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再生医学与健康創新中心
Centre for Regenerative Medicine and Health
Hong Kong Institute of Science & Innovation, Chinese Academy of Sciences

Standard Operating Procedure *for*
General Good Safety Practices in Clean Zone

DOUCMENT PARTICULARS	
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Authorized by: **Name/ Title/ Signature**	**Prof. Pan Guangjin** **Director of CRMH**

General Good Safety Practices in Clean Zone

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01	09 Jan 2023	01 Feb 2023	01 Aug 2023	New SOP

General Good Safety Practices in Clean Zone

Table of Contents

A) Objectives

This document describes the general good safety practices and administrative procedures used by *Centre for Regenerative Medicine and Health, Hong Kong Institute of Science & Innovation, Chinese Academy of Sciences Limited* (refer to CRMH below), staff, and students to handle cell cultures in clean zone.

B) Scope

The documents applies to all personnel entering and working in the clean zone. Other safety concerns such as cryogenic, fire, and electrical safety are not included in this document.

C) Facility Covered

Clean zones in CRMH, 5/F, 15 Science Park West Avenue, Hong Kong Science Park, Pak Shek Kok, Hong Kong

D) Responsibilities:

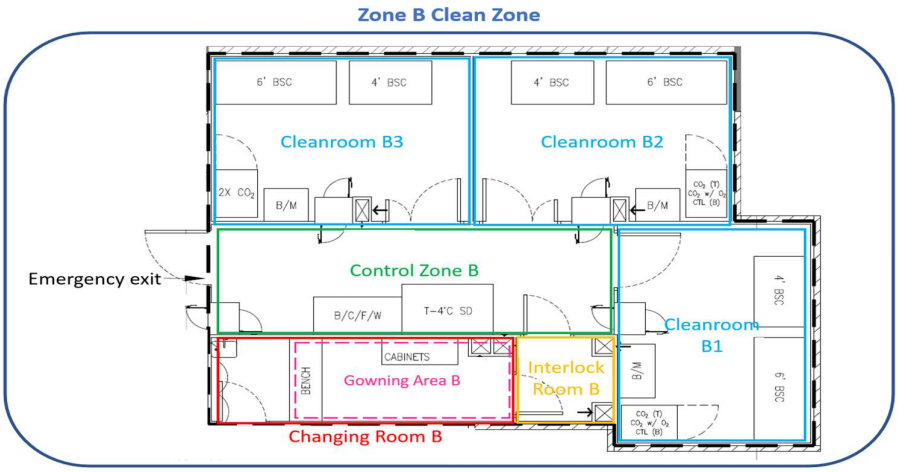
1. CRMH Safety Committee oversees the execution and reviews the SOPs from time to time. When the experiment may impact the general safety to the Centre, CRMH Safety Committee has the final decision if that experiment could be conducted in the Centre.
2. F&OC and team managers (or their delegates) implements the SOPs approved by CRMH Safety Committee.
3. Every member working in the clean zone should adhere to the established clean room SOPs diligently, share the appointed laboratory duties, and consider the impact of every action taken in the laboratory.

E) References:

1. International Organisation for Standardisation. *Cleanrooms and associated controlled environments – Part 5: Operations*. ISO 14644-5: 2004, 2004.
2. Health and Safety Executive. *The SACGM compendium of guidance.* 2007.
3. U.S. Department of Health and Human Services. *Biosafety in Microbiological and Biomedical Laboratories, 6th Ed.* 2020.

F) Nomenclature & Definition:

1. Names of rooms/areas of a typical clean zone in CRMH:



Floor plan of a typical Clean Zone in CRMH.

2. Biosafety Level 2 (BSL-2)

		Examples
Biosafety Level 1 (BSL-1)	- Appropriate for defined and characterized strains of biological agents - Not known to cause disease in immunocompetent adult humans	Lactobacillus acidophilus, Escherichia coli K12
Biosafety Level 2 (BSL-2)	- Appropriate for handling moderate-risk agents that cause human disease of varying severity by ingestion/through percutaneous or mucous membrane exposure - Agents may cause infection, but effective treatment and preventive measures are available	Adenovirus, Lentivirus, pathogenic strains of staphylococcus
Biosafety Level 3 (BSL-3)	- Appropriate for agents with a known potential for aerosol transmission - Agents may cause serious and potentially lethal infections, and are indigenous or exotic in origin	Clostridium botulinum, Dengue virus, SARS-Coronavirus
Biosafety Level 4 (BSL-4)	- Exotic agents that has a high individual risk or life-threatening disease by infectious aerosols - No treatment is available	Ebola virus, herpes simiae virus

The above risk criteria are used by the US Centers for Disease Control and Prevention to define the four levels of biosafety.

G) Procedures

1. *Training*

1.1 Every research personnel working in the laboratory should have received BSL-2 laboratory by F&OC and team managers (or designated person assigned by Principal Investigator), and have shown necessary skills to comply with the guidelines and work in BSL-2 laboratory.

1.2 Research personnel should sign the CRMH Training Log (Appendix 1) under the witness of F&OC or team managers to acknowledge that they have received the required trainings and the copies of the SOPs.

1.3 Research personnel should make sure that they have completed the trainings required by F&OC and the team manager. Type of training can be referred to the training checklist (Appendix 2).

1.4 F&OC, team managers, and the research personnel should keep all the training records until that research personnel has left the CRMH laboratory for > 1 year.

2. *Security & Access To The Clean Zone*

2.1. Person who enter the clean zone must have the permission of the team manager and F&OC.

2.2. The team manager must enforce the rules that control access to the clean zone.

2.3. Approval from team manager and notification to F&OC is required in advance for conducting experiment during non-office hours.

3. *Items Storage In The Clean Zone*

3.1 Inventory

3.1.1 Dedicated area(s) and/ or box(es) is assigned for each research personnel for storage inside cleanroom.

3.1.2 It is recommended that the team manager shall have an inventory list of chemicals and reagents inside the cleanroom. The stock-taking shall be performed periodically, and the inventory list shall be updated timely.

4. *Risk assessment*

4.1 The Risk Assessment Sheet (Appendix 3) should be completed by the research personnel and approved by the team manager prior to working on a new project. Do not start working prior to approval of the team manager.

4.2 Copy of the signed Risk Assessment Sheet must be sent to F&OC for retention.

4.3 When there is a concern on the general safety to the Centre, CRMH safety committee will discuss if the experiment could be conducted in the Centre.

4.4 The risks of the approved projects shall be reviewed annually.

4.5 The research personnel has to update the team manager timely when there is a change in the research direction of the project. Re-assessment of the

potential risks and re-approval for the commencement of the project before the annual review if necessary.

4.6 **When the experiment involves using lentivirus/ adenovirus/ adeno-associated virus, a separate Risk Assessment Sheet (Appendix 3) for handling these viruses has to be filled in.**

5. General safety practices

5.1 Research personnel should make sure the following is readily available before entering and working in the control zone.

5.2 PPE should be provided.

5.3 Eye wash bottles and first aid kit should be readily available.

5.4 Chemical and biological spill kits should be in place.

Figure 1 Biological & Chemical spill kits

5.5 The log sheet of the safety kits including eye wash bottles, first aid kit, and spill kits must be documented timely. Research personnel has to notify team managers and F&OC when these safety kits are going to out-of-stock. The stock of these safety kits must be replenished timely.

5.6 The expiry dates for spill kits, eyewash bottles, and first aid kits should be checked yearly by F&OC.

5.7 Personnel who enter the clean zone must always wear the suitable PPE.

5.8 Do not enter the clean zone when feeling unwell.

5.9 Protective spectacles are recommended for people wearing contact lenses or without glasses.

5.10 Perform all procedures to minimise the creation of splashes.

5.11 No bare parts of the body should be exposed.

5.12 Mobile phones should be put into a specific plastic bag available in gowning area.

5.13 Open wounds should be covered with a suitable band-aid.

5.14 Eating, drinking, smoking, handling contact lenses, and applying cosmetics are not permitted inside the clean zone and open laboratory.

5.15 Mouth pipetting is not permitted.

5.16 An open flame is not allowed unless approval from the team manager and F&OC is obtained.

5.17 Laboratory personnel must display an adequate level of personal hygiene.

5.18 Laboratory personnel must follow and uphold the established SOPs diligently.

5.19 SOPs shall be made readily available on the iPad inside the clean room.

5.20 Materials without labelled name may be discarded without further notice.

5.21 Research personnel must immediately notify the team manager and F&OC in case of an accident.

6. Biological safety

6.1 A universal biohazard symbol must be present at the entrance of the clean zone, and should include:

6.1.1 Clearly stated “Biosafety Level 2”;

6.1.2 Names and contacts of Principal investigator and team manager;

6.1.3 Names and contacts for emergency.

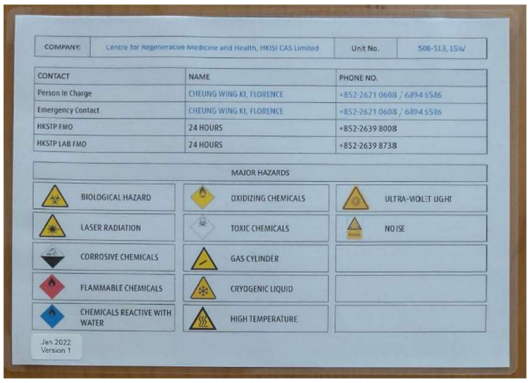


Figure 2 Sample of Biological Hazard Label

6.2 Wash hand thoroughly before leaving the clean zone

6.3 All technical procedures should be performed in a way that minimizes the formation of biohazardous aerosol and droplets. Procedures which have a risk of aerosolization should be conducted in Biological Safety Cabinet (BSC).

6.4 Work surface must be decontaminated using appropriate disinfectant after any biohazardous spills, and before and after using that work surface.

6.5 Maintenances of the BSC, incubator, centrifuges, passbox, freezer and refrigerator against biohazardous contamination can be referred to “SOP for maintenance of clean zone”.

6.6 Risk assessment against biological agents which would be used in clean zone must be completed prior to the commencement of the experiment in clean zone.

6.7 Biological waste must be segregated according to the physical nature, i.e., liquid or solid. After being kept temporarily in the designated area of the clean room, the waste will be transferred to the designated area of the open laboratory, treated, and disposed according to the “SOP for Waste Disposal”.

6.8 Biological spills shall be dealt with according to the “SOP for Spills and Exposure”.

6.9 The UV lights for the clean zone should be turned on for 30 mins in the morning after taking out the wastes, and at the end of the shift.

6.10 Make sure no person is staying in the clean zone prior to turning on the UV lights.

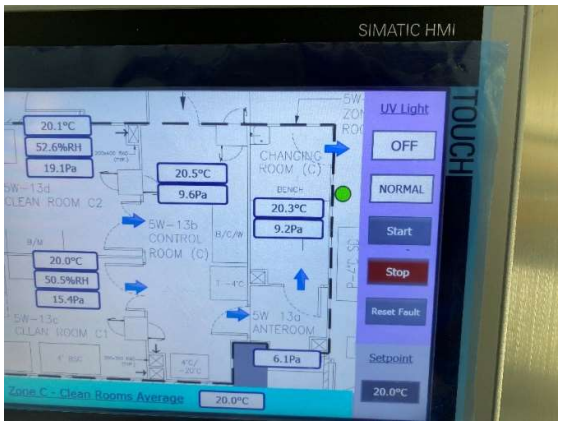


Figure 3 Location of the UV light on the touch screen

7. Chemical safety

7.1 The appropriate PPE must be equipped when handling all chemicals.

7.2 All chemicals must be clearly labelled, and the inventory record of the chemicals shall be updated timely.

7.3 Flammable, toxic, corrosive, and other hazardous materials must be handled in a fume hood outside of the clean zone unless prior approval is obtained from team manager. All these materials shall not be stored inside the clean zone.

7.4 Pour more concentrated solutions into a less concentrated solution to avoid vigorous exothermic reactions.

7.5 Tighten caps on containers before transporting chemicals, and use a compatible secondary container when transporting chemicals.

7.6 Chemical waste should be transferred to the designated area in the open laboratory according to the “SOP for Waste Disposal” and must be disposed of according to “The Waste Disposal (Chemical Waste) (General) Regulation (Cap. 354C)” set out by the Government of Hong Kong SAR.

7.7 Chemical spills shall be dealt with according to the “SOP for Spills and Exposure”.

H) Accident & Incident Reporting

1. Research personnel shall alert team manager and F&OC staff verbally when the situation allows.
2. After an accident or incident, research personnel (either the injured in an accident or the witness of an incident) are required to complete the Accident & Incident Report Form (Appendix 4) **within 48 hours of accident or incident**.

3. Team manager shall assist the research personnel to complete the Accident & Incident Report Form and send to F&OC. For serious accident/ incident, the Accident/ Incident Report Form will also be sent to the Director and Deputy Director of the Centre.
4. Finally, F&OC will send the scanned copy of the completed form to SHE Office of HKSTP by email she_office@hksto.org **within 72 hours of accident or incident**.
5. In addition to the reporting of accidents or incidents to HKSTP by completion of the Accident & Incident Report Form (Appendix 4), CRMH are required to inform the Labour Department of any serious accidents in accordance with local legislations, i.e. the Occupational Safety and Health Ordinance (Cap. 509) and Employees' Compensation Ordinance (Cap. 282).
6. Details of the Accident and Incident Reporting Procedures can be referred to the Section B02 of the HKSTP SHE Handbook (Part II)- Laboratory & Research Safety Requirements.

I) Abbreviations:

1. BSL-2: Biosafety Level 2
2. BSC: Biological Safety Cabinet
3. CRMH: Centre for Regenerative Medicine and Health, Hong Kong Institute of Science & Innovation, Chinese Academy of Sciences Limited
4. F&OC: Facility and Operations Compliance Department
5. HKSTP: The Hong Kong Science & Technology Parks Corporation
6. PI: Principal Investigator
7. PPE: Personal Protective Equipment
8. SOP: Standard Operation Procedure

J) Appendixes

Appendix 1: CRMH Training Log Template

Appendix 2: Training Checklist

Appendix 3: Risk Assessment Sheet

Appendix 4: HKSTP Accident & Incident Report Form

Appendix 1

CRMH Training Log

Training:

Date of Training	Type of Training*	Research Team (Rp1/ Rp2/ Rp3)	Name of Research Personnel	Signature of the Research Personnel	Name and Affiliation of Trainer(s)

*** Type of Training: F** – Face-to-Face; **V** – Video; **Z** - Zoom; **Other (please specify)**

Training checklist

		✓ when completed
1.	**Entrance procedures**	
	Approval to use the cleanroom	
	System check such as Temperature, Humidity, Pressure, UV	
	CRMH-SOP-002: SOP for Clean Zone Entry & Exit	
	CRMH-SOP-004: SOP Gowning and De-gowning in Clean Zone	
	Laboratory setting with explanation of interlock door systems and pressure changes	
2.	**Clean zone practices**	
	CRMH-SOP-001: SOP for General Good Safety Practices in Clean Zone	
3.	**Handling of supplies/equipment**	
	CRMH-SOP-003: SOP for Material Entry & Exit of Clean Zone	
	Packaging and labelling of materials	
	Storage and Inventory maintenance of self-owned materials	
	Use of equipment in clean room	
	CRMH-SOP-008: Adenvovirus/ Adeno-associated virus/ Lentivirus Handling Safety and Risk Management in Clean Zone	
4.	**Communication inside the clean room**	
5.	**Emergency procedures**	
	Emergency procedures and locations of first aid boxes and eye wash bottles	
	CRMH-CR-SOP-007: SOP for Spills and Exposure in Clean Zone	
	Alarm for other mechanical systems failures	
	Accident/ Incident reporting	
6.	**Waste disposal and housekeeping**	
	CRMH-CR-SOP-005: SOP for the Collection & Disposal of Waste in Clean Zone	
	CRMH-CR-SOP-006: SOP for Maintenance of Clean Zone	

Risk Assessment Sheet

Notes:

(i) This list is to be completed by the research personnel and be approved by the team manager prior to working on a new project.

Section to be completed by team manager

Part I - General Information	
Name of PI	
Project Title	
Biosafety Level Required	
Brief summary of project (Max. 250 words)	
Procedures to be carried out **(e.g. cell culture, centrifugation, disposal etc.)**	

Part II – Chemicals/Dangerous Goods/Drugs/Compressed gas/ Nanoparticles **(If "Yes", please answer the following questions. If "No", please go to Part III)**	**Yes**	**No**
Will you handle any hazardous chemicals/dangerous goods/drugs in clean zone? (If Yes, please provide a list of the hazardous chemicals/dangerous goods/drugs)		
Is a dangerous goods licence required? (If Yes, please provide the license to F&OC)		
Any special storage condition is needed for the chemicals in clean zone?		

Risk Assessment Sheet

Will you use any compressed gas cylinders in clean zone?		
Do you need to handle any nanomaterials in clean zone?		
Will you generate chemical waste in clean zone? **(Definition of chemical waste: chemicals that have not been in touch with biological agents)**		

Part III – Biological Agents		
What is the biosafety level required? **Biosafety Level _____**		
What biological materials will be used in the project?	**Yes**	**No**
Bacteria (e.g. E.Coli, HB101) **If yes, please state all agents to be used:** **_____**		
Viruses or viral vectors (e.g. Adenovirus, Adeno-associated virus, Lentivirus) **If yes, please state all agents to be used:** **_____**		
Fungi, parasites **If yes, please state all agents to be used:** **_____**		
Human cell lines **If yes, please state all agents to be used:** **_____**		
Animal cell lines **If yes, please state all agents to be used:** **_____**		
Clinical samples **If yes, please state all agents to be used:** **_____** **If identifiable human material is used, please attach the supporting document as indicated in the HKSTP Ethics Guide for Human Research (point 7c) as applicable.**		

Risk Assessment Sheet

***Materials = Biological materials including but not limited to tissues, organs, blood, plasma, skin, serum, DNA, RNA, proteins, cells, hair, nail clippings, urine, saliva, or other body fluids**		
Others **If yes, please state all agents to be used:** **_____**		
Will you generate clinical waste?		
Are the prophylaxis measures performed? (e.g. vaccination if provided)		
Has the risk assessment for virus vector work carried out? **If yes, please attach the MSDS of the virus, protocol and the assessment record.**		

□ I declare that I have the related skill set and knowledge to conduct cell culture/ experiment as described in the Project Summary in the CRMH clean zone.

□ I adhere to the established clean room SOPs diligently, share the appointed laboratory duties, and consider the impact of every action taken in the laboratory.

_____ _____

Signature of Applicant Date

Risk Assessment Sheet

Section to be completed by team manager

Part IV – Safety Provisions	**Yes**	**No**
Is the biosafety level of the clean zone suitable to the user to conduct experiment described in the Project Summary in our clean zone?		
Are the SOPs readily available for applicant?		
Does the applicant pass the written test about the clean room SOPs?		
Does the applicant pass the practical test (e.g., Gown/ De-Gowning) about the clean room SOPs?		
Does the applicant understand the CRMH-SOP-008 and the risk in the association of adenovirus/ adeno-associated virus/ lentivirous if these virus will be used in the experiment?		
Does the applicant understand the emergency procedures?		
Should the application/ project be discussed further in the Meeting of CRMH Safety Committee?		

□ I have discussed this application with PI. We **approve** the applicant to conduct cell culture/ experiment described in the Project Summary in my team's clean zone.

□ I have discussed this application with PI. We **disapprove** the applicant to conduct cell culture/ experiment described in the Project Summary in my team's clean zone.

(Note: Record of this application is not required to sent to F&OC)

□ I have discussed this application with PI. We have concern about the safety of the experiment to the Centre. **Further discussion** is needed during the **meeting of CRMH Safety Committee**.

_____ _____

Signature of Team Manager Date

HKSTP	**Safety, Health and Environment Office** Accident & Incident Report Form	SHE Form L02 (Official use only) Reference No.:

Note: This report form should be completed and sent to the Safety, Health & Environment (SHE) Office of HKSTP within 72 hours of the accident or incident. The information provided herein will be used for investigation and compiling accident statistics.
In case of work-related accident to employee resulting in death or partial incapacity, the concerned unit of HKSTP or the client should fill in the relevant form provided by the Labor Department of Hong Kong and return it in duplicate to the Commissioner for Labor within the statutory required period.

1. Accident / Incident Information		
Date:	Time:	Location:
Type of Area: □ Office □ Laboratory / Workshop □ Others (Please specify):		
2. Nature of Accident / Incident		
□ Personal injury	□ Fire / Explosion	□ Spillage of hazardous substances
□ Flooding	□ Unpleasant smell	□ Damage to property / equipment
□ Others (Please specify):		
3. Personal Details (For the injured or person concerned)		
Name:		Sex: □ Male □ Female
Post Title:		Phone No.:
Division / Company Name:		
Company Address:		
Nature of Injury: □ Amputation □ Burn □ Contusion □ Fracture □ Laceration □ Sprain □ Others (Please specify):		
Part of Body Injured: □ Hand □ Leg □ Head / Face □ Eye □ Others (Please specify):		
The injured received medical treatment: □ Yes □ No		
The injured was hospitalized: □ Yes □ No		
The injured took sick leave: □ Yes (No. of days:) □ No		
4. Accident / Incident Reported By		
Name:		Signature:
Post Title:		Date:
5. Accident / Incident Report Endorsed By		
Name:		Signature:
Post Title:		Date:

HKSTP	**Safety, Health and Environment Office** Accident & Incident Report Form	SHE Form L02 (Official use only) Reference No.:

Please fill in details about the accident / incident in the next page.

6. Brief Description of Accident / Incident
7. Causes of Accident / Incident
8. Recommendation for Prevention of Recurrence

For Internal Use by SHE Office of HKSTP	
Further investigation required: ☐ Yes ☐ No	Investigation Report No.:
Accident / Incident Classification Code:	
Accident / Incident Cause Code:	
Remark:	