Agenda for the 17th meeting of the Biosafety Committee of the University of Hong Kong. (A sub-committee of the Safety Health and Environment Committee).

To be held on Thursday, October 20th 2016, 11.00 a.m. Room 412 at Professorial Block, Queen Mary Hospital.

1. Minutes of the 15th meeting of the Biosafety Committee (October 9th 2015)
The minutes of the previous physical meeting of the Biosafety Committee were circulated in March 2016 and members approved them by e-mail. For completeness they are attached as Appendix 1.

2. Matters arising from the minutes of the 15th meeting (action points etc.)
The secretary arranged for the minutes to be uploaded to the safety office website.

3. Agenda of the 16th e-mail based meeting
The agenda of the 16th meeting has been uploaded to the Safety Office website as a record of the matters considered. As all responses were acknowledging receipt of the document and there were no comments on the proceedings this will be the document kept instead of any minutes.

4. Introductory course in biosafety
The next introductory course in biological safety will be held in January 2017. If members are aware of staff or students who might benefit please bring it to their attention. The slides used in a previous session have been uploaded to the Safety Office website and links to the courses files can be found on http://www.safety.hku.hk/homepage/bio.html.

5. Risk assessments and guidance on retrovirus vectors
Over the past few years a number of departments have submitted risk assessments for approval of work with retrovirus vectors on the form RA3 (http://www.safety.hku.hk/homepage/pdf/RA3.doc). A typical form (appendix 2a and my response (appendix 2b) are included as examples of the issues involved. From this and other responses it was clear that the questions could be improved to ensure the applicants better understood the intent of the questions. Consequently an updated RA3 form is included as appendix 2c and as can be seen the modifications are only minor in nature.

In the process of revising the form the secretary reviewed the current guidance on retrovirus vectors and realized that there were a number of links in the document that were out of date along with some new information that should be incorporated. An updated version of the guidance is included as appendix 2d (The version supplied is one that tracks the changes made to the original document in order for members to be able to follow what information has been updated)

The secretary would welcome comment on the document particularly if members feel other material should be included or the guidance structured in a different way.

6. Biosafety Policy update

6.1 Referencing other committee documents in the biosafety policy

A number of the recent documents the committee has approved such as "The Guidance on Good Microbiological Practice" should be mentioned in the appropriate section of the Biosafety policy e.g. Section 5.3 is on good microbiological practice. Consequently the secretary has updated the relevant sections and included the updated document as appendix 3.

i) Reference to the good microbiological practice has been included in section 5.3
ii) Reference to the risk assessment document has been added to section 3.4
iii) Reference has been made to the handling of clinical samples document in section 5.10.
iv) Reference to the Biosafety level 2 document has been made in section 5.4

6.2 Update of Section 5.4

Section 5.4 of the current policy was an abbreviation of a longer section in a previous version and on reflection the section is somewhat confused. A much clearer explanation of risk groups and levels of containment is found in the risk assessment document approved several years ago. The secretary proposes to replace the current section 5.4 with the information in the risk assessment document (with a few simple edits to reduce its length). *Members are asked for comments, approval and advice on whether the updated policy would need to be approved by SHEC.*

7. Biosafety basics

The secretary is occasionally asked about the need for import or export licenses. *Do members think it would be of value to summarize/consolidate the import export requirements for biological materials in one document? Are there other basic biosafety areas that members feel would benefit from better documentation?*

7.1 The secretary now has 5 presentations with handouts that cover biosafety basics. In order not to make this meeting too long they are not presented here but will be at the next meeting. *Have members any experience of putting courses online? What are their experiences of the university lecture recording system? Do members use any of the other centrally provided systems?*

8. Hazard/Risk group classification updates (For information)

In many countries, infectious agents are categorized in risk groups based on their relative risk. Depending on the country and/or organization, this classification system might take into consideration the pathogenicity of the organism, the mode of transmission and host range, the availability of effective preventive measures (e.g., vaccines), the availability of effective treatment (e.g., antibiotics.) and other factors such as local considerations.

8.1 UK Approved list

The UK regulators (HSE) have published a revised version of the Third Edition of the Approved List of Biological Agents following advice from the Advisory Committee for Dangerous Pathogens (ACDP). The Approved List is a legally binding standard in the

UK and classifies biological agents hazardous to humans into hazard groups (HG). The revisions to the Approved List include a re-classification of Zika virus (reclassified from HG3 to HG2), inclusion of Middle East Respiratory Syndrome coronavirus (HG3) and a new classification for type 2 poliovirus (HG3). When the type 2 component is withdrawn from the trivalent poliovirus vaccine, attenuated strains of type 2 poliovirus will also be classified as HG3. Types 1 and 3 polio virus will remain as HG2. See http://www.hse.gov.uk/pubns/misc208.pdf for the full list.

8.2 Risk Group Database App

ABSA International (the new name for the American Biosafety Association) have developed an extensive risk group database (https://my.absa.org/tiki-index.php?page=Riskgroups) that includes information on the risk groups of infectious agents as assigned by various countries and whether they are human or animal pathogens or simply apathogenic. To increase the utility of the information they have created a free App available for Apple and Android devices which allows access the ABSA Risk Group Database on mobile devices.

9. Follow up on the US Gain of Function moratorium (For Information)

Following on from point 3 of the last meeting and a series of for information points in other meetings the National Science Advisory Board for Biosecurity (NSABB) who oversee gain of function work (GOF) have released a 100+ page Final Report – "**Recommendations for the Evaluation and Oversight of Proposed Gain-of-Function Research**" (May 24, 2016). For the full report please see:- http://osp.od.nih.gov/sites/default/files/NSABB_Final_Report_Recommendations_Evaluation_Oversight_Proposed_Gain_of_Function_Research.pdf. Appendix 4 contains a brief review on the concerns about GOF as a reminder (from point 3 of the last meeting) and the main findings and recommendations of the report.

Part of the report refers to the Risk and Benefit Analysis of Gain-of-Function Research, Final Report from Gryphon Scientific published in April 2016. http://www.gryphonscientific.com/wp-content/uploads/2016/04/Risk-and-Benefit-Analysis-of-Gain-of-Function-Research-Final-Report.pdf

The secretary believes the crucial comment contained in the report on the 1009 page risk benefit analysis is:-

"The report effectively illustrates that the harmful events being modeled are low probability (see Figures 6.2 and 6.4 in Gryphon's report). Only a small fraction of laboratory accidents would result in a loss of containment. Of those, only a small fraction would result in a laboratory acquired infection, and of those, only a fraction would spread throughout the surrounding community (or to the global population). The NSABB recognizes the challenge of analyzing low-probability, high-consequence events for which little data exists and appreciated attempts to make this point clear in the risk benefits analysis."

NSABB also commissioned an ethical analysis of the gain of function research. For the full report see: Selgelid, M., April 2016. http://osp.od.nih.gov/sites/default/files/Gain_of_Function_Research_Ethical_Analysis.pdf.

The implications for HKU are at present unclear, primarily because the authorities have not responded to the recommendations. Currently the only department within HKU that receive funds from NIH/CDC (as far as the secretary is aware) are the School of Public Health and they currently do not use these for GOF studies. The secretary expects there will be more stringent controls including some form of closer oversight on the work that can be carried out with NIH/CDC funding. Whether the arrangements we have put in place for extra scrutiny of this type of study will meet their requirements may be clarified next year with the scheduled visit of CDC to the school of public health.

10. A Note from CDC about the Federal Select Agent Program (For information)
Three federal reviews of the select agent program were released last autumn, each containing recommendations designed to strengthen the federal government's biosafety and security practices and oversight, both through the Federal Select Agent Program and at a broader national level.

Over the past several months, the Federal Select Agent Program has assessed the recommendations and implemented an action plan with appropriate program changes and improvements to address these recommendations. Efforts have focused on four main categories of improvement, the inspection process (both facility inspections and inspection reporting), customer service, incident response, and transparency and public engagement.

The CDC has created a website in order to keep stakeholders updated on the work that is underway at CDC and to inform you of the changes to the program that you will begin to see as these items roll out. The website, now available at http://www.cdc.gov/phpr/dsat/review_progress.htm, is designed to extract and summarize the recommendations relevant to CDC's role within the Federal Select Agent Program, collect them in one place, outline actions that have been identified to address each, and provide an update on progress towards implementation of those recommendations.

11. Proposed reviews of key international Biosafety Advice (For information)

11.1 The WHO Laboratory biosafety manual
The WHO Laboratory biosafety manual (Laboratory biosafety manual, Third edition. Geneva: World Health Organization; 2004 http://www.who.int/csr/resources/publications/biosafety/WHO_CDS_CSR_LYO_2004_11/en/) originally published over 30 years ago has provided practical guidance on biosafety techniques for use in laboratories at all levels. As the third edition was published in 2004 the need for a revision has been discussed by WHO and there is general agreement that a revision should be undertaken. At a 2015 meeting of their biosafety task force recommendations regarding revision of the WHO Laboratory biosafety manual were made and participants emphasized that:

i) Revision to the Manual is a necessity and a priority.
ii) A needs survey would be beneficial in determining how best the Manual can suit the user's requirements.
iii) A guideline or standard for the assessment and validation of containment processes and procedures, including BSL3 facilities, would be useful either within the revision or as a standalone document. As yet the secretary is unaware of any timescale involved with the project or who would carry out the revision.

11.2 Biosafety in Microbiological and Biomedical Laboratories (BMBL) 5th edition
Since publication of the first edition by National Institutes of Health (NIH) and the Centers for Disease Control and Prevention (CDC) in 1984, the Biosafety in Microbiological and Biomedical Laboratories (BMBL) has become the cornerstone of biosafety in laboratories in the United States and in many countries around the world. The BMBL has been revised periodically over the past three decades to refine the guidance it provides based on new knowledge and experiences - allowing it to remain a relevant, valuable, and authoritative reference for the microbiological and biomedical community.

Seven years after the release of the printed BMBL 5th edition, a revision is being considered by the NIH and the CDC. To inform the revision, the agencies have asked the National Academies of Sciences, Engineering, and Medicine to assist in soliciting input from a broad set of stakeholders. This is an invitation for all users of the BMBL to participate in a virtual town hall meeting and share their thoughts on the next revision of this document, particularly which information should be deleted from, modified in, or added to the BMBL sections. Common themes from this forum were discussed in a workshop on May 12, 2016 in Washington, DC at the National Academy of Sciences.

11.3 Revision of Part 3 of the UK Scientific Advisory Committee for Genetic Modification (SACGM) Compendium of Guidance
The SACGM Compendium of Guidance is being revised in a phased manner. The revised Part 3 of the Compendium, which relates to the containment requirements for genetically modified microorganisms, was available for review and comment via HSE's microbiological hazards on-line community. Those interested were asked to provide feedback on the drafted guidance via a feedback form before the end of 2 May 2016.

11.4 Revision of ACDP guidance on 'deliberate work' with biological agents
The new guidelines "Management and operation of microbiological containment laboratories" will replace ACDP's 2001 publication "The management, design and operation of microbiological containment laboratories" and the 2005 publication "Biological agents: managing the risks in laboratories and healthcare premises" except Part 2 "Working in Healthcare" which will remain as a standalone document.
This new publication is intended to provide the benchmark standards for laboratory (deliberate use) work at containments levels 2 and 3 including relevant links to requirements of Specified Animal Pathogens Order(s) and Genetically Modified Organisms (Contained Use) Regulations. In addition to containment standards, the guidance will cover fumigation; sealability; spillage procedures; microbiological safety

cabinets and waste management. It is envisaged that in future this “core document” will be supplemented by electronically linked topic-specific guidance.
The new guidance was consulted on from 2 May 2016 for six weeks via HSE’s microbiological hazards on-line community and publication may well be before the end of 2016.

12. Recent laboratory acquired infections and incidents in the news (for information)

12.1 A Laboratory acquired case of Zika reported in Pittsburgh area
Prior to the current case, there were four reports of laboratory acquired Zika virus infections, although the route of transmission was not clearly established in all cases. The Allegheny County Health Department (ACHD) says a female contracted the virus from a needle stick while working with Zika virus in a laboratory. Her symptoms have resolved and she has been discharged from hospital.

12.2 Mystery of a laboratory acquired HIV infection (edited from Promed mail)
Please note this study was published as an abstract and presented at a conference. These data and conclusions should be considered to be preliminary until published in a peer-reviewed journal.

Italian researchers are trying to unravel a mystery: How did a European laboratory worker become infected with human immunodeficiency virus (HIV) from a non-infectious strain?

"We are looking at a perfect storm of errors," Claudia Alteri, PhD, a researcher at the University of Rome Tor Vergata, told MedPage Today. "We cannot exclude any mode of infection at this time." At the annual Conference on Retroviruses and Opportunistic Infections, she explained that her laboratory was asked to investigate the incident, which did not occur in Italy.

The infected laboratory worker -- whose identity, including sex and age, are being withheld -- only found out about the infection when the person was tested in the process of donating blood and was determined to have an active HIV infection. The worker denied all the known risk factors: no sexual behavior consistent with HIV infection, monogamous sex partner was HIV-negative, no injection or IV drug use, and no history of blood transfusions or invasive medical procedures.

Adding to the mystery, the laboratory worker also said that no laboratory accidents had occurred. The worker did not recall any broken gloves, cell medium splash, percutaneous injury such as a needle stick, or anything else that might have caused an exposure.
Yet, Alteri and her colleagues found, the genetic sequence of the HIV virus in the worker's body was almost identical to an HIV construct that the worker was using in experiments in the Biosafety Level 2 laboratory. That construct was not supposed to be infectious.

The investigators believe that somehow a competent HIV virus from a Biosafety-3 laboratory found its way into the lower-safety level laboratory. That in itself might not have caused the infection, but also present were experiments using the vesicular stomatitis virus (VSV) The laboratory worker was conducting pseudotyping procedures that required plasmid encoding for the G glycoprotein of VSV, Alteri said. VSV can increase virus infectivity 20- to 130-fold, she said.

What happened next is speculation, the researchers said. They think that, somehow, the competent HIV virus was able to share its genes with the non-infective construct, rendering the construct infectious. And that, in turn, became attached to the VSV.

"VSV can infect any cell in the body," said molecular biologist John Coffin, PhD, of Tufts University in Boston. "So it is possible that the virus infected the worker through direct contact or through the lungs if the virus was in an aerosol form," he told MedPage Today. What the researchers do know, Alteri reported in her oral presentation and at a press conference, is:

"HIV-1 contagion occurred in the period when the person was working on HIV-1 pseudoviruses production with defective constructs in a bio-safety 2 laboratory containment." "All those procedures should not have included any infective vector."

"Nevertheless, an infectious HIV-1, NL4.3/JRFL molecular clone, probably present in the laboratory at the time, entered the chain of HIV-1 pseudoviruses that the worker was handling, most likely causing the infection."

What Alteri and her colleagues have not confirmed is when and how the infectious molecular clone entered the pseudoviruses production; what was the mode of contagion since no reported event that might explain what happened has ever been reported or recalled; and if the use of the VSV favored the contagion.

The bottom line, though, is the worker is now HIV-positive and is being treated with antiretroviral therapy. "This is an interesting and disturbing case," Coffin said as he moderated the press conference, "of an individual in an research laboratory who through a series of rather inadvertent accidents became infected with HIV."

He said the episode suggests that, in some laboratories, "there has been a little bit too much familiarity with the use of HIV vectors, which can be very valuable in gene therapy. I think there has been a certain amount of biosafety fatigue in laboratories that needs to be revisited by institutional biosafety committees. These kinds of accidents just shouldn't happen."

Primary Source: Conference on Retroviruses and Opportunistic Infections
Source Reference: Alteri C, et al "HIV -1 laboratory contagion during recombination procedures with defective constructs" CROI 2016; Abstract 18LB, available at: <http://www.croiconference.org/sessions/hiv-1-laboratory-contagion-during-recombination-procedures-defective-constructs>

12.3 Anthrax inactivation and distribution errors (edited from Promed mail)

ANTHRAX - USA (04): LABORATORY ERRORS, GAO INVESTIGATION REPORT
Source: The Virginian Pilot [edited]
<http://pilotonline.com/news/military/local/the-army-mistakenly-shipped-live-anthrax-to-hampton-roads-gao/article_d45608f3-8b58-5372-89f8-2b5fab1e5e81.html>

Potentially deadly live anthrax spores were mistakenly sent to a laboratory in Hampton Roads from an Army facility in Utah, according to a map in a government watchdog report.

The Army has said samples of anthrax that were supposed to have been inactivated were sent to 194 federal, academic and commercial laboratories in every state, 9 countries and 3 U.S. territories. There were a total of 575 shipments of live anthrax delivered to labs from 2004 through 2015, although the Army says no illnesses were reported.

The mistaken shipments were 1st discovered in May 2015, when a private company in Maryland notified the Centers for Disease Control and Prevention that it found live spores in a shipment from the Army that should have contained only dead spores. The company was developing a diagnostic test to identify biological threats. A subsequent investigation found that live spores were mistakenly sent from Utah to 88 primary recipients, who then sent samples to 106 2ary recipients.

The Army has not specified which laboratories received the live samples. But a Government Accountability Office [GAO] report released last week included a map that shows a laboratory in Hampton Roads was one of the primary recipients. The GAO said it could not elaborate on specific sites beyond the map [see map on online link. - Mod.MHJ]. This map from a GAO report shows where anthrax was delivered.

The CDC is prohibited by law from disclosing the names or locations of laboratories that handle anthrax and other deadly toxins. But 122 labs are registered and authorized to work with anthrax in the United States, according to CDC spokesman Jason McDonald.

The strain that was shipped from the Army's Dugway Proving Ground in Utah's western desert was an "extremely harmful" variety that was the same as those sent in letters to 2 U.S. senators and multiple media outlets in a 2001 attack, according to the Army. At that time, 22 people contracted anthrax and 5 of them died. The military works with biological agents to develop countermeasures for U.S. troops.

Yet Army officials said in a news conference in January [2016] that safeguards were in place so that nobody was threatened due to the errant shipments. "At no time were lab technicians, or the American public, at risk based on these inadvertent shipments," said Maj. Gen. Paul Ostrowski, who investigated the mistaken deliveries. Ostrowski noted that technicians who work with anthrax always wear protective equipment, and it was

shipped in a secure manner in a liquid vial. Anthrax is spread by skin contact with infected animal tissue, bites from insects that feed on infected animals, inhalation and ingestion of contaminated undercooked meat. "So again, not aerosol. Anthrax or _Bacillus anthracis_, is mostly placed in an aerosol venue," Ostrowski said.

The GAO report that contains the map showing the anthrax deliveries focused on other incidents where various pathogens weren't inactivated before shipment. The report found 21 instances - 11 more than labs previously reported - between 2003 and 2015. The report also said the actual number could be higher because there's no standardized way for labs to report a problem or a way to easily access databases.

[To read the full GAO 16-42 report quoted above, go to:
<http://www.gao.gov/products/GAO-16-642>.
The report: "High-Containment Laboratories: Improved Oversight of Dangerous Pathogens Needed to Mitigate Risk", GAO-16-642, Published:
Aug 30, 2016. Publicly Released: 21 Sep 2016 is available.

There is a parallel report on mitigating risks: <http://www.gao.gov/products/GAO-16-871T>, "High-Containment Laboratories: Actions Needed to Mitigate Risk of Potential Exposure and Release of Dangerous Pathogens", GAO-16-871T:
Published: Sep 23, 2016. Publicly Released: 22 Sep 2016.

The report covers 21 incidents involving 7 different pathogens and 11 federal laboratories, 5 private laboratories, and 5 academic labs. It lists a series of protocol deficiencies and erratic reporting. And from which NECESSARY stricter regulations are and will be issued on this topic.

13. Dates of next meetings.
The next two Biosafety Committee meetings have been tentatively scheduled for 9th March 2017 and the 19th October 2017. These dates are intended to be flexible and will be confirmed nearer the time with committee members by e-mail.