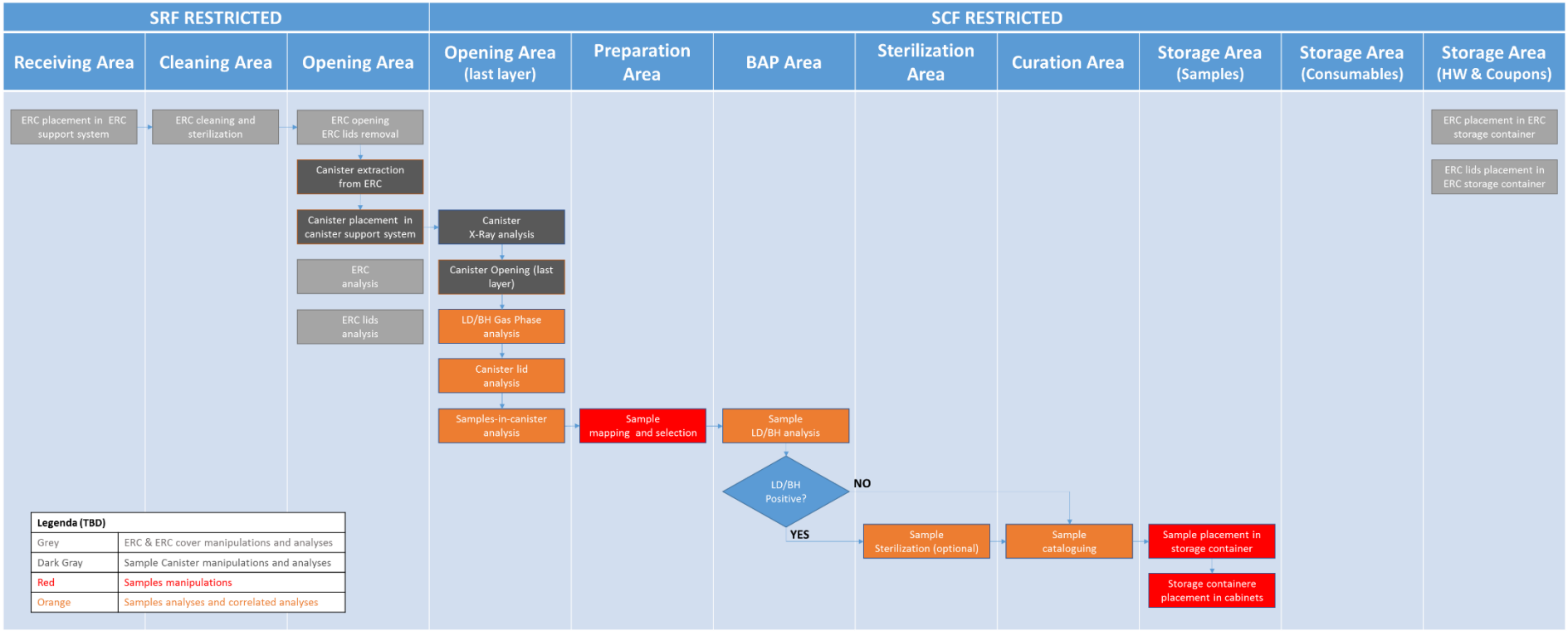

Figure 8. Flow of operations for restricted science areas.

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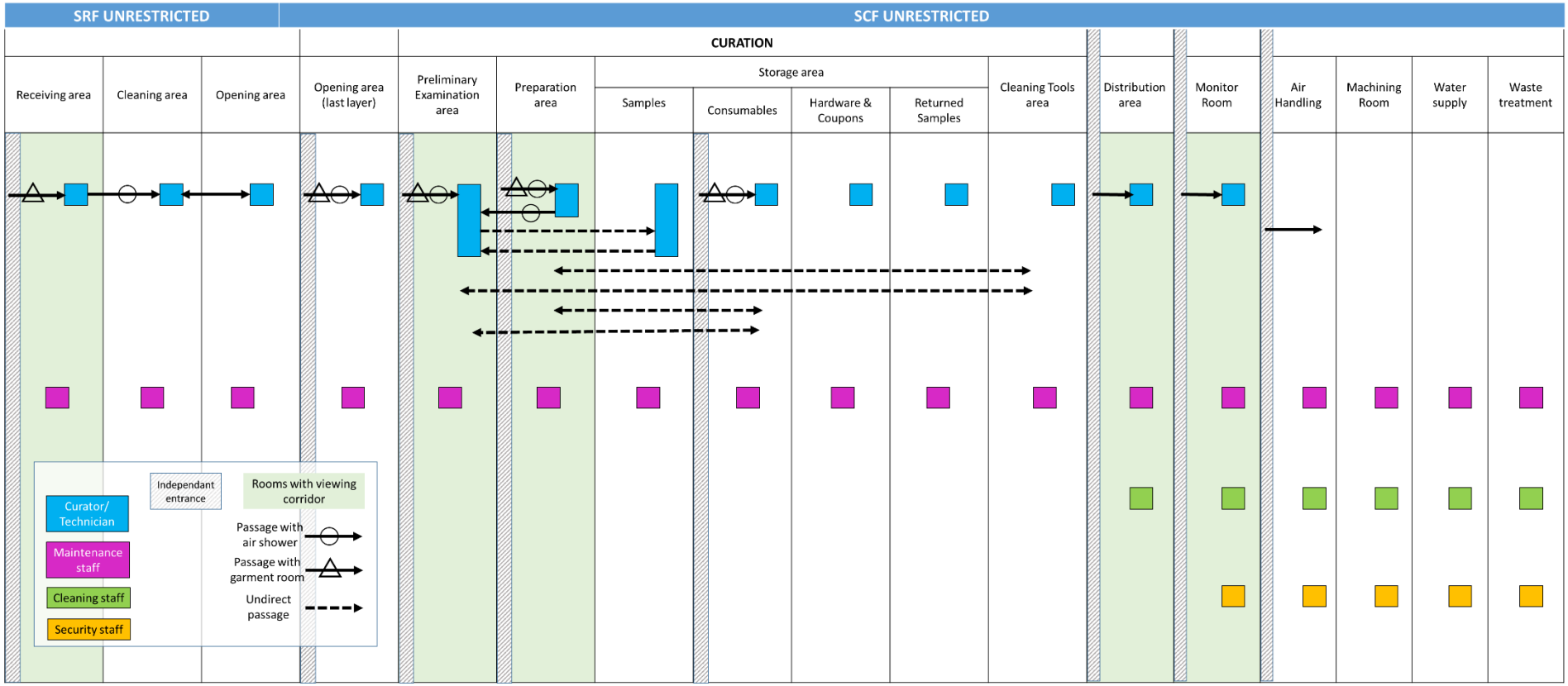

Figure 9. Flow of workers.

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4. Functional Layouts

The first step was to define the functional relationships and adjacency of each room or area of the FUs. To do so we defined the environment of each room, regarding cleanliness, containment levels (for restricted samples), presence of humans and/or robots, etc. (see tables 6 and 7). We took into account the flows of activities, samples and staff (see section IV.3).

All functional layouts are presented in Appendix.

Analogue / Mock-Up Facility

This FU is meant to be built before the other scientific FUs, and has several purposes:

- Testing of materials and building techniques, before applying those to the other scientific FUs.
- Testing of protocols and instruments, by using analogue samples.
- Storing a sufficient collection of analogue samples.
- Training and vetting of staff.
- Development of containment solutions and equipment for the restricted facility.
- Participating to the public outreach program.

We designed this FU to be rather small (compared to the other FUs), as a "sandbox" allowing curators, researchers, engineers, technicians and contractors to test and validate protocols, equipment and materials before using them on the precious returned samples. The AMUF features notably a full shower suit (replica from the one for restricted FUs), a "villi system" (see next page), a storage room, a replica of an examination room and a smaller room to be used for material testing.

The AMUF will not receive any ERC, so we did not include a high-bay.

Returned sample Laboratories: general design decisions

Restricted FUs and unrestricted were treated separately, for the following main reasons:

- Instruments cannot be shared between restricted and unrestricted samples (Franchi et al., 2016).
- Instruments will need to be modified in order to fit into villi or DWI.
- Additional facilities will be required for BAP/LD.
- Retrofitting not sustainable (SEA, 2012).

For both unrestricted and restricted FUs, we joined SRF and SCF in the functional layout. It is not a strong requirement, but it makes the transfer and opening of the sample canisters easier.

At the interface of SRF and SCF, we included a Material Airlock coupled with a Dirty Tool room. These rooms are used as an airlock on entrance of the ERC/Sample canister, or during the life of the facility, to bring instruments and tools needing maintenance that would disturb the operation of the facility or the cleanliness and containment conditions if done inside of the laboratory. A last use for this room is to take out decommissioned instruments. For that reason, the Dirty Tool room is accessible from any part of the laboratory, using corridors.

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The Vault will be adjacent to the Preliminary Examination Room so the samples can be accessed and stored without delay.

Doors for entering rooms are scaled for either people (single door) or instruments (double doors). In general, doors open contrary to the air flow, so that they will close automatically.

Receiving facility

Receiving facilities (Unrestricted and Restricted SRF) are composed of a high-bay, able to accommodate a truck and potentially cranes if the ERC is too heavy to be moved "manually". A fully enclosed unloading dock has been chosen as part of the ERC for cleanliness/containment and for security reasons.

An unloading process was considered, and opening of external layers with mostly human operators, even for a restricted sample return (although in that case, positive pressure suits should be used), considering the need of flexibility and adaptability to different types of ERCs, and to unknown condition within each layer of the ERC.

The ERC goes through a cleaning and opening room, and then the sample canister is introduced in the SCF. Layers of the ERC are also introduced in the SCF, to be curated in a dedicated storage room.

Condition of cleanliness and containment, as well as transfer mechanisms from one room to the other are dependent on whether the samples are restricted or not.

Villi

For the SCF part of the functional layout, we followed recommendations of the D4.2 in trying to keep the largest instruments outside of the cleanrooms and/or contained areas. This system, based on intertwining contained/clean areas and non-contained ones, was nicknamed “villi”, and is detailed below.

The purpose of keeping instruments outside of the working areas is manifold:

- Minimize particles-emitting and off-gassing sources inside the DWI and cleanrooms.
- Limit the need to decontaminate (fragile) instruments (for restricted samples).
- Allow staff to operate some of the instruments without going through gowning procedures, and to work in a more relaxed environment.
- Allow maintenance from outside (without disturbing the entire laboratory).

Such a system requires to develop through barrier technologies, such as what is used in Fort Detrick (Maryland, USA, see figure 10).

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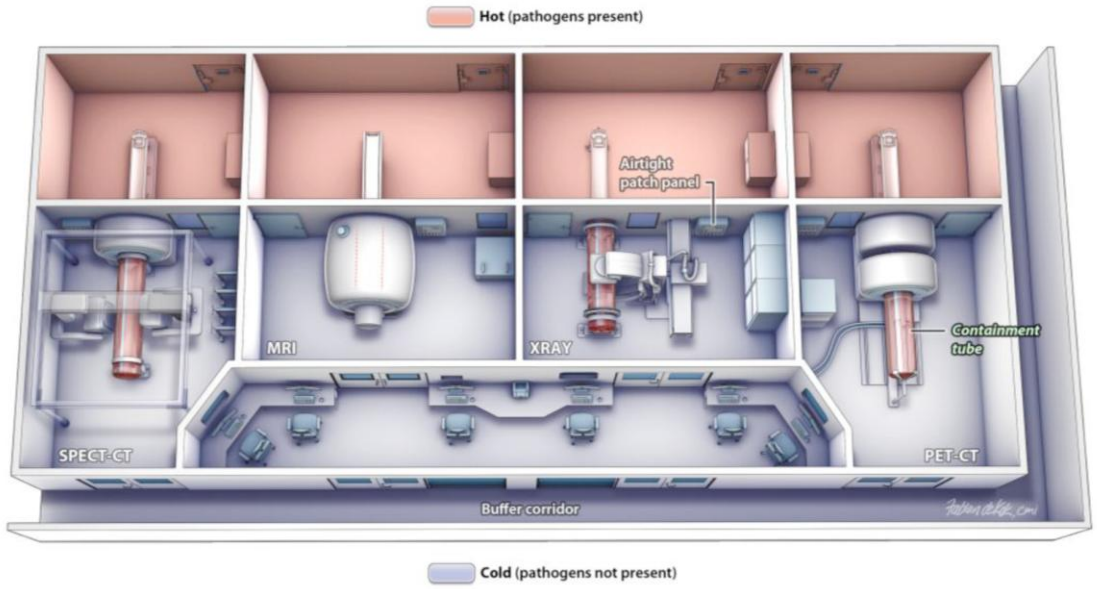

Figure 10. Schematic of the imaging suite at the NIAID Integrated Research Facility (de Kok-Mercado et al., 2011).

Figure 11 shows a functional layout for the "villi" solution.

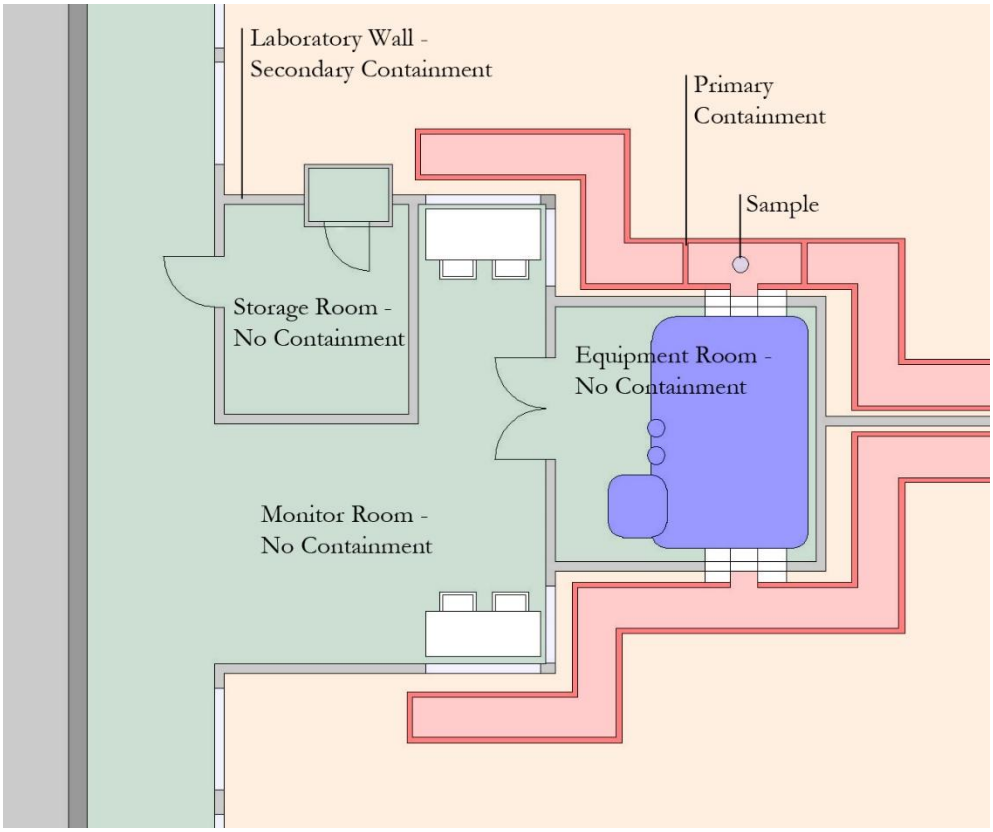

Figure 11. Graphic representation of one villus. *A villus is composed of a non-contained working room (in green), hosting an instrument (in blue). Samples are kept within the primary containment layer (in red), with secondary containment being the laboratory room (in orange).*

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Each instrument room can be equipped to handle special requirements, such as low vibrations, or magnetic field suppression, etc. The limited size of the room is then an asset to achieve these requirements at low costs, and with known technologies. However, detailed design work may be required to separate the external functions of equipment from the functions that will be housed in the contained area.

Unrestricted laboratory functional layout

The Unrestricted SCF is split into two sub-sections; one extremely clean part for pristine and analogue samples, and a section for returned samples, spare hardware storage and preparation of samples to be disseminated to external laboratories.

Table 6. Parameters for the Unrestricted SRF and SCF. *Frequency: 1 = every day; 3 = very week; 9 = rarely. Cleanliness level: 1 = ambient; 2 = medium; 3 = clean; 4 = ultra-clean. People vs Robots: 1 = people only; 2 = Robots only; 3 = both possible. Light blue indicates high cleanliness areas, dark blue indicates lower level cleanliness areas, and green indicates no cleanliness level.*

	Areas	Frequency of use	Cleanliness level	People vs. Robots	Air shower to enter	Changing room
SRF						
#01	Receiving area	9	1	1	N	Y
#02	Opening/ Cleaning area (cycle)	9	3	3	Y	Y
#03	Material Airlock	9	2	1	N	N
SCF						
	High Cleanliness Curation					
#04	Preliminary Examination area	1	4	3	Y	Y
#05	Vault (Samples)	3	4	3	Y	Y
	Medium Cleanliness Curation					
#06	Sample preparation	3	3	3	Y	Y
#07	Contamination/Cleanliness Assessment	3	3	1	Y	Y
#08	Work room readmit. samples	3	3	2	Y	Y
#09	Cleaning tools area	1	3	3	Y	Y
#10	Storage area (readmit. samples)	9	3	3	Y	Y
#11	Storage area (HW & Coupons)	9	4	3	Y	Y
#12	Storage rooms (consumables)	1	3	3	Y	Y
#13	Dirty Tool room	9	2	1	N	Y
#14	ISO 5 Corridor	1	3	1	Y	Y
#15	ISO Airlock	3	3	1	Y	Y
	Outside of cleanroom					
#16	Instrument alcove	1	1	1	N	N
#17	Monitor room	1	1	1	N	N
#18	Distribution/Packaging room	3	1	3	Y	Y
#19	Buffer corridor	1	1	1	N	N
#20	ISO 4 Changing room	1	1	1	N	N
#21	ISO 5 Changing room	1	1	1	N	N

Work on samples should be conducted in positive-pressure gloveboxes filled with an inert gas (see D1.3 and D3.1). Staff entrance is possible through a gowning suite adapted to the level of cleanliness.

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The receiving area for samples is shared with the general receiving area (for instruments, consumables, maintenance needs, etc.).

Flow of samples and staff is usually through doors, with the occasional use of an air shower.

Restricted laboratory functional layout

In this laboratory, the main design driver was the way the samples were being handled. At this stage of the project, in the absence of a clear protocol for Sample Early Characterisation / Preliminary Examination (SEC/PE) and Life detection / Biohazard Assessment Protocol (LD/BAP), we chose to make possible different types of approaches.

Table 7. Parameters for the Restricted SRF and SCF. *Frequency: 1 = every day; 3 = very week; 9 = rarely. Cleanliness level: 1 = ambient; 2 = medium; 3 = clean; 4 = ultra-clean. Containment Level: x = none; m = medium; h= high. People vs Robots: 1 = people only; 2 = Robots only; 3 = both possible. Yellow indicates medium containment levels, or gradual containment levels, Orange indicates the highest containment level.*

	Areas	Frequency of use	Cleanliness level	Containment level	People vs. Robots	Air shower (entry)	Changing room	Decon. Shower (exit)
SRF								
#01	Receiving area	9	1	m	3	N	Y	N
#02	Opening/ Cleaning area (cycle)	9	3	h	3	Y	Y	Y
#03	Material Airlock	9	2	m	3	Y	Y	Y
SCF								
	Contained curation							
#04	Examination area	1	4	h	2	Y	Y	N
#05	Vault (Samples)	3	3	h	2	Y	Y	N
#06	Contamination/Cleanliness Assessment	3	3	h	3	Y	Y	Y
#07	Storage Area (HW & Coupons)	9	3	m	3	Y	Y	Y
#08	Tool room/Dirty Room	9	2	h	1	Y	Y	Y
#09	Material Airlock	9	2	h	1	Y	Y	Y
#10	Corridor	1	3	h	1	Y	Y	N
	Non-contained rooms							
#11	Instrument alcove	1	1	x	1	N	N	N
#12	Monitor room	1	1	x	1	N	N	N
#13	Storage rooms (consumables)	1	2	n	3	N	N	N
#14	Storage rooms (general)	1	2	n	3	N	N	N
#15	Sterilisation area	9	3	h	3	Y	Y	Y
#16	Changing room	1	2	n	1	N	N	Y
#17	Suit changing rooms	1	2	m	1	N	N	Y
#18	Corridors	1	1	n	1	N	N	N
#19	Bathrooms	1	1	n	1	N	N	N
#20	Janitor room	1	1	n	1	N	N	N

The biggest part of the facility, thought for SEC and PE is designed to host a number of interconnected DWIs. Since a DWI is the primary and secondary barrier, staff can access the laboratory without a suit, using only a gowning suit. Staff will not be required around the exterior

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of the DWIs because the remote control of the robotic manipulators within it. However for emergencies, such as emergency procedures and maintenance of the DWI then it may be necessary to have airtight suits for workers to use, or some form of accessing the inside of the isolator using gauntlets or haptic systems.

Another part of the restricted SCF is designed to use either MSC3 as primary containment, or a full positive pressure suit. Staff entrance for this part is through a changing facility, whether using a suit of not, where staff will be required to don protective clothing before entering the restricted area.

A material airlock with decontamination capacities between those two parts allows for flows of instruments and staff if needed. This airlock, by isolating completely both parts of the laboratory, allows for a complete shut-down of one part (for maintenance, or in case of emergency) without impacting the other part.

5. Sizing of FUs

Sizes of rooms have been defined according to the activities to be conducted inside. Since protocols are not completely defined at the moment, sizes might change according to input from WP2 "Planetary Protection" and WP4 "Instruments and methods". Specific areas have been custom sized (and are described below), while more common parts of a laboratory (gowning, changing rooms, air shower, etc.) have been sized according to our visits to existing facilities, and interactions with the designers at Merrick and Company. Sizes indicated are minimum sizes. When the functional layouts were defined, the sizes may have changed to a certain extent.

Analogue / Mock-Up Facility

Table 8. Sizing for the Analogue / Mock-Up Facility.

	Areas	Length (m)	Width (m)	Height (m)
#01	Test room	9	10	8
#02	Instrument alcove	5	5	4
#03	Monitor room	4	4	4
#04	Suit suite	…	…	…
#05	Material suitability room	4	4	4
#06	Storage room	5	5	4

Unrestricted laboratory

The SRF needs to accommodate a transportation vehicle for ERC and should be high enough, to accommodate for example a temporary cleanroom or a crane. Because there is no issue of biohazard, the same docking station can be used for instruments and pieces of equipment.

Opening/Cleaning area should be large enough for relatively big return capsules.

Preliminary Examination Areas are the largest rooms in the unrestricted SCF, and are planned to accommodate up to 20 gloveboxes.

Sample Preparation and Contamination/Cleanliness Assessment areas are wide enough to allow two working stations (or counters) on opposite ends and to still have ample space for two people to stand in between.

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Dirty Tool rooms are scaled so that large pieces of equipment can go through for maintenance and cleaning purposes.

Instrument Alcoves are designed with large machinery in mind and they can – and probably should – be considered according to the pieces of equipment they will house (cf. D4.2). Some large pieces of equipment will require stabilizers while others may need a faraday cage. Monitor Rooms are large enough for observation windows and desks to be accommodated inside.

Table 9. Sizing for the Unrestricted SRF and SCF. *Light blue indicates high cleanliness areas, dark blue indicates lower level cleanliness areas, and green indicates no cleanliness level.*

	Areas	Length	Width	Height	Iterations
SRF					
#01	Receiving area	10	13	8	1
#02	Opening/ Cleaning area (cycle)	5	8	4	1
#03	Material Airlock	4	5	4	1
SCF					
	High Cleanliness Curation				
#04	Preliminary Examination area	9	10	4	2
#05	Vault (Samples)	6	6	4	1
	Medium Cleanliness Curation				
#06	Sample preparation	4	4	4	1
#07	Contamination/Cleanliness Assessment	4	4	4	1
#08	Work room readmitted samples	3,5	7	4	1
#09	Cleaning tools area	3,5	3,5	4	2
#10	Storage Area (readmitted samples)	4	5	4	1
#11	Storage Area (HW & Coupons)	4	4	4	1
#12	Storage rooms (consumables)	3	3	4	3
#13	Dirty Tool room	7	10	4	1
#14	ISO 5 Corridor	…	…	…	…
#15	ISO Airlock	…	…	…	1
	Outside of cleanroom				
#16	Instrument alcove	5	5	4	2
#17	Monitor room	4	2	4	4
#18	Distribution/Packaging room	7	7	4	1
#19	Buffer corridor	…	…	…	…
#20	ISO 4 Changing room	…	…	…	1
#21	ISO 5 Changing room	…	…	…	1

Restricted laboratory

As in the case of unrestricted laboratory, the SRF needs to accommodate a transportation vehicle and should be high enough. However, we plan another docking station for pieces of equipment, when containment measures are not necessary.

Opening/Cleaning area should be large enough for relatively large return capsules, with a pass-box large enough between the docking station and the opening/cleaning area.

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Preliminary Examination Areas are the largest rooms in the restricted SCF, and are planned to accommodate up to 20 gloveboxes or DWIs.

Dirty Tool rooms are large enough for the big equipment to fit through for maintenance and cleaning purposes.

Instrument Alcoves are designed with large machinery in mind and they can – and probably should – be considered with the equipment it will house. Some large equipment will require stabilizers while others may need a faraday cage. Monitor Rooms are large enough for observation windows and desks. In the case of restricted samples, the through-barrier engineering is of the upmost importance, to ensure integrity of the barrier.

A sterilisation area is necessary, to get decommissioned equipment and waste outside of the laboratory. This room should be equipped with several possibilities of decontamination (autoclave, incinerator, etc.), and lead to the outer buffer corridor.

Table 10. Sizing for the Restricted SRF and SCF. *Colours show the level of containment, from none (white) to high (red).*

	Areas	**Length**	**Width**	**Height**	**Iterations**
SRF					
#01	Receiving area	10	13	8	2
#02	Opening/ Cleaning area (cycle)	5	8	4	1
#03	Material Airlock	4	5	4	1
SCF					
	Contained curation				
#04	Examination area	9	10	4	3
#05	Vault (Samples)	4	5	4	1
#06	Contamination/Cleanliness Assessment	4	4	4	1
#07	Storage Area (HW & Coupons)	4	4	4	1
#08	Tool room/Dirty Room	7	5	4	1
#09	Material Airlock	3	4	4	1
#10	Corridor	…	…	…	…
	Non-contained rooms				
#11	Instrument alcove	5	5	4	5
#12	Monitor room	4	2	4	4
#13	Storage rooms (consumables)	3	4	4	7
#14	Storage rooms (general)	3	4	4	1
#15	Sterilisation area	5	6	4	1
#16	Changing room	…	…	…	1
#17	Suit changing rooms	…	…	…	1
#18	Corridors	…	…	…	…
#19	Bathrooms	…	…	…	2
#20	Janitor room	…	…	…	1

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Work Space

Table 11. Sizing for the Work Space. *Dimensions are in meters.*					
	Areas	**Length**	**Width**	**Height**	**Iterations**
Workers					
#01	Security booth	2	3	4	2
#02	Entrance desk	5	4	4	2
#03	Entrance hall	10	15	4	1
#04	Meeting rooms	14	10	4	3
#05	Guest offices	5	5	4	2
#06	Single offices	3	3	4	5
#07	Shared offices	4	3	4	7
#08	Administration rooms	3	4	4	5
#09	"Mission control" room	12	8	4	1
#10	Archive room (papers)	16	4	4	1
#11	Server room	10	4	4	1
#12	Security camera room	5	5	4	1
#13	Social rooms	4	5	4	2
#14	Cafeteria	20	8	4	1
#15	Toilets/Bathrooms	8,5	5	4	1

Areas are large enough to fulfil their intended purpose (and considering the total number of employees that is foreseen for the ESCF; cf. D3.1 and below) but may somewhat differ when a more substantial design will be developed. For instance, in this case (table 11) we account for a large bathroom unit that accommodates for over 40 persons with male, female and disabled access bathrooms. If the design needs a bigger area, then it might be wiser to have multiple smaller bathrooms.

For the most part, the working areas consist of shared offices with multiple meeting rooms ideally located in between them to favour interactions between employees. Single offices are considered for the administrative staff and curators. The Server room is rather narrow and long knowing that we have considered multiple racks in a side by side configuration. Its location, if possible not next to an exterior wall, will need to be as much as possible far away from potential sources of interference (i.e. from power plants or lifts, etc.). An Archive Room is also included to allow the storage of hard copies of the different documents (i.e. based on different visits of similar facilities and curation expertise, hard copies will still be used in the next decades even if more and more digital files are increasingly generated). It is also a narrow, "corridor-like" room, so the documents can be stored in cupboards or archive cabinets with drawers. A large Mission Control room (roughly over 100 m²) is added to the areas for scientific committee works or emergencies meetings. It should be possible to sit over 40 people in this area. It can also be used for press conference or other purposes yet to be defined according to the needs.

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V. Common features for unrestricted and restricted samples

1. Staff breakdown

Below is an exhaustive list of staff expected to work in the facility with their respective function(s), including an estimate of the minimum number needed for the ESCF to operate. The number of employees is highly dependent of the state of the ESCF (FUs built, mission arriving or already curated, etc.).

The following list considers an integrated approach for the facility. If the design concept is broken down to different units, there might be replicas needed.

The presented list was first compiled based on expertise of the WP3 team members, some input from the WP4 and then completed using other various sources, including personal working at the JSC (NASA) and JAXA.

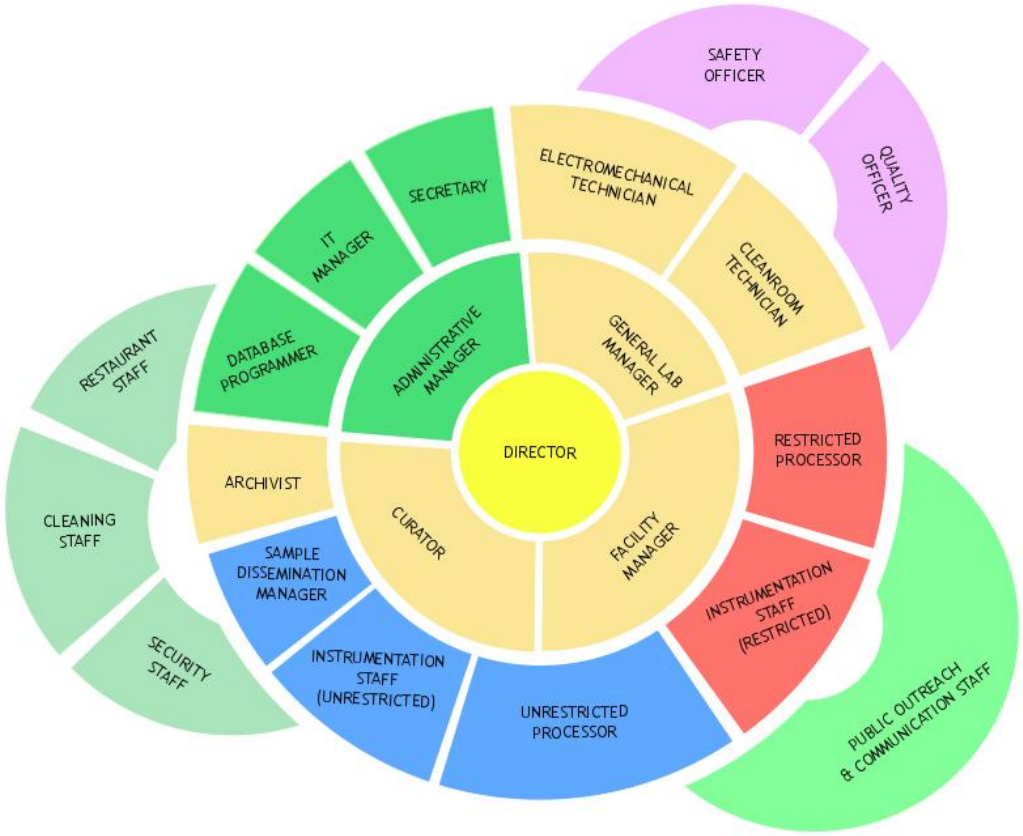

Figure 12: Proposed Organigram of the ESCF.

Administrative staff

The administrative staff do not deal directly with the samples and are required whether the facility is hosting unrestricted or restricted samples.

Director of the facility: Directs and manages all the facility operations. 1 full time person.

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Administrative manager and Secretary: In charge of the business planning, finances, human resources, etc. Supports staff, handles personnel issues and assists with various other administrative tasks. 2 full time persons.

Quality officer: Writes and reviews operating procedures in collaboration with science staff. Carries out quality audits. Interacts with external quality assessors. 1 full time person.

Safety officer: Provides safety advice, risk assessments and planned maintenance schedules for the facility. Carries out safety audits. Interacts with regulators. 1 full time person.

IT manager: Handles the day-to-day computer and network related issues. 1-2 full time person(s). Can be outsourced to an external company. If the facility is included in an already existing institution, there is no need of a dedicated worker.

Database manager/programmer: In charge of the database software (to develop, manage and maintain database(s) and the general website of the facility). 1-2 full time person(s).

Public outreach and Communication staff: Organizes the activities of the Public outreach unit, promote the ESCF through communication media. Liaise with local associations and authorities for ensuring open communication. 1-2 full-time person(s).

Security staff: In charge of the security of the site and its assets. 4-6 full time persons. Can be outsourced to an external company. If the facility is included in an already existing institution, the number of dedicated workers could be reduced if they already operate at the required level.

Restaurant staff: Applicable if catering is on site. Deals with the operation of the restaurant. 4-5 full time persons. If the facility is included in an already existing institution, no need for dedicated workers.

Cleaning staff: In charge of the cleaning of the non-restricted areas (i.e. non-cleanroom parts) of the facility. 1 full time person. Can be outsourced to an external company. If the facility is included in an already existing institution, no need of a dedicated worker.

Science staff for general functions

Science staff deal with samples and maintenance of the facility.

Curator: Responsible for the curation of the samples. In charge of the handling, documentation, preparation, preservation and distribution/allocation of the samples. Also assumes managerial roles, supervises personnel and is involved in education and public outreach. The same person can be curator for multiple collections. 1 per mission and/or set of samples, full time.

General (laboratory) supervisor/manager: Provides oversight of day-to-day technical and scientific functions of the facility. 1 full time person.

Facility manager/engineer: Responsible for ensuring that the building operates correctly and is correctly maintained. May be responsible for contracting out servicing and maintenance (i.e. filter testing, room air flow validation, autoclaves, primary containment, equipment testing, etc.). 1 full time person (?).

Archivist: Tracks the records associated with samples (loans, publications, etc.). Can be associated with the sample dissemination manager, at first. 1 full time person (?).

Cleanroom technician: Responsible for keeping the laboratories clean, cleaning the tools, helping with organization in the laboratories, etc. and of the training of facility staff and visiting researchers. 1-2 full time person(s).

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Electromechanical technician: Fixes and maintains things in the laboratories (lights, microscopes, heat-sealers, etc.) and of the major infrastructure systems that supply the laboratories (i.e. air-handlers, liquid and gaseous N systems, UPW systems, etc.). Only light works, considering there will be full maintenance once or twice a year done by an external company. Can also build small custom things for the cleanrooms. 1-2 full time person(s).

Science staff for unrestricted samples

Sample dissemination manager: Responsible for dissemination of the samples to external science laboratories (and to education institutions). Deals with loan agreements, contracts, shipping and receiving of the samples, education and public outreach, etc. 1 full time person.

Unrestricted processor: Performs the preliminary examination on sample containers and samples. Prepares samples for dissemination, according to requests. Processors are cross-trained to be able to work on several collections and several techniques. Training is performed with analogue samples. Unrestricted processors cannot work on potentially biohazardous samples, since it requires a specific and demanding training. 2 full time persons (to be increased with time and multiplication of the samples/collections).

Instrumentation staff: WP4 (Instruments and Methods) plans a suit of 13 instruments in total to perform the SEC on unrestricted samples (see D4.2). To properly run these instruments, a minimum of 9 (full time) persons is envisaged by the WP4 team.

Science staff for restricted samples

Restricted processor: Specially trained scientists/technician/engineer to handle restricted samples. Work on samples in the BSL-4 part, on life detection (including BAP). Must work in pair and for a limited time inside of the laboratory. 2-4 full time person(s). In case a robotic approach is preferred, workload will be reduced.

Instrumentation staff: WP4 (Instruments and Methods) plans a suit of 13 instruments in total to perform the SEC on restricted samples (D4.2), independently of Life Detection and Biohazard Assessment Protocol. To properly run these instruments, a minimum of 9 (full time) persons is envisaged by the WP4 team. LD and BAP will require additional instruments (see WP2 deliverables), and hence additional staff.

In total, we estimate between 30 and 50 staff independently on the choice of scientific FUs (unrestricted or restricted).

An increased number of personnel will be required at each mission arrival. These personnel may be a combination of permanent staff and visiting or contractual staff. Experience from previous sample return missions shows that there is intense pressure to obtain results quickly, and fatigue within science teams and technical staff is likely to be an issue. One member of the Lunar Sample Preliminary Examination Team (LSPET) described being in a "daze of exhaustion" after three weeks of analysing Apollo 11 samples (Taylor, 1994). In a curation setting, especially for Mars samples, fatigue could further lead to breaches in protocol that could undermine both scientific and public confidence. Accordingly, considerable attention should be paid to developing plans for mitigating fatigue issues – for example, by having extensive training and a program of rotating staff, especially during the first few weeks to months after a sample return mission.

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2. Database and cataloguing of samples

Sample cataloguing will begin as soon as the samples are removed from their containers. This cataloguing will serve as the permanent record for each sample and will include various types of information and data. The cataloguing system will need to follow a standard and methodical approach. Such methodologies are currently used in many international institutions such as museums and national laboratories and many electronic cataloguing and databasing solutions are available. Curatorial procedures/workflows should be incorporated into the cataloguing system. Sample cataloguing will be a regular and constant part of the curatorial tasks during preliminary examination and well into the future.

A main purpose of curation is to catalogue the samples, in order to:

- Make them available to the science community for in-depth research.
- Make them partially available to the public for display in museums and other outreach activities.
- Keep constant track of the location of the samples.
- Keep constant track of the analyses and subsampling activities.

The software will act as a logbook to track and document all the actions performed on the (sub)-samples inside EURO-CARES and in external laboratories.

The sample categories of the database will be:

- Pristine samples (within original containers).
- Work samples.
- Aliquots and preparations for staff training, sample classification, and subsample for allocation to external laboratories.
- Allocated and returned aliquots and preparations.
- Analogues samples.
- Hardware and pieces of the spacecraft.
- Coupons and witness plates.

Datasets linked to each sample will include:

- Identification (e.g. labelling, origin, imaging, state of matter, mass).
- Pictures of in-situ sampling and of next stages of the samples.
- Paths in and out of the SCF.
- Conditions (T, P, etc.) from the sampling site to the arrival in the SCF.
- Classification (e.g. structural, compositional).
- Preparation (e.g. type of preparation/mount, preparation/mount description and imaging).
- Location (e.g. sample container/location in the facility).
- Allocation (e.g. requested samples, location outside the curation facility, research purposes and methods duration of the loan/donation, expected results).
- Documentation (e.g. internal/external data and reports, scientific publications).
- Public (selected data on-line, e.g. sample description and availability for research).

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All the above information will be obtained and documented during the following procedures/actions:

- Cataloguing (identification, location).
- Classification (to be meant as preliminary/basic classification).
- Pre-delivery (preparation and allocation).
- Post-delivery (check of returned samples for research, storage).

Efficient data collection and storage in the various laboratories of the facility will make use of state-of-the-art electronic devices (e.g. internet, wireless audio-video recorders, bar-coded samples, subsamples and preparations, etc.) enabling unambiguous link of data sets to samples.

As with any IT system, care will be taken for the security of the system, during internal use as well as in those circumstances external users can access the database, e.g. external scientists providing or searching for information.

3. Manipulation of samples

Sample handling and manipulation systems will have to be capable of handling samples of different shapes and sizes and personnel operating those systems will have to be trained to deal with different types of material. The use of analogue materials will be very helpful because technologies/equipment can be tested prior to being validated for use in the facility and personnel can also be trained using these materials. During sample handling and manipulation there will be close collaboration between the curation personnel who will be carrying out these operations and the scientists that will participate in the Preliminary Examination. Sample handling and preparation will be a regular occurrence (happening on a daily basis) during the Preliminary Examination phase and shortly after as the samples will be of great interest to the scientific community. However, over time it is anticipated that the requests for new samples will gradually diminish with the reuse of samples that have already been prepared for earlier investigations e.g. polished sections of samples. It will be important that the skills honed by personnel during the early stages are maintained and also passed onto new personnel through time. This could also be achieved through regular training on analogue samples.

Manipulation without physical contact reduces contamination of samples as low as possible and protects the workers for restricted return samples. Table 12 shows a few envisioned possibilities for contactless manipulation:

Table 12. Techniques of contactless manipulation.

Technique	Notes	Ref	Pro	Cons
Optical tweezers	Atomic scale up to 100μm	S.K. Joshi, WP3 workshop	No direct contact, no opening container	Not good with metal. Heating of the particle
Tractor beams	Objects up to mm	S.K. Joshi, WP3 workshop	No heating	Needs dense atmosphere
Optical levitation	Objects up to kg	S.K. Joshi, WP3 workshop		Unstable, needs high energy
Electrostatic forces	Hayabusa samples	JAXA SCF		

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4. Materials

The materials that could be used for containers, tools or gloves (everything that could be in close or direct contact with the samples) are discussed in this section. Building materials (walls, floors, paint, etc.) are not considered here.

In general materials with a low rate of particles production, a low rate of outgassing and a simple element to measure in case of contamination are favoured. A review of both metallic and plastic materials is given below.

Metallic materials

Metallic alloys should be preferred to other rigid materials such as carbon fibre and other carbon compounds (e.g. SiC, TiC) because of their lower outgassing rate (at least by one order of magnitude Craig Jr, 1980).

The following properties should be considered in the selection of the metallic alloys:

- *Outgassing rate.* A low outgassing rate is needed in order to minimize the risk of forward contamination.
- *Rigidity and resistance to breakage.* This has to be considered only in case of transport outside the ESCF in order to withstand to shocks (i.e. it is not a fundamental property for containers that remain inside the ESCF).
- *Thermal conductivity.* This should be taken into account in case the samples need to be maintained at a reduced temperature and hence thermal insulation from the container is required.
- *Cost.* This is something to be considered if two or more materials have similar properties.
- *Electromagnetic properties.* Electrostatic and/or magnetic charging can change the properties of the samples, or make the manipulation of small-sized particles difficult. On the contrary, some materials can shield the samples from magnetic fields.

We do not consider density in this trade-off analysis, since the amount of samples to be transported is expected to be low (in the order of some grams) and hence containers' size is also expected to be relatively small. Therefore, container/box mass is not critical, contrarily to boxes aimed at transporting entry and return capsules (whose masses can be in the order of 10^2 kg), for which density is crucial for materials' selection (Longobardo et al., 2016). A summary of the considered properties is given in Table 13.

Table 13. Physical properties, thermal properties *(Patrick, 1973; Edelmann, 1992; Koyatzu et al., 1996; Huttel, 2014; Moshey, 1982)* **and costs of metal alloys** *(derived from an analysis of the current market prices).*

Alloy	Outgassing rate (10^{-6}torr l s^{-1} cm^{-2})	Young's modulus (GPa)	Thermal conductivity (W/m . K)	Cost (€/kg)
Stainless steel	0.05	195-215	16-24	1.3-1.5
Aluminium	0.6	70-80	230	1.5-1.7
Magnesium	1	40-45	120	1.6-1.8
Titanium	0.1-0.3	85-130	6	10-12
Copper	0.7	120-150	400	4-4.5

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Outgassing rate and cost are the only criteria to take into consideration for transport of samples inside the ESCF, if no need of low-temperature storage. For both criteria, stainless steel is by far the most appropriate material. Young's modulus should also be taken into account for transport outside of the facility; stainless steel is again the most suitable alloy because it has the highest rigidity.

If the samples have to be kept cold, titanium may be more appropriate than stainless steel because it guarantees a better thermal insulation. However, its high outgassing rate (two orders of magnitude larger than stainless steel) and cost (~7 times more than stainless steel) might preclude its use. A combination of two (or more) alloys can also be considered.

Plastic materials

According to WHO requirements, plastic material should have a good mechanical resistance and a low permeability. In addition, a low outgassing rate is a fundamental property, since it minimizes the risk of contamination to the samples. Plastics should be chemically inert as well, to avoid any reactions with the samples, or with chemicals used during analyses.

Longobardo et al. (2016) evidenced that the polymers with the lowest outgassing rate are Polyurethane (or Adiprene, polyether or polyester di-isocyanate copolymer), Teflon (tetrafluoroethylene polymer), KEL-F (or Neoflon, chlorotrifluoroethylene copolymer) and Perfluoroelastomer (or Kalrez, tetrafluoroethylene-perfluoromethylvinyl ether copolymer).

The following trade-off has been performed on these four materials and is based on:

- Wear/abrasion resistance.
- Water permeability (water resistance is a needed property).
- Nitrogen permeability (since the containers can be filled with nitrogen).
- CO_2 permeability (since CO_2 might be released from Martian samples or used as the atmosphere to mimic Mars during sample handling).
- Linear coefficient of thermal expansion (it should be low in order to minimize the risk of permeability increase due to thermal expansion of the plastic material).
- Cost.

Table 14 summarizes the properties of the four polymers.

Table 14. Properties of Polyurethane, Teflon, Neoflon and Kalrez (Peacok, 1980). Peacock (1980) does not indicate the permeation data of Kalrez and the reported values are relative to Viton (having similar permeation properties). Costs have been derived from an analysis of the current market prices.

	Wear/ abrasion resistance	Water permeability (10^8scmm s^{-1} cm^{-2} cm atm^{-1})	Nitrogen permeability (10^8scmm s^{-1} cm^{-2} cm atm^{-1})	CO_2 permeability (10^8scmm s^{-1} cm^{-2} cm atm^{-1})	Linear coefficient of thermal expansion (10^5 $°C^{-1}$)	Cost (€/kg)
Polyurethane	Excellent	260-9500	0.4-0.11	10-30	3-15	0.3-0.4
Teflon	Excellent	27	0.14	0.12	5-8	5-20
Neoflon	Very Good	0.5	0.004-0.03	0.02-1	4-7	20-60
Kalrez	Excellent	40	0.05-0.3	5.8-6.0	23	3000-5000

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Polyurethane is not suitable due to its high values of permeability. Kalrez has overall good mechanical and thermal properties, but it is extremely costly compared to the other polymers.

Teflon and Neoflon (KEL-F) are the best trade-off. Linear coefficient of thermal expansion are similar; Neoflon has a lower permeability to water, nitrogen and CO_2, but also a lower resistance to abrasion and is at least three times more expensive than Teflon.

We thus conclude that for the plastic bags in which the sample containers would be placed, Neoflon is more indicated, since samples' insulation is the most important issue, and knowing that wear and abrasion have a low probability to occur since plastic bags are expected to include small sample containers.

Otherwise, for covering the internal walls of the sample containers, Teflon would be preferred since cheaper, whereas insulation would be guaranteed by the external layers (i.e. plastic bag, if present, and the rigid box).

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VI. Unrestricted samples

1. Curation and storage

Curation in the facility has two main goals: first, curating *sensu stricto* i.e. storing, handling and managing the samples as a valuable scientific resource for generations of researchers to study, then conducting basic analyses on the samples and associated hardware (SEC and PE). Whilst there are similarities in many of the curatorial processes during both phases of activity, there are some differences in personnel and equipment resources that will be required.

During sample receiving and SEC/PE, there is a close connection between the needs of the scientific investigations and those of the curation and management of the samples. Given that it may be the case that the exact nature of the samples is uncertain e.g. if a core sample has remained intact or whether frozen samples have remained frozen, it is critical that a high-degree of flexibility in terms of both technology and personnel training is factored in.

The method of sample storage will be highly dependent on the type of samples returned from space. At a minimum, the sample storage environment should be controlled in terms of environment (cleanliness, temperature, humidity, atmosphere, etc.). There are different levels of control possible – the sample microenvironment, such as the environment within a single sample storage vessel (e.g. a tube, box, etc.) and the wider environment e.g. glove-box, cabinet in addition to room-level control. The closer we get to the sample, the more stable the environment will have to be. Access to the storage area should be monitored, in term of security (see III.3) and to allow this stability of environment. Sample storage environments should be monitored regularly using an electronic system with built-in alarms should any issues be detected.

It will likely be necessary to have such multi-level approach to storage, especially for particularly sensitive samples such as those that are frozen or which contain volatile components.

An important part of curating unrestricted samples is the dissemination to external facilities. Curators may ensure that samples are prepared accordingly to the external researchers' needs and swiftly sent, but they must also consider the order of analyses that can be performed (some analyses will destroy some characteristics of the samples), and must make sure that the claims are from an appropriate laboratory.

Samples that are returned from scientific study but which can be reused must be kept separate from those which are considered pristine.

2. Contaminants and cleanliness

For unrestricted FUs, there is no biological threat to the environment. Liquid waste should be treated only for potentially harmful chemicals, existing laboratories will already have protocols in place to deal with these chemicals. Solid waste having been potentially in contact with samples (disposable tools, gloves, etc.) will be stored and carefully searched for sample particles before disposal with other waste following traditional systems.

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3. Cleaning

In cleanrooms, the main process to ensure cleanliness is by the filtration of the inlet air. Additional cleanliness protocols can be undertaken, by sweeping the laboratory's surfaces with IPA wipes or with ultra-pure water, on a regular basis.

A specific vacuum cleaner (e.g. http://biobubble.com/products/hepa-vacuum/) could be used, especially for changing rooms.

In addition to the filtration of air within the laboratories, it is possible to remove particulate material and staff upon ingress by using air showers. Air showers are airlocks separating rooms of different cleanliness levels, with an active removal of particles and air filtration. They have an interlocking door systems, meaning that once inside the air shower, the worker cannot exit before the scrubbing process (30s to 120s) is completed. On the way out, air showers are generally not used and serve only as airlocks. The shape of an air shower can vary, from a small cubicle with two or three doors, to a tunnel for larger equipment to be brought into a cleanroom. They can be equipped with a static ionization system, which might prove very useful for laboratories handling small particles.

The use of an air shower depends on the facility and its use. They are present at Hayabusa Curation Facility, JAXA; Stardust Curation Laboratory, NASA; etc., but not present within Genesis Curation Facility, NASA; Hayabusa Curation Facility, NASA; etc. Based on the interviews we conducted, the usage of air showers is based more on customs and habits of the facility manager rather than on comprehensive studies of air shower efficiencies. However, the facilities lacking air shower were all retrofitted spaces. Lack of space might be an explanation for not installing an air shower within a facility.

In our understanding, air showers are extremely helpful in keeping a low and stable level of particles contamination (https://www.alnmag.com/article/2002/12/how-do-air-showers-fit-contamination-reduction-plan). They are small (a few m^2) and easy to integrate in a floor plan. Their cost is negligible (http://www.liberty-ind.com/airshower-cost.html) compared to the whole building. Moreover, they help reinforce the psychological effect that cleanliness is extremely important, while being an acceptable procedure for workers, contrary to other cleanliness measures.

Our conclusion is that air showers should be used and strategically placed in the facility. We identified two possibilities that may coexist in the ESCF:

- Closed air shower, or closed air tunnel. This type or airlock is integrated in the workers path, to separate cleanliness levels. They can be laminar or turbulent. The latter is faster in use and should be preferred.
- Open air showers are corridors of clean air around facility: These units operate 24 hours a day, continually filtering the air by recirculating it past a HEPA/ULPA filter and creating an "air curtain." The idea is that by continuously filtering the air, the chances of having loose particulate material in the facility is reduced. Where traditional air showers operate using high velocity air to dislodge particles, these air showers tend to work by filtering high volumes of air. In effect, you are keeping the general environment in the whole facility clean in anticipation that personnel will be bringing contaminants into the facility no matter what you do. This type of air shower works well in high traffic areas where

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changing garments is not practical, but you still want to reduce the number of contaminants.

Cleaning should also be considered for tools and instruments, since a major concern is sample cross-contamination, especially for the processing of multiple samples collected from different environments. To avoid sample cross-contamination, all curation equipment (sample handling and preparation tools, containers, etc.) should be able to be thoroughly cleaned between operations on different samples. In the situation where equipment cannot be cleaned to the required levels, then it would be necessary to replace with new equipment. Depending on the type of equipment it may be possible that only the part(s) in direct contact with the samples would require replacement rather than the entire equipment. These issues can be identified during the testing and verification process for the sample handling, manipulation and preparation equipment and informed decisions can be made then.

4. Protection of workers and samples

In the case of unrestricted samples, workers' safety from biological agents is not an issue. The only concerns is to protect the samples from external contamination. We recommend the use of positive-pressure gloveboxes kept under an inert atmosphere.

Cleanroom garments

Cleanroom garments are adapted to the level of cleanliness and must be cleaned and packed accordingly. A study has been considering the effect of particle contamination reduction with usage of cleanroom garments, versus garments and additional undergarments. The study showed a reduction of nearly 50% in biological contaminants (skin flakes, hairs, etc.) when cleanroom style undergarments were used (Moschner, 2002).

However, a complete change can be straining for the workers and expensive. The use of clean room undergarments should be addressed depending on the procedures that will be completed, if a further reduction in particulates is required for a process then undergarments can be worn.

Minimizing the sources of contaminants

As developed in section III, instruments deemed to be prone to produce contaminants (particles or outgassing), will be kept outside of the cleanrooms.

5. Robotics vs. human

Robots and humans

In the previous deliverable, D3.3, an extended discussion on the advantages and disadvantages of robots compared to humans was presented together with the possible improvement of the functional requirements of the ESCF robots may allow. From our previous discussion it was clear that it will not be robots OR humans but robots AND humans. The idea is to use robots (including automatic tools, robotic manipulation, artificial intelligence (after more development), etc.) to conduct the repetitive and fine manipulation tasks. For example, a robotic manipulation would make sense to sort and catalogue small particles/grains, especially in the case of regolith samples (as the technology already exists, Micro Support Co. www.microsupport.co.jp/en/).

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The following information presented was obtained from meetings and discussions with a number of robotics experts, high-containment experts, curators of collections and a variety of colleagues from different fields and expertise. Information extracted from the WP3 Workshop, from previous EURO-CARES deliverables and publications, as well as from unpublished reports were also used.

We first identified all the main tasks that could possibly be undertaken in the case of unrestricted samples using robots and robotic systems in the facility. These tasks are also to be conducted with the restricted samples. A questionnaire was prepared and circulated to experts on the use of robotics in scientific facilities, follow up discussion were held with the experts. The results from the survey and discussions are summarised below.

This section will not define which areas will have robotics in the ESCF, but to evaluate what procedures can be undertaken (or not) with robotics and how this can be completed. However, it should be noted that the use of robots and/or humans will have direct implications on the design of the facility and, thus, their usage should be discussed as early as possible in the planning and design process.

In total we have identified five main tasks and applications for which the use of robotic systems would make sense:

- Opening of the sample container
- Extraction of the sample(s) from the container
- (Micro-)Manipulation of the sample(s)
- Transfer of the sample in the scientific instrument (for SEC/PE)
- Re-packaging and transfer of the samples to the storage room

Some of these tasks are highly dependent on a number of factors and parameters that were unknown or not defined at the time this report was compiled e.g. sample material, size of samples, etc. In some cases, the applicability of the use of a robot can be greatly affected by these factors and parameters. For example, for the (micro-) manipulation of the samples, without previous knowledge of their size how diverse and non-homogeneous they will be, their properties, etc. it is difficult to define how suitable robotic systems will be.

Different types of robots and their suitability for different tasks

We have distinguished here three different main types of robots that are:

- Fully autonomous robot (i.e. capable of self-adaptation to the situation)
- Autonomous robot programmed for a specific task (object and path planned in advance or at the time of carrying out the operation, based on the specificity of the task to be conducted)
- Teleoperated robot (i.e. controlled by a human operator) and Cobots (collaborative robots)

Table 15 summarizes how suitable or not suitable the different types of robots are in function of the different tasks to be conducted.

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Table 15. Suitability of the different types of robots to operate different types of tasks *(based on a questionnaire). "0" in case the robot is "not suitable", "1" in case it is "quite suitable" (or suitable under specific conditions), and "2" in case it is "suitable". It is to be noted that in some cases, specific conditions can drastically change the suitability of one type of robot; in such a case some text is added.*

Type of robot / Task	Fully autonomous robot	Autonomous robot programmed for a specific task	Teleoperated robot and Cobot
Opening of the sample container	2	1-2	0 (or 1 in case it does not go as planned)
Extraction of the sample(s) from the container	0	0	1
(Micro)-manipulation of the sample(s)	0	0	1-2
Transfer of the sample in the scientific instrument	0-2 (0 in case the sample is not fixed on/in a specific holder)	0-2 (0 in case the sample is not fixed on/in a specific holder)	1-2
Transfer of the samples to the storage room	2 (automated storage and retrieval system)	1 (if automated system and retrieval system not used)	0

From the results of our survey, it appears that for robots the most difficult task to be conducted is the (micro-) manipulation of samples due to the number of uncertainties on the nature, size (range and homogeneity), properties, etc. of the samples to be manipulated. However, the use of Cobots is likely the best available solution at the present time. It involves direct physical interaction between a human and the machine, "hand in hand". An example can be seen at www.percipio-robotics.com/index.php/en/ and new developments are very encouraging (Lu, 2016).

The transfer of the sample in the scientific instrument for SEC/PE (if the samples are fixed/mounted on a specific holder) was felt to be a task that would be suitable for robots as would be the opening of the sample container and the transfer of the samples to the storage room. In the case of the transfer of the samples to the storage room, an automated storage and retrieval system (ASRS) was thought to be the best solution. ASRS are commonly used in many industrial sectors such as pharmaceuticals (e.g. BoxPicker™ Automated Pharmacy Storage System), warehousing and libraries, etc. (figure 13). The advantages in using such a system are numerous, including accuracy (tracks permanently the position of the samples and records all the movements and eliminates human errors), security (as humans do not have access to the storage area), possibility of working in extreme environments (such as at cold temperatures and gases), time saving and allows efficient use of storage space.

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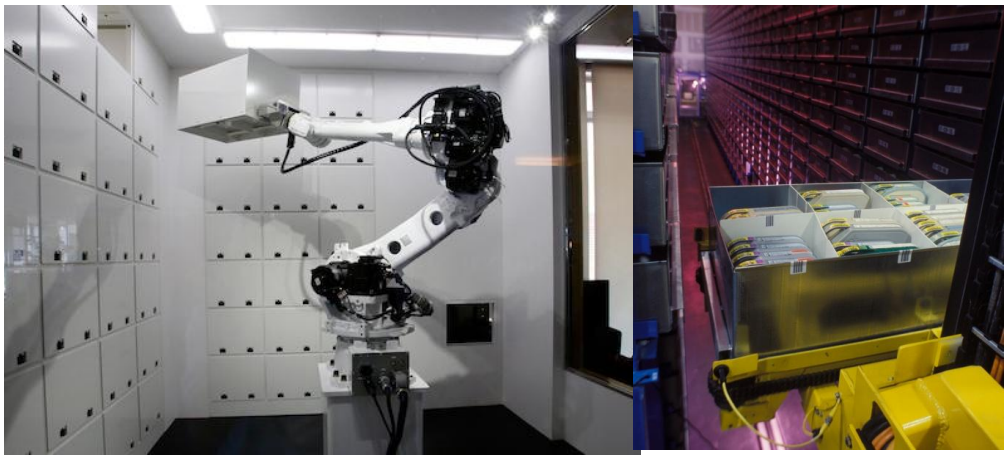

Figure 13. Examples of automated storage and retrieval systems (*sources: left, Public domain; right, Wikimedia commons).*

Challenges and solutions

Robots and robotic systems would need to operate in a clean environment without shedding of particles from motors or joints. At present there are robots working in cleanrooms that were developed specifically to meet the requirements of clean environments (typically used by semiconductor companies; Mathia, 2010), such as:

https://www.robots.com/applications/cleanroom

http://www.staubli.com/en/robotics/6-axis-scara-industrial-robot/specialized-robot/cleanroom-semiconductor-robot/

http://www.kuka-robotics.com/taiwan/en/products/industrial_robots/special/clean_room_robots/

In most of these cases, appropriate coatings have been developed to encase robots for working in clean environments. These coating materials are able to contain any leakage and can be decontaminated. However, these coating materials were developed to limit particulate contamination but not molecular contamination. Certain coatings and lubricants may off-gas and produce molecular contamination with the sample environment. Cleaning can also be challenging (Saito et al., 2017) and more research is needed to provide an adequate system. To summarize, some solutions to adapt robots to the work environment inside the ESCF already exist but still an assessment on whether they are inorganically and/or organically clean enough needs to be conducted. Cleaning protocols would also need to be defined and assessed but again this would depend on the location of the robot and the process it is required to complete.

In recent years, alternative (lighter) materials have been developed for the construction of robots (i.e. robots are generally constructed with aluminium, steel or titanium) including different types of composite materials and plastics. As the joints and motors are the main sources of contamination (i.e. friction creates particle contamination, lubrication used off gases), one solution is to keep them partially outside of the working environment. The use of non-conventional robots may also be a solution, such as "soft robots" (i.e. robots characterized by non-conventional structures, constructed with soft and deformable materials like silicone, rubber, plastic, etc.). In general, soft robots are continuous deformable structures that do not have joints

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and have no motors on board. Such robots have a number of advantages over traditional rigid robots. Their deformable structures allow them to adapt to the environment; this could allow for example grasping and manipulation of samples with unknown/undefined properties (such as size or even consistency). However, they may be less suitable for high precision tasks. Shen (2016) discusses that most soft robots are currently only at the prototype stage, but future developments should be highly considered for use in the ESCF. A good example of a recent and successful development is STIFF-FLOP (STIFFness controllable Flexible and Learn-able Manipulator for surgical OPerations; www.stiff-flop.eu/index.php/en/). Reader can find more information on soft robots here: http://softrobotics.org/.

Apart from the contamination risk from moving parts and lubricants, one of the issues of the robot is the gripper. Research is needed to develop suitable grippers for both efficiency and of non-contamination (knowing that this task is complicated by the to some extent unknown nature of the samples and their properties). Currently, a number of different physical effects are used to guarantee a stable grasping between a gripper and the object. There are four general categories of robot grippers (Monkman et al., 2007), namely:

- Impactive (such as jaws or claws; physical grasping of the sample, not very suitable in the case of small samples)
- Ingressive (such as needles or pins; physically penetrates into the sample, not suitable in our case)
- Astrictive (suction forces are applied to the sample surface; whether by vacuum, magneto- or electroadhesion)
- Contigutive (requires direct contact for adhesion to take place; use of a glue, surface tension or freezing)

The purpose of this report is not to review all different types of robot grippers, this is something that would need to be completed during the design and planning phases of the ESCF.

Current usage of robotics in curation facilities

Currently robotics are not generally used at the NASA Johnson Space Centre curation facility in Houston (USA) with the exception of a semi-automated micro-manipulator which is used for picking small cosmic dust grains (it is currently not done in a cabinet environment but rather on a laminar flow bench). However, in the case of Mars 2020, the plan is to drill onsite rock samples to make them conform to shape and size to be handled robotically. Past experiences of the use of robotics is limited to very few experiments such as the use of a robotic manipulator (i.e. a small robotic arm) in an advanced curation glove box (Bell et al., 2013).

At the Planetary Material Sample Curation Facility (PMSCF) of the Japan Aerospace Exploration Agency (JAXA) in Sagamihara (Japan), micromanipulators are used for handling very small particles. They consist of a specially designed electrostatically controlled micromanipulation system which is operating in an ultra-pure nitrogen environment (Yada et al., 2014). The group also constructed an electrostatically controlled micromanipulation system composed of commercial based instruments which could be used both in a clean booth of an electron microscope room and also in a glove box filled with nitrogen. Theoretical information on electrostatic particle manipulation has previously been documented by Saito et al. (2007).

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VII. Restricted samples

1. Curation and storage

Curation and storage principles are similar to unrestricted samples when it comes to SEC/PE and storage, but sample containers will be required to be held in more secure facilities both in terms of Biosafety and security principles. However, the dissemination activities are not as straightforward as for unrestricted samples. Potentially biohazardous samples cannot leave the ESCF without either being proven to be free of life or sterilised using a validated method, as such the containers for the restricted samples must be constructed similar to those identified in D6.3 (Longobardo et al., 2016), i.e. a two- or three-layered package.

The requirements of the sample container strictly depend on the planned analyses on the sample. Currently, the laboratory personnel that require the samples also provide the sample container to the Curation Facility (e.g. this is the procedure used for Stardust samples). For internal ESCF sample transport, the container should be composed of a sample collector, a collector protection and metallic walls (possibly internally Teflon-coated) aimed at insulating the samples. This can be modified to reflect the type of sample e.g. regolith, rock, gas, ice, liquid.

When the sample is transported inside the ESCF, the pressure system (coupled with collector protection) is optional (since the internal environment is controlled) but is mandatory when the transportation occurs outside the ESCF. Figure 14 (right) shows a basic design of sample container.

The sample container would be the most internal layer of the double or triple packaging.

The additional layers aim to:

- Protect the sample(s) from forward contamination.
- Protect the container from vibrations/shocks during (ground/air) transportation.

Therefore the container should be included in a rigid and cushioned box. The box material should have low outgassing rate, in order to avoid contamination in case of container damage/breakage during the transportation. When samples need to be preserved at low temperatures, a low thermal conductivity material should be used in order to minimize heat exchange with external environment. Low temperature inside the box would be guaranteed by a cooling system, involving liquid nitrogen or a refrigeration plant. A trade-off among metallic materials is performed in the "Materials for samples containers" section.

In order to reduce forward contamination, it should be considered to fill the outer metallic layer with an inert atmosphere of nitrogen or argon gas. Trade-off analysis performed in D6.3 shows that nitrogen would be preferable due to its lower cost and to the fact that its larger reactivity and thermal conductivity are not critical for transport of extraterrestrial samples.

During the transportation phase, box pressure should be monitored in real-time: indeed, pressure change may be ascribed to box leakage or forward contamination. It would be possible to perform a further contamination evaluation after the arrival of the box to destination, by placing one or more witness plates inside of the box.

Additional precautions must be adopted in case of transport of restricted samples, i.e.:

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- The sample container should be surrounded by an absorbent material in order to prevent a risk of fluid leakage (e.g. phase transition in Martian samples).
- A layer consisting in a bag of non-outgassing plastic material must be added between the sample container and the metallic box. Whereas the double packaging (container + metallic box) reduces the risk of forward contamination, the risk of backward contamination arises for restricted samples and a safer packaging must be adopted in this case. According to World Health Organization (WHO) guidelines (WHO, 2015), this triple packaging (container + plastic bag + metallic box) is mandatory for samples which may hosts life forms. It failed only in 106 cases on 4.92 million (0.002%), hence this packaging can be considered safe (WHO, 2015).
- A real-time monitoring of the pressure inside the box during the transport could be needed. D6.3 shows different instrumentation/techniques that could be used to this purpose.

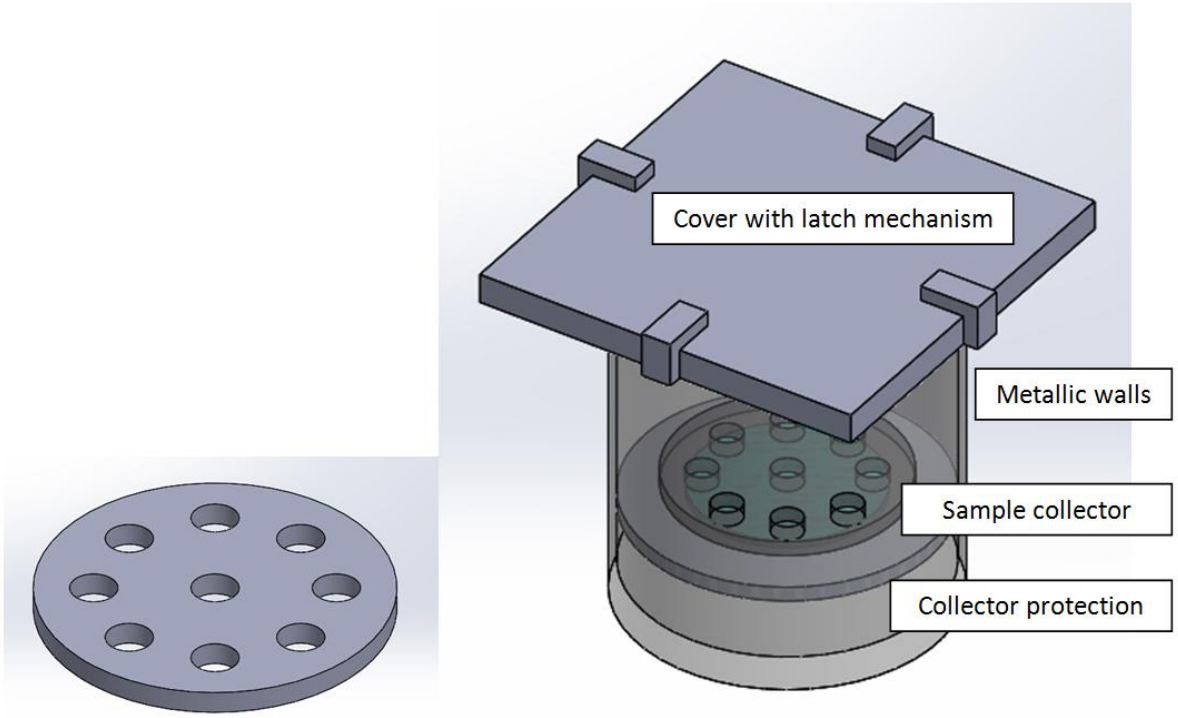

Figure 14. *Left:* Sample collector ("racket" model). *Right:* Basic design of a sample container. *Depending on the study to be performed, a window of transparent material should be added in order to allow optical analyses of the sample(s).*

2. Biological sterilization

Samples

There will be a requirement to sterilise any restricted return samples before they can go out of the ESCF for external studies, either before it has been proven to be free of lifeforms or if lifeforms have been identified. This is a prerequisite of the PP guidelines (COSPAR, 2002). Returned samples will be primarily composed of cored rock samples and regolith. If the sample presents a high porosity, which is the case for regolith, organisms might use pores and fissures as a microenvironment. This may only be determined through microscopic analysis of the rock, meaning it will need to be considered as contaminated internally until proved otherwise.

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Sterilisation of these rock and regolith samples will only be achieved by using an energy-based technology that can penetrate to their interior, such as heat or radiation. Validation will need to be undertaken to ensure that the appropriate parameters are met for effective sterilisation without altering the physical or chemical properties of the sample material and influencing future testing. More details on these methods are included in the D2.3 "Sterilisation and Cleaning" of the EURO-CARES project (Leuko et al., 2017).

Waste

Solid waste decontamination

Autoclaves

Autoclaves have historically been used to provide an effective method of sterilisation of laboratory waste (Block, 2001). The most effective way of sterilising waste before it can leave a high containment laboratory is through autoclaving. Within a BSL-4 laboratory the autoclave is required to be double-ended, with interlocking doors. The external doors should only be able to be opened once a cycle has been completed to all of the parameter set points. This stops unsterilized material from being released from the laboratory.

The European standard 12347 describes the minimum operating parameters that must be exceeded for a correct autoclave cycle. There are a number of different autoclave cycles that can be used and these will reflect the waste that is being processed, i.e. high liquid volumes, or highly absorbent loads. Validation of the cycle can be completed using either chemical, physical or biological methods, or a combination of more than one. Spores of the bacteria *Geobacillus stearothermophilus*, are recommended as the biological indicator organism, as these are resistant to moist heat. Chemical indicators that change colour after exposure to the required conditions can be used, or using thermocouple recorders to establish the same conditions have been achieved are available to be used.

If the autoclave cycle fails then the waste inside can be returned to the laboratory and the autoclave repaired. Autoclaving provides a well-established and easily validated methodology of sterilising waste generated in the laboratory, using monitored physical parameters.

Incinerators

Incinerators use combustion at high temperatures to reduce the waste within it to non-combustible ash. Incineration is used as the final stage of the solid waste disposal process, where waste is incinerated after autoclaving. As such there are no incinerators housed directly within BSL-4 containment facilities. The EU Directive 2000/54 stipulates that incineration must be used in animal BSL-4 facilities for the disposal of animal carcasses, although other technologies are being investigated as alternatives, such as alkaline hydrolysis. The use of incinerators is often highly regulated under national regulation.

The most standardised design of incinerator is the dual chamber incinerator. In this design the waste is fed into the bottom chamber which is operated at a temperature ranging from 870-980°C, the oxygen content within this chamber is also regulated, allowing the control of the oxidation of the waste and fixing of the carbon. Waste gasses from this chamber are allowed to move to the second chamber, which is above the first one, where extra air is introduced to burn

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the waste gasses from the first chamber. The temperature in the second chamber is higher than in the first at >1093°C (Block, 2001).

Generally, incineration after a validated autoclave cycle is unnecessary as there is little benefit and the incineration process is costly and environmentally unfriendly.

Liquid waste

The majority of the liquid waste produced within a BSL-4 facility is from either positive pressure suit decontamination showers or from personal showering. Small volume processes completed in the BSL-4 facility will also be collected in the effluent system. The effluent system must have two HEPA filters in series if it uses atmospheric ventilation to stop any contamination within the gases from being released in the environment (Chosewood and Wilson, 2009).

The effluent treatment system must be completely sealed to prevent any leakage of effluent. Special measures need to be put in place for high containment facilities handling large animals, such as being constructed to be gas-tight at a pressure of 1KPa (Barbeito et al., 1995). Large animals cannot be contained within primary containment such as cabinets, so the room is treated as the primary containment. The animals produce a large quantity of potentially contaminated waste that cannot be completely collected and autoclaved such as within a non-animal high containment facility and therefore the effluent treatment system must be designed to a higher standard. The material the effluent treatment equipment is constructed of must be able to withstand any chemicals that are used in the treatment process and also used in the laboratory. Currently the preferred method of treatment for the effluent is heat, produced by steam, this is because it is easier to validate, control and therefore reproduce (WHO, 2004). Other methods can be used such as chemicals or heat and chemicals in combination. After treatment the effluent can be cooled and discharged to the main sewer (HSE, 2009), or if the treatment is chemical then the effluent must be neutralised and/or returned to a neutral pH prior to discharge. The construction of the effluent system should allow for regular inspection of the pipework, with no pipework being hidden from view e.g. by enclosures. Any drains and U-bends incorporated into the system must be able to be sealed or engineered to prevent drying out to stop any air from the effluent treatment plant from returning to the laboratory. The pipework should be able to be sterilised *in situ* to reduce the need for human intervention during operation.

The effluent system should work on a gravity feed because this removes the need for back up devices in the event of a pump or power source failure. The treatment vessels must be situated in a plant room that is bunded, to contain any leaks or spillages from the treatment vessels. This bunding must be able to hold the capacity of the treatment vessels plus an additional 10% (HSE, 2009). This needs to be demonstrated by filling the bunding with water to this level and then being held over a period of time with no loss. In larger facilities that are envisaged to be in continual use then it may be appropriate to use two processing tanks as once one reaches the fill level and the treatment is undertaken the other tank allows the laboratory to continue to operate. The processing tanks should be able to continually stir their contents to maintain homogeneity of the effluent during treatment.

Validation is completed using biological indicators, such as spores of *Geobacillus stearothermophilus*. After validation, monitoring of the physical parameters can be completed to determine if the process if effective, prior to release of the treated effluent to drain.

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Tools

Decontamination of tools will be completed either by sealing within an autoclave pouch and then autoclaving if thermostable or, if thermolabile, treated chemically, either gaseous or liquid. If the tool cannot be decontaminated then single use tools can be procured for the facility. It will be important to identify and validate the selected technique in appropriate conditions.

Rooms

The surfaces of the laboratory and rooms will initially be treated using a liquid disinfectant to remove the gross contamination from them, often after this as the final step in the decontamination process a gaseous application of a decontamination chemical will be used. For this process there is a range of techniques and technologies that are available for use, e.g. formaldehyde, chlorine dioxide and hydrogen peroxide (Beswick et al., 2011). More details on these processes are found in the D2.3 "Sterilization and Cleaning" of the EURO-CARES project.

Showers for suited workers

On exit from a suited BSL-4 facility the exterior surfaces of the suit must be decontaminated before it can be removed. As all the sample handling procedures will have been undertaken within primary containment then any contamination should be at a low level on the suit. The showers should be linked directly to the laboratory exit via airtight doors. The shower will be at a positive pressure to the laboratory but at a lower pressure to the changing area to create a flow of air into the laboratory away from the areas where personal protective equipment (PPE) is not necessary. There are a number of different choices for the shower design with arrangement and type of shower nozzles that can be used. Showerheads that become clogged easily should be avoided, the National Institutes of Health (NIH) facility in the USA use shower heads that can be detached and cleaned easily to stop them becoming clogged (Crane et al., 1999). The effluent from the showering process is collected in the effluent treatment facility.

At present there is no defined guidance for the type of chemical that should be used in the decontamination shower or the cycle parameters (Klaponski, 2011). Whilst the facilities can choose their own respective chemical, the introduction of the EU Biocide Directive will limit those that can be used in the future. For example, Microchem which is used in some USA and Canadian facilities cannot be used in Europe. During 2010, PHE received information from a range of BSL-4 facilities around the world on their shower cycles, this is shown in Table 16.

Table 16. Shower cycles used in BSL-4 facilities.

Facility	Chemical cycle (L)	Rinse cycle (L)	Total volume (L)	Type of detergent/disinfectant
A	68	160	228	Microchem
B	10	35	45	Microchem
C	60	30	90	Desintex
D	10	35	45	Microchem
E	10	35	45	Microchem
F	10	35	45	Microchem
G	33	60	93	Microchem
H	24	115	139	Microchem

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The shower cycle decided for a new facility will need to be validated to determine its efficiency. A study completed by PHE investigated a shower cycle using Desintex against two different positive pressure suits (Chemturion, ILC Dover and BSL-4 suit, Honeywell) and the contamination positioning on the suit. The study found that increased removal from the suit was facilitated by using a brush, the removal from the different suits varied, and that the positioning of the contamination on the suit caused variances in the removal levels. This indicates that there is no set showering regime for use in the facility and different cycles will be developed on the choice of suit, potential level of suit contamination, work being undertaken and shower/nozzle delivery system used.

Redundancies are built into the shower set-up where a gravity fed tank of chemical disinfectant is always available so the suits can be decontaminated in the event of a power loss. This emergency tank needs to be large enough to wash and decontaminate the maximum number of suits that will be in the laboratory at any one time.

In both types of BSL-4 facility (cabinet line and suited) the operators will be required to also pass through a personal shower before exiting the laboratory. This will follow the removal of the positive pressure suit or in a cabinet line laboratory after removal of the individual's scrubs. Effluent from the shower after cabinet line, isolator or animal facility is treated in the effluent treatment system before discharge.

3. Protection of workers and samples

In the case of restricted samples, the safety of workers is an issue, alongside with the non-contamination of samples.

As mentioned in the *Design Theoretical Approach* section (IV.4), there are three possibilities:

- Cabinet Line Laboratory
- Suited Laboratory
- DWI Line Laboratory

This section will detail the different laboratory types and how they could be applicable to a sample return facility.

Cabinet line laboratories

There are three different types of MSC used in microbiology laboratories, classes 1, 2 and 3. Each of these classes use a combination of directional airflow and high air change rates to prevent exposure of workers to any microbial aerosol within the working area of the cabinet. Both class 1 and 2 cabinets are open fronted and require the worker to directly insert their arms into the cabinet to handle the samples, whereas the class 3 cabinet forms a physical barrier between the worker and the samples. Within Europe, cabinet performance is specified in the European standard EN 12469:2000 for biotechnology performance criteria for microbiological safety cabinets (BSI, 2000).

MSC3

The MSC3 is designed to offer the highest level of protection to the worker and the surrounding environment whilst also protecting the work from particulate and biological contamination

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(Chosewood and Wilson, 2009). The cabinets are generally constructed with a front window made of clear Perspex or safety glass and an airtight seal, which is held in place using locking nuts to the carcass of the metal cabinet. The glove ports, through which the sample manipulation occurs, are either through the window or below the window through the cabinet's body. Whole arm length gauntlets are secured to the gloves ports. The gauntlets are usually constructed of rubber but can be made of other material as long as it confers the level of protection and dexterity required by the users. Figure 15 shows a MSC3 cabinet in operation at PHE (Porton, UK).

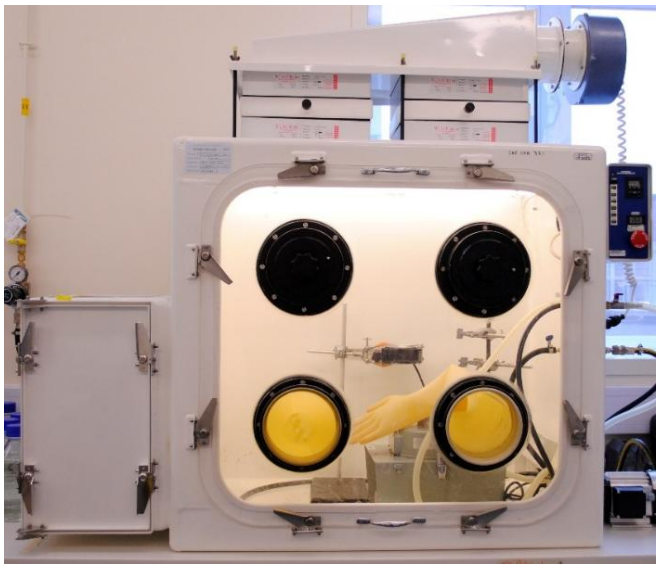

Figure 15. A MSC3 in operation at PHE Porton (UK).

An inflow of air is drawn through a single HEPA filter, passing over a baffle plate ensuring the air is mixed thoroughly within the cabinet. Air is then drawn out of the cabinet through double HEPA filters by a fan unit positioned after them. The fan unit operates at a higher flow rate than can be drawn through the inlet HEPA filter to ensure negative pressure is maintained within the cabinet. A number of cabinets can be linked together to form a cabinet line (discussed in more detail below), this provides a greater flexibility of sample processing tasks than could not be performed in a single MSC3. But for smaller operations, a single MSC3 can be used. Some of the MSC3 will have a pass box or other transfer systems to allow samples or equipment to be removed or to enter the cabinet during operation. Barbeito and Taylor's (1968) experiments during the 1960's on the protection afforded by an MSC3 in operation and showed that the cabinet was effective at containing an aerosolised bacterial challenge. Further experiments also proved that when the gloves were removed from a cabinet in operation, it could still provide a high degree of protection (Barbeito and Taylor, 1968). The MSC3 should be operated at less than a negative pressure of 250 Pa with a minimum volumetric inflow of air of 0.05 m^3/s for each cubic metre of cabinet volume, as specified by the standard BS EN 12469.

The MSC3 exhibits a very high protection factor when operating correctly and allows the users to work without the necessity for respiratory protection or constraining suits. But the cabinets can be difficult to work with and restrictive due to the positioning of the glove ports. The high airflow and turbulent environment is unsuitable for handling some materials such as powders.

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Cabinet line laboratories

Cabinet lines are made up of a number of MSC3 that are connected together to form a spine. From this spine, further MSC3's are connected and will be used for manipulation of the samples and to house the specialist equipment that is required for processing, e.g. microscope, analysers, etc. The cabinet line spine is used to move the samples along to the necessary cabinet branch where the manipulation/analysis can be performed.

Material entering a cabinet line in a BSL-4 facility will be passed through a dunk tank filled with a validated liquid disinfectant. The sample container must therefore be waterproof to avoid ingress of the disinfectant. The container will be immersed for a defined period of time before it is then transferred to the cabinet line and opened. At the terminal end the cabinet line will be connected to a double sided autoclave, which is used to sterilise any material that is removed from the cabinet line. Live samples, or other material that cannot be autoclaved can be packaged and either passed through the dunk tank or fumigated before removal from the cabinet line, rather than being autoclaved.

Testing of cabinet lines are not included within the European standard EN 12469, as this only details the tests required for single MSC3 cabinets, but the general principles can be used for cabinet lines. This will need to be discussed and agreed with the host country's regulatory agency.

The use of a cabinet line can be restrictive for the workers, but training can be completed more quickly than for a suited laboratory (Hilliard et al., 2007). This is because workers progressing from working in lower containment levels to BSL-4 will already have experience working with cabinets, but the majority of workers will not have previously worked with the positive pressure suits used. Operators working within the cabinet line are required to wear specific laboratory clothing that consists of disposable underwear and operating theatre scrubs with a lab gown. These will be removed on exit prior to a personal shower and then autoclaved before washing outside of the laboratory.

Flexible film isolators

Flexible film isolators (FFI) have been used in the UK for working with risk group 4 agents and infected small animals (van der Groen et al., 1980). FFI are thought of as non-standard MSC3, where a metal frame is constructed with a flexible canopy covering it. It increases the flexibility of the work that can be completed within the FFI compared to a MSC2 or 3 because the design can also include a number of half suits on the floor of the isolator allowing operators to be inside, increasing the usable surface area (figure 16). There are glove ports around the exterior of the isolator allowing for the operation of larger pieces of technology. FFI usually operate at a significantly lower pressure differential and air change rate than a MSC3 cabinet, this can be changed depending on the use of the isolator. A fan unit, with battery back-up, is used to generate the pressure differential and air changes within the isolator. Bennett et al. (2005) have shown that the isolators can achieve a high degree of protection, similar to MSC2 and 3, even when gloves are removed or canopies ripped.

Modified FFI have been used for the transport and treatment of infected patients with high risk group agents, such as during the recent West African Ebola virus epidemic, where infected workers were transported by plane to specialist treatment facilities and then housed in large isolators during treatment.

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Figure 16. A solid frame isolator used in a BSL-4.

Cabinets provide a high degree of operator and product protection. They can be adapted to the specific procedures that will be carried out within them using different arrangements, lower inflow of air, ultra HEPA, different gauntlets, but they do have limitations on the dexterity and size of equipment that can be placed within them. FFI have been developed to provide a solution to these problems by the use of half suits, the workers can operate from within the isolator in conjunction with those using gauntlets on the exterior surfaces. Flexibility of use can be incorporated into a cabinet line by future-proofing it with the design of sections where further cabinets can be attached containing additional equipment. This allows the modification of operations performed within it as newer equipment becomes available.

Suits

Positive pressure suits are used within all BSL-4 laboratories, except in the UK where the regulating body required the construction of cabinet line high containment laboratories when the facilities were built, as primary containment for the worker as opposed to a MSC3 cabinet line or flexible film isolator. With the operator wearing the positive pressure suit specific procedures with the infectious agent will be undertaken in a MSC2 to reduce the possibility of release to the wider environment because suits will only help to protect the worker, not the laboratory environment. However, for non-normative process such as large animal experiments, suits can be used as the main containment system. Positive pressure suits have been used within the nuclear industry with a long history of safe use.

There are currently two main manufacturers of fixed gas line positive pressure suits for use in BSL-4 laboratories; ILC Dover (USA) and Honeywell (France) (Walker et al., 2011). Positive pressure suits have an airline fitted to the suit through which breathing air is supplied, either from bottles or air compressors. The air is generally supplied into the suit from a detachable air line through a valve incorporating a HEPA filter on the outside and through a noise reducing mechanism. The suits incorporate a number of one way exhaust valves which are situated beneath splash covers. The airflow into the suit is higher than that leaving it, so the suit becomes positively pressurised and inflates. The positive pressure of the suit to the laboratory environment

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is one of the mechanisms that confers resistance to the user, by stopping the ingress of aerosolised particles, the other is by the physical barrier given by the suit.

Although the operation of the two main suit types is similar, there are large differences between them. The Honeywell BSL-4 suit operates at a higher airflow rate, 470-950 L/min, than the ILC Dover Chemturion suit, 142-155 L/min, meaning that a more powerful compressor is required for operation, especially if there is more than one Honeywell suit being operated at the same time. During emergencies, if the compressor fails, then, often a compressed air bottle back-up system is employed, again meaning that more bottles will be required with the Honeywell suits.

The suits are manufactured using different materials which can be affected in different ways by the disinfectant chemicals (Kümin et al., 2011) and should be investigated prior to use in a facility. The Chemturion suit is made of durable chlorinated polyethylene (Chloropel™), which is a blue colour and more rigid that the Honeywell suit. The Chemturion has a large clear forward facing visor made of polyvinylchloride (PVC). The Honeywell BSL-4 suit is constructed of a polyester fabric coated with PVC, with the panels sealed using high frequency welding. This provides a lighter weight suit. Again the suit has a clear visor, but this is completely around the head of the wearer. The suits can be seen in figure 17. Whilst the Chemturion suit is supplied in three sizes, small, medium and large, the Honeywell BSL-4 suit can be made to the wearer exact dimensions. This means that whilst a single Chemturion suit can be used for multiple workers the Honeywell BSL-4 suit will only be suitable to a specific individual (unless a number of people have the same measurements).

Figure 17. A Honeywell BSL-4 positive pressure suit in a decontamination shower mock up.

The operator protection factor of positive pressure suits has been investigated by a number of different laboratories (PHE, UK and Spiez, Switzerland). The work completed showed that both suits conferred a high level of operator protection factor to the user (Kümin et al., 2011; Steward and Lever, 2012). Testing of the suits showed that under extreme movements it was possible to briefly negatively pressurise the suits and force some air inwards to the suit through the one way

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valves but this was for a short duration and the ingress of aerosolised particles was very low. This ingress can be eliminated through correct training of the workers to use smooth steady movements.

Working within those suits can be difficult, with the extra weight of the suit resting on the shoulders of the worker. The temperature of the incoming air needs to be carefully regulated to avoid the overheating of the worker. The noise of the incoming air can also be an issue for long duration use of the suit and communication. The Chemturion suit has a higher noise level within the suit compared to the Honeywell BSL-4 suit, but both usually require the worker to wear hearing protection when used for extended periods of time (Steward and Lever, 2012). The noise within the suits also makes communication difficult between workers in the suits and to outside of the laboratory. Push to talk radio systems and head units are used within the suits. This also allows workers external to the laboratory to contact those within it in an emergency case.

Regular inspections and tests are undertaken on the suits to ensure they operate effectively. Visual inspections involve monitoring of the welds and zips prior to use of the suit, which the suit is physically tested using a pressure hold test to ensure there is no microscopic damage to it, using the European standard EN 464:1994.

The layout of the laboratory needs to allow the manoeuver of the worker in an inflated suit without danger of knocking into any equipment or damaging the suit.

DWI Line Laboratory

The third possibility is a train of DWIs, with a full robotic integration for sample manipulation. Concept of one DWI is explained below (section VII.4).

In that case, the workers can wear simple lab coats, and the samples are not in contact with any external contaminants, but the ones caused by the DWI itself.

Personal Protection Equipment

Workers attire

Within both cabinet line and suited BSL-4 laboratory, safe operating procedures include that the workers must remove their own clothes prior to entry into the laboratory (Hilliard et al., 2007). Within the cabinet line laboratory, disposable underwear is worn under operating theatre style scrubs, which are then covered by a rear fastening gown (solid front). The clothing worn in a suited laboratory will depend on the operator's preference. Within both laboratory types, the only personal item that can be worn is glasses knowing that on exit they must be washed in the personal shower with the worker. On exit of the laboratory, the clothing will be removed and either disposed of via incineration or sterilised using an autoclave, if reusable.

Gloves

The main interface between the worker and the infectious material being handled in a BSL-4 facility is either gauntlets in a cabinet line laboratory or gloves on a positive pressure suit. Before entering the laboratory, the worker will always put on a set of personal gloves. The gloves attached to positive pressure suits will be made of neoprene or heavy duty household cleaning gloves, where the gauntlets on the cabinet line are generally made of rubber, although other

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materials with better disinfectant compatibility are now available. Therefore, in each laboratory there are two layers of protections between the potential contamination and the worker's hands.

Biological laboratory gloves are usually manufactured from either latex or nitrile and are useful for a secondary barrier if used correctly (Mansdorf, 1987). Training must still be given to the worker in good laboratory practice as any contamination on the exterior of the gloves can still be transferred to other surfaces or the worker's face with poor practices similar to if no gloves were worn at all.

Gloves can be affected by the disinfectants used for decontaminating a laboratory, leading to permeation and penetration of the gloves by the infectious agent. A number of studies have been undertaken to identify the chemical agents that can permeate gloves, and European standards have been produced e.g. BS EN 374-2:2014 Protective gloves against dangerous chemicals and microorganisms, determination of resistance to penetration. Alcohols can penetrate a range of glove materials, one study showed that alcohol was detected within the gloves tested after 10 minutes exposure (latex, nitrile, and a synthetic polymer) (Baumann et al., 2000).

Perhaps one of the major criteria for selection of gloves is worker dexterity. Different materials can have an effect on the dexterity of the worker. In a comparison between latex and nitrile gloves there was a slight decrease in fine dexterity movements when workers used nitrile gloves, but during gross dexterity testing no difference was detected (Sawyer and Bennett, 2006). The dexterity of the worker is further decreased when a secondary layer of glove is worn (increasingly so with the thickness of the second layer, i.e. rubber gauntlets).

These points show that there are a number of options for use for glove materials in the facility, for both primary and secondary barriers. Careful consideration needs to be given as to what processes will be undertaken and then the most appropriate gloves can be chosen for this process. For example, if a chemical cleaning is used, then, the gloves material will need to be tested against the chemical to determine if they are compatible. Whilst a material might provide excellent dexterity, if they are prone to breakage or become easily permeable, then an alternative option might need to be sorted that decreases dexterity but provides more protection.

For the removal of the samples from the Earth return capsule (ERC), workers could wear positive pressure suits to protect themselves from any sample contamination if there had been a non-nominal landing and ERC containment failure, since cleanliness is less of an issue.

4. Robotics vs. human

Robots needed

In the case of curation activities of restricted samples, both containment and cleanliness are required. Three possible methods to simultaneously maintain both requirements were presented in Space Studies Board (2002) and in Rummel et al. (2002) (figure 18).

Knowing that conventional isolators are prone to leakage and that both principles, of "protecting the outside from the inside" using negative pressure and "protecting the inside from the outside" using positive pressure are not usually used together in one place, two main solutions (that we are aware of) are presented, a "double-walled glovebox" (Beaty et al., 2009; "FLAD team project") and a DWI system (e.g. Vrublevskis et al., 2016).

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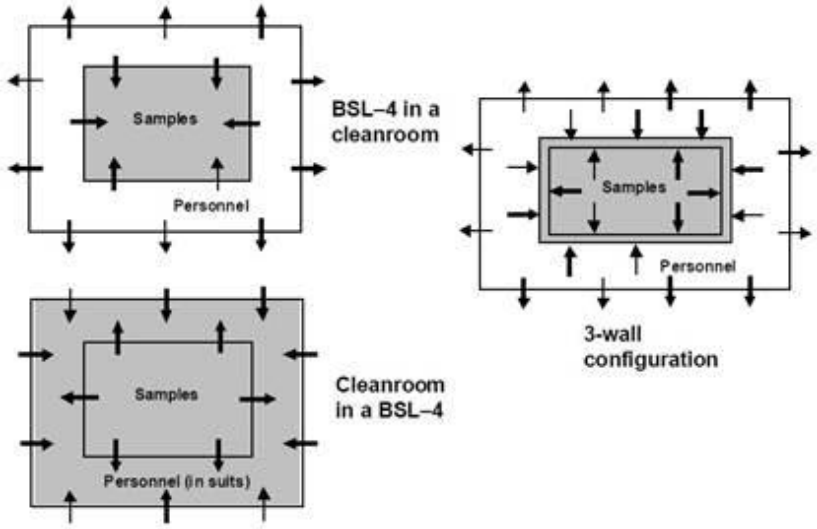

Figure 18. Different options to simultaneously maintain both containment and cleanliness *(modified from Space Studies Board, 2002). Arrows show gas flow (via leakage) caused by pressure differentials in the spaces shown.*

The "double-walled glovebox" consist of a glovebox linked to a double-walled Class III Biological Safety Cabinet with reduced pressure between the walls (figure 19). In Beaty et al. (2009) it is presented as a concept with a need of more work to be conducted before to be validated. Recently, in 2016, a somewhat more detailed concept was presented by J.S. Ellis; All the details can be seen on pages 27 to 31 of the presentation that was given in the framework of the WP3 meeting by Ellis, see here: http://www.euro-cares.eu/files/WP3_Vienna/Presentations/Ellis_EUROCARES_WP3_2016_PRESENTATION.pdf.

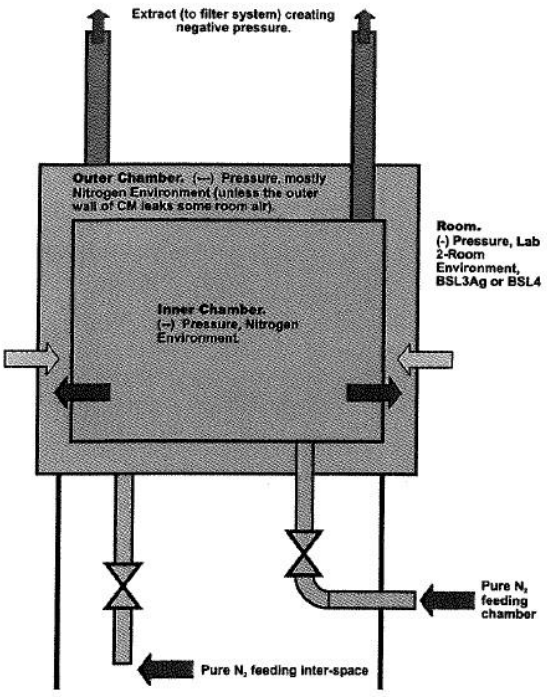

Figure 19. Conceptual double-walled Class III Biological Safety Cabinet *(Beaty et al., 2009)*

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Even this concept is interesting, it is not only very challenging, but the gloves cannot always guarantee the "double walls" principle (i.e. the biocontainment requirements are not adhered) and contaminations issues due to the use of gloves for example would have to be seriously considered.

The DWI system is based on the principle that containment and cleanliness is maintained by the pressure regime, using filtered dry inert gas (figure 20). With this "box within box" principle, the only way samples can be handled is with remote manipulation and thus the use of robotic systems is mandatory. For this reason, the DWI must be capable of housing a robotic manipulation system (see previous section on the different types of robotic systems that were suggested for unrestricted samples and associated discussion) and interfacing with a range of analytical instrumentation. Interfaces need to be available to pass the samples into and out of the isolator. The DWI system does not require high airflows, what is important especially in case of fragile, dust (like), samples that would possibly be manipulated within this system (i.e. we do not want (parts of) the sample to end-up in the HEPA filters).

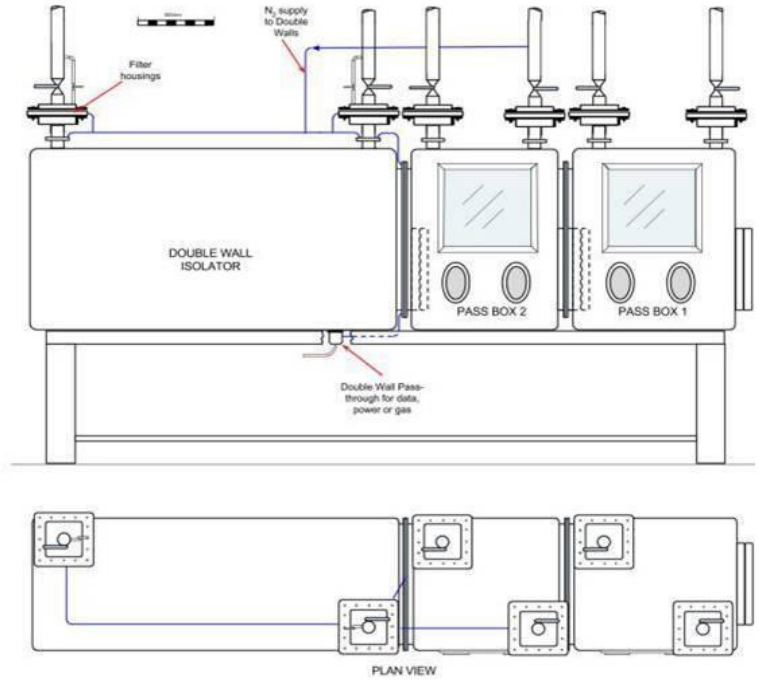

Figure 20. DWI preliminary concept design *from Vrublevskis et al. (2016), More details can be seen in the presentation that was given in the framework of the WP3 meeting by Vrublevskis et al., see here: http://euro-cares.eu/files/WP3_Vienna/Presentations/Vrublevskis_EUROCARES_WP3_2016_WIsystems_PRESENTATION.pdf.*

Research works are currently in progress on this type of DWI system but for the moment it seems to be the only viable method that can be used for most of the SEC and PE. For further examination, later stage of LD and BAP, where cleanliness of the samples is not an issue anymore, a MS3 cabinet commonly used in BSL-4 could then be used.

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Current usage of robotics in contained environment

The use of robotic systems to handle pathogenic agents has been proposed as a way to increase the safety of BSL-4 facilities by reducing potential operator exposure. Robotic systems are widely used in microbiology laboratories (for diagnostic procedures) and in biotechnology/pharmaceuticals (for high throughput screening of antimicrobial compounds). However, due to high capital costs and economics they are only used when the sample throughput is very high. Because of the low incidence of highly pathogenic agents within humans and the additional capital burden of containment measures, and knowing that the conducted work is rather individual, robotic systems have until now not been used to any extent at high containment. Nevertheless, robotic systems have been considered for use in BSL-4 facilities as it would allow to separate any operator from the process. In that respect, a system is being developed in a European laboratory in which antiviral compounds screening is carried out using a robotic process line within a metal isolator. This device is currently being evaluated at BSL-2 but has been designed to operate at BSL-4 if required. For use in high containment systems any robotic system will have to withstand liquid and gaseous disinfection to prevent cross contamination of samples and allow servicing and maintenance.

Usage of robotics in clean and contained environment

A few studies on handling and (remote) (micro-)manipulation systems for restricted samples have been completed or are currently in progress, such as for example Stewart (2010), Nelson and Mani (2011), and Vrublevskis et al. (2016). However, on the basis of these studies, no concrete system was yet produced and tested.

A number of studies on facilities to receive, contain and curate restricted samples, called for the use of robotics. An example is in Beaty et al. (2009) where robots are either used for the entire spectrum of tasks to be conducted within the SRF, such as for the preparation, analyse, transfer of the samples, etc. or for only a subset of these tasks. As already mentioned in the case of the unrestricted samples, the use of robotic systems has direct implications on the concept of the facility, and, thus, the extent of their usage, which is mandatory in the case of restricted samples, should be properly considered already in the first steps of the concept design.

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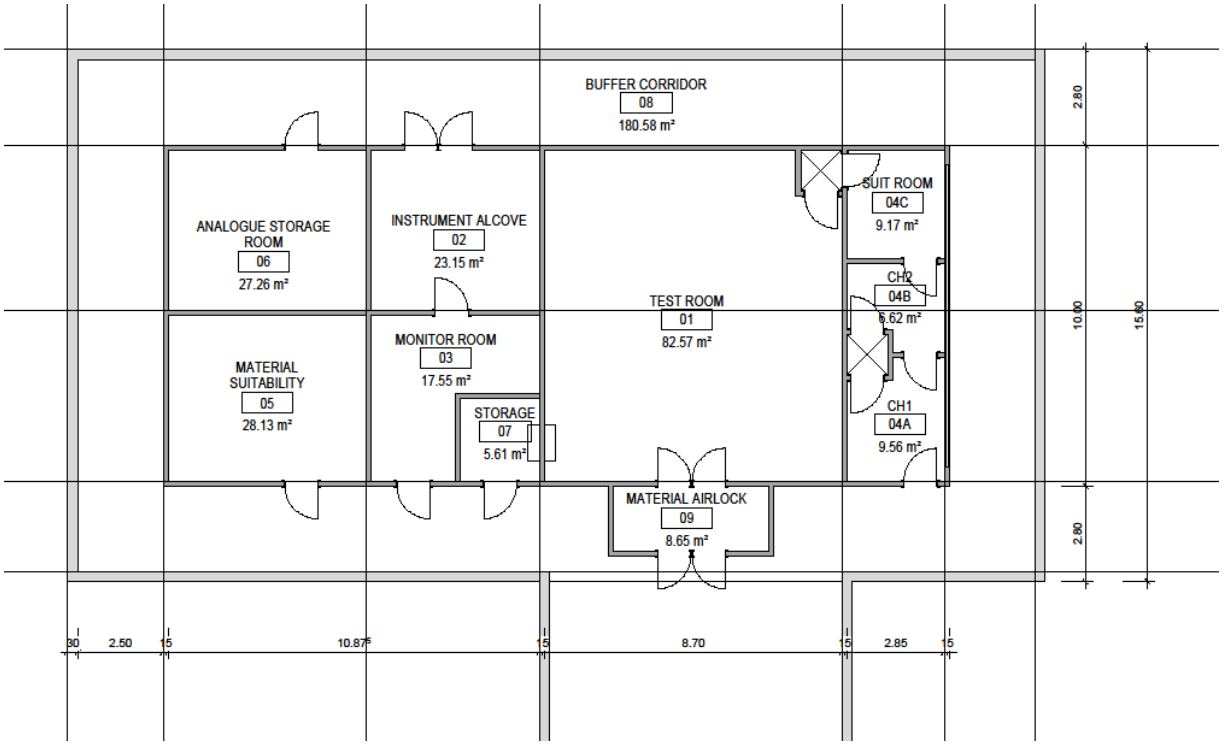
X. APPENDIX



Analogue/Mock-Up Facility function layout.

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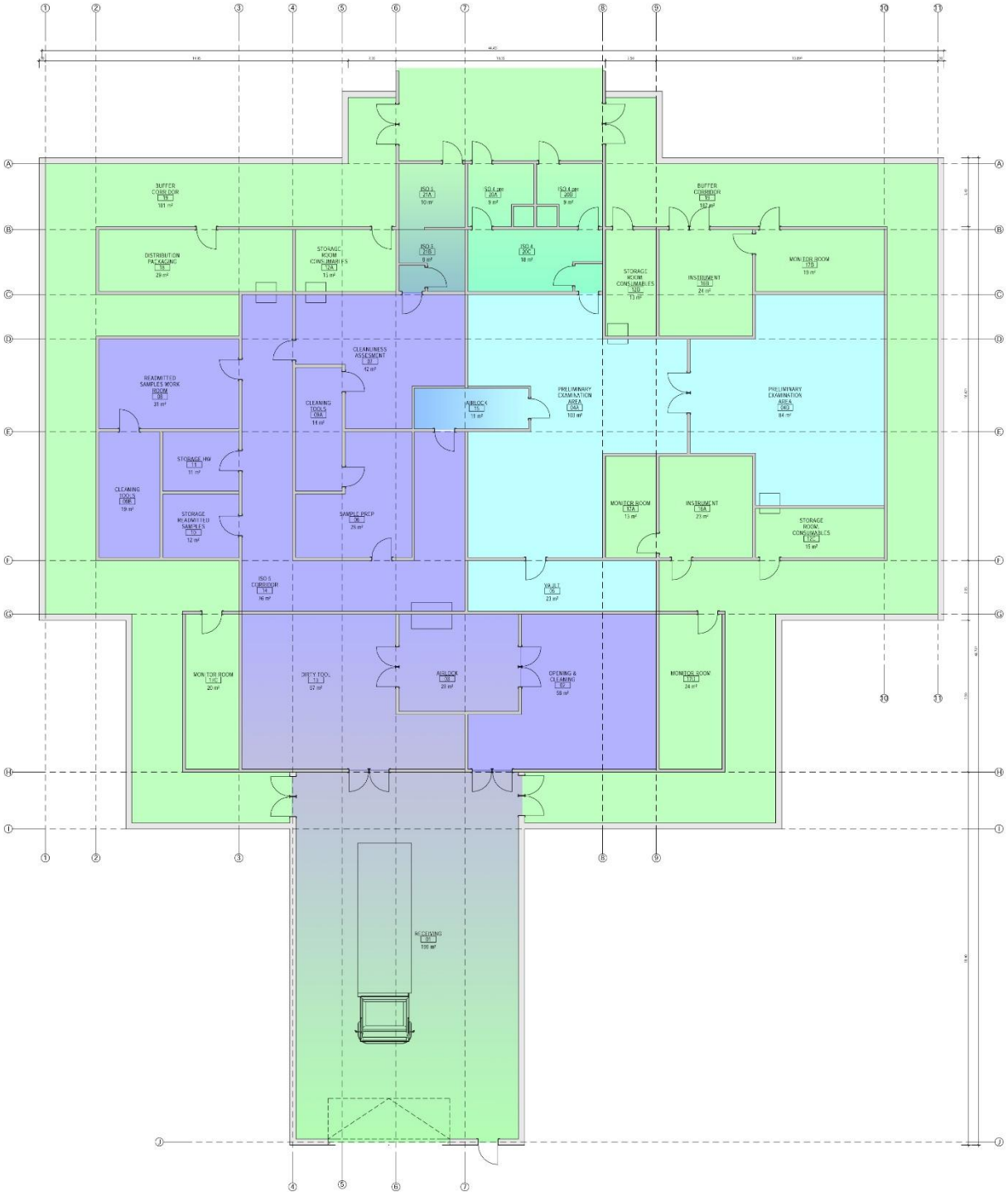

Unrestricted SRF and SCF functional layout. Colours indicate the levels of cleanliness from green (ambient) to light blue (high level of cleanliness).

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Restricted SRF and SCF functional layout. Green indicates areas that are not contained. Pink indicates the contained areas where work is conducted using DWIs or MSC3. Orange indicates areas where a suit is necessary.

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