

BIOBANKING IN TIMES OF COVID-19

Web Conference #1 Risks and Opportunities (April 1, 2020) recording Web Conference #2 Pre-Analytical Processes (April 7, 2020) recording

Disclaimer: These are individual questions coming from the web conference participants. This document serves as a summary of exchanged experiences and does not represent legal guidelines.

All information about the BBMRI.QM web conferences: Biobanking in Times of COVID-19, including recordings and presentations, can be found here: https://www.bbmri-eric.eu/services/bbmriqm-covid

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GENERAL QUESTIONS AND ANSWERS

- Q: Can biobanks around the world be included in the COVID BBMRI-ERIC Directory?
- **A:** Yes, BBMRI-ERIC offers to include biobanks in the Directory see https://directory.bbmri-eric.eu/menu/main/app-molgenis-app-biobank-explorer/biobankexplorer. Please see the presentation of Petr Holub on BBMRI-ERIC website.
- **Q:** A general question: I believe it would also be feasible to look at the functional readout of the genetic information that you have collected. Standardized metabolomic tests could contribute to patient stratification (after positive testing) and thereafter for therapy monitoring (responder/non-responder). If someone is interested, I shall be happy to share information via email!
- A: Contact: bijon.chatterji@biocrates.com
- **Q:** What type of samples are you collecting right now? Since we still don't know what type of studies will be carried out. We are not sure what type of samples to be stored: Whole blood? Plasma? Serum?
- A: See presentation of Lukasz Kozera 7 April 2020 on the BBMRI-ERIC website.
- Q: It would be useful to know how biological samples should be handled safely?
- **A:** In any case handling biological sample is recommended to be carried out as described in the WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y



- **Q:** Are there currently dedicated funds/EU calls for the sampling and the implementation of biobanks with COVID-19 samples?
- **A:** Any information can be given by Francesco Florindi, Please see info at the BBMRI-ERIC website: https://www.bbmri-eric.eu/covid-19
- **Q:** How does BBMRI envision collaborating with Third Countries outside Europe on COVID-19, particularly with countries in Asia, Eastern Europe, and Africa? The GCPA and SIDCER work in these areas and we are aware of a need for collaboration coming from several of these countries. We are also aware of legal and regulatory hurdles, here in Europe and in the respective countries.
- A: BBMRI-ERIC is open for global collaboration.
- **Q:** Any partnerships with any African countries for samples/data since the prevalence of the disease there is low?
- **A:** African biobanks are invited to be included in the Directory see https://directory.bbmrieric.eu/menu/main/app-molgenis-app-biobank-explorer/biobankexplorer. Any collaboration with African biobanks needs to be initiated individually, but is supported where possible by BBMRI-ERIC.
- Q: How will BBMRI work with countries, especially China, that cannot send samples outside their borders?
- **A:** Chinese biobanks are invited to be included in the Directory see https://directory.bbmri-eric.eu/menu/main/app-molgenis-app-biobank-explorer/biobankexplorer Any collaboration with Chinese biobanks needs to be initiated individually, but is supported where possible by BBMRI-ERIC.
- **Q:** What should those of us do who run biobanks in countries where COVID-19 has not really taken hold (yet!)? What should we do to prepare for as biobankers? Please advise.
- **A:** Follow the info given at the web conference on 7 April 2020, and see the WHO guidelines and presentations of Lukasz Kozera and Helmuth Haslacher on the BBMRI-ERIC website.
- **Q:** Could you also please share the links where we could find all the documents related to the safety regulations and the quality of samples and their associated data?
- **A:** See a list of documents https://www.bbmri-eric.eu/services/bbmriqm-covid and https://www.bbmri-eric.eu/services/bbmriqm-covid and https://www.bbmri-eric.eu/services/bbmriqm-covid and https://www.bbmri-eric.eu/services/bbmriqm-covid and https://www.bbmri-eric.eu/services/standardisation/
- Q: I'll like to know whether Brexit will impact UK companies' participation.
- A: UK is a Member of BBMRI-ERIC https://www.bbmri-eric.eu/national-nodes/

CLINICAL ASPECTS AND BIOBANKING

- Q: What about asymptomatic patients in high-risk populations?
- **A:** Their samples might be interesting from the epidemiological point of view. Please stress the fact that we need detailed information concerning symptoms and first of all timing of symptoms. Then associated clinical data are essential. This will be underlined during the presentation on 7 April 2020.
- **Q:** Would it be interesting to know the patient's previous pathologies? Is there a classifier of the severity of the pathology? If so, I find it interesting to incorporate these data: previous pathologies and severity.
- **A:** Information on existing diseases will be very important when it comes to data analysis. Disease coding according to ICD-10-CM. COVID-19 codes can be found CD-10-CM Official Coding Guidelines for COVID-19 April 1, 2020 -September 30, 2020 at the <u>CDC</u>.
- **Q:** How do we have to manage samples from patients from whom we do not know the COVID status; do we need specific caution concerning frozen tissue?



- A: In this COVID-19 situation but also in general, all samples must be treated as potentially infectious. The WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the ISO 15190 gives safety recommendations in sample handling.
- **Q:** The risk is that in the normal diagnostic cases patients without complaints might be carriers of COVID-19. The samples might contain virus. Therefore, vigorous methods are needed in the lab to work with these samples. Therefore, samples are no longer collected for the tissue bank. Is that the proper way to handle this?
- A: Performing risk analysis on the process handling in such cases is essential. Setting up measures and actions to protect the safety of the processor is key. See WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y
- **Q:** Would it be possible that through BBMRI-ERIC, all biobanks are establishing a table with risk management/handling of HBS versus the nature of the HBS collected?
- **A:** BBMRI-ERIC could support this in a Working Group, if requested.
- Q: What about the security measures taken by investigators that will conduct samples analysis?
- A: Investigators underlie the same security measures WHO
 Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the internal risk assessment performed by the hospital/laboratory/hygiene department (biosafety department)/biobank.
- **Q:** Should we stop activity because there is a risk that patients in normal care can be infected without complaints and thus carry the risk to contaminate the collection?
- A: In this COVID-19 situation but also in general, all samples must be treated as potentially infectious. The WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the ISO 15190 give safety recommendations in sample handling. You could mark a biobank collection as collected during the COVID-19 crisis (started in China November 2019 Entered Europe January 2020).
- Q: We conduct research for cancer clinical trials and collect/bank bloods during radiotherapy. Patients were not routinely being screened for COVID-19, and we do not receive updates on whether the patients were subsequently diagnosed with the virus. We usually process samples in a Cat 2 laboratory. Should researchers be concerned about defrosting and using these patient blood samples in future experiments? Does formalin fixation of tissue deactivate the virus?
- A: In this COVID-19 situation, but also in general, all samples must be treated as potentially infectious. The WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the ISO 15190 give safety recommendations in sample handling. You could mark a biobank collection as collected during the COVID-19 crisis (started in China November 2019 Entered Europe January 2020). Currently CDC has recommendations to this issue on influenza virus. https://www.cdc.gov/ncezid/dhcpp/idpb/specimen-submission/influenza.html. Based on this observation we assume, that all other viruses are no longer infectious after formalin fixation, because of the chemical bonding of proteins. Still to be verified for COVID19.
- Q: What specific safety precautions must be taken for long-term storage of samples?
- A: See for all general aspect in how to operate a biobank the Standard <u>ISO 20387:2018</u> Biotechnology Biobanking General requirements for biobanking e.g. for Biosafety issues (3.8 Biosafety, 4.1.1, 6.3.2, 7.3.2.2, Annex A). Include a risk-assessment approach to set up your biobank-procedures.



- **Q:** What about blood collected from infected and symptomatic patients? Can they be processed and aliquoted in BSL-2 labs or is better to use level 3 labs? Do you need to inactivate the samples before aliquoting?
- **A:** See WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the internal risk assessment performed by the hospital/laboratory/hygiene department (biosafety department)/biobank.
- **Q:** My hospital is not a COVID-hospital, but we are one of the hubs in Lombardy for cancer patients. Thus, we will start a prospective project for screening asymptomatic and pauci-symptomatic healthcare personnel of our Institute in terms of NP swabs and IgG and IgM antibodies. For this latter test, do you have any suggestion about assays with acceptable levels of sensitivity and specificity?
- **A:** We will not recommend particular brands since we are not performing validation ourselves. In fact, this topic was raised in the recording of 7 April 2020.
- Q: In general, how sure is it that asymptomatic patients have high viral loads like patients with severe complaints? As a consequence, should ALL biobanks collecting and freezing fresh materials stop collecting samples from the non COVID-19 diagnostic process to prevent contamination of the collection with COVID-19?
- A: Please see recording of 7 April 2020.
- Q: Do you collect samples during illness or after a patient is cured?
- **A:** Researchers may wish to collect samples at different time points.
- **Q:** Which procedures are followed to prepare serum or plasma? In BSL-2 or BSL-3 labs? Are you using virus inactivator?
- **A:** In a routine diagnostic lab, workers do not inactivate virus. Please follow WHO and ECDC guidelines. Please see the discussion in the recording of 7 April 2020.
- **Q:** As a University department responsible for SARS-CoV-2 isolation and detection in patients' material, we are thinking about establishing a section for this virus in our Biobank. The primary material collected from patients are nasopharyngeal swabs in buffer, so the idea is to store the remaining buffer for short-term storage and then isolate the RNA of the virus as the final biobanking material. I would like to kindly ask you for your opinion about this approach. Does it make sense to you?
- **A:** We cannot give an opinion on projects, but we recommend thinking about storage of multiple samples. In addition to virus RNA, it would be very interesting to assess the immune response of the COVID-19 patients, hence blood samples might be useful as well.
- **Q:** What biosecurity measures are carried out in biobanks? Exclusive shipping containers and boxes, but freezers too?
- A: See WHO guidelines for shipment: https://apps.who.int/iris/handle/10665/331337 and WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the internal risk assessment performed by the biobank/hospital/laboratory/hygiene department (biosafety department).

PRE-ANALYTICAL AND ANALYTICAL PROCEDURES

- Q: How should the DNA isolated from whole blood samples be treated in terms of biosafety?
- **A:** Please see the publication of Chang et al., Transfusion medicine reviews, 21th February 2020. Certain publications indicate that active virus might be present in mononuclear cells. Performing risk analysis in such cases is essential.



- Q: And peripheral blood mononuclear cells? At what BSL level?
- **A:** Please see the publication of Chang et al., Transfusion medicine reviews, 21th February 2020. Certain publications indicate that active virus might be present in mononuclear cells. Performing risk analysis in such cases is essential.
- **Q:** I was wondering if there was any reason to be concerned about the frozen patient blood samples (and the FFPE tissue blocks) that were collected and stored before/during the outbreak.
- A: In this COVID-19 situation, but also in general, all samples must be treated as potentially infectious. The WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the ISO 15190 give safety recommendations in sample handling. You could mark a biobank collection as collected during the COVID-19 crisis (started in China November 2019 Entered Europe January 2020).
- **Q:** Is there any information about the SARS-CoV-2 virus load in nasopharyngeal samples versus blood samples (serum or whole blood)?
- A: Yes, please see recording of 7 April 2020.
- **Q:** Should we manipulate the blood samples and their derivatives (plasma, serum, etc.) with the same biosecurity measures that are used for respiratory samples?
- A: See WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the internal risk assessment performed by the biobank/hospital/laboratory/hygiene department (biosafety department).
- Q: How infectious is serum collected in SST?
- A: Please see recording of 7 April 2020.
- **Q:** We need to know if we can work with COVID-19 samples (Peripheral blood, plasma and serum), to process and store them. Would it be possible to do it in a BSL-2 lab?
- A: See WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the internal risk assessment performed by the biobank/hospital/laboratory/hygiene department (biosafety department)
- Q: At what level should saliva collected in a lytic solution be handled?
- **A:** Please follow WHO guidelines; any specimen containing active virus should be handled in BSL-3 standard.
- Q: What safety precautions are required with respect to freezer storage of extracted RNA?
- **A:** WHO Guideline https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and the internal risk assessment performed by the biobank/hospital/laboratory/hygiene department (biosafety department)
- Q: Is there an advice/best practice on the number of samples and volume of storage tubes?
- **A:** Follow the manufacturer's manual for collecting and storing samples (vaccutainers, tubes, etc) and see https://www.bbmri-eric.eu/services/standardisation/ if applicable.
- **Q:** Does that mean that we should work in a BSL-3 lab? So, if we only have the possibility to work in a BSL-2 lab, does that mean that we cannot work with COVID-19 samples (Blood: Plasma/Serum)?
- **A:** Check your own sample handling processes and check your activities against WHO Guidelines https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y



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- **Q:** I would like to know how to preserve at -80°C saliva samples from COVID-19 patients for future researchers. Could I use RNAlater or Quiazol??
- A: We have not validated any of these protocols, so it is difficult to advise on that matter.
- **Q:** Would it be possible to provide some information about tissue handling and storage? And how can tissue-specific biobanks participate best these days (regarding COVID-19). Are there projects including tissue biopsies?
- **A:** BBMRI-ERIC has not developed such procedures. If required we may consider establishing a working group on such matters.
- **Q:** Are BSL-3 precautions mandatory for the processing and storage activities performed by biobanks. How must the long-term storage of samples be done comparing to our best practices?
- **A:** No, in certain conditions BSL-2 is enough; BSL-3 is required when working with live virus. It is very important to perform individual risk analysis.
- **Q:** My question goes to biosafety concerns. I'm not sure what BSL level would be necessary when processing blood for lymphocytes isolation using gradient centrifugation. Even knowing that for blood it is recommended BSL-2 I am not sure if in the case of blood cells (PBMC-peripheral blood mononuclear cells isolation) the BSL should be BSL-2 or BSL-3.
 - And what if we want to culture these lymphocytes to carry on immunologic assays?
- A: Please get your advice to your specific sample type at https://apps.who.int/iris/bitstream/handle/10665/331500/WHO-WPE-GIH-2020.2-eng.pdf?sequence=1&isAllowed=y and perform a risk analysis.
- Q: Are there any determined "minimum data set (MDS)" of COVID-19 patients?
- **A:** We proposed that data sets should ideally concentrate on:
 - · Disease severity, duration and outcome
 - Antibodies titer (IgM and IgG)
 - CT imaging of lungs, alternatively X-ray
 - Clinical symptoms (fever, dry cough, shortness of breath, muscles pain)
 - Blood count and other lab results especially at the moment of hospital admission,
 - Treatment protocol (antivirals, antimalarial, tocilizumab, GCs)
- **Q:** Are there any specific time intervals for serum/plasma sample collections during disease?
- A: Currently none have been defined.
- Q: Do you suggest heat inactivation for serum samples?
- A: We do not recommend such a solution.
- **Q:** Is it possible to store nasal aspirates/swabs or Bronchoalveolar lavage (BAL) samples in a biobank which has BSL-2 level laboratories?



- **A:** According to WHO recommendations, work with a live virus should be performed in BSL-3 standard. Please perform a risk analysis.
- **Q:** What about infected serum/plasma samples? If we need to aliquot samples in a BSL-2 lab, do we need to inactivate the samples before in an appropriate BSL-3 lab?
- **A:** Please follow WHO guidelines, follow a comprehensive risk analysis on your sample handling processes, any specimen containing active virus should be handled in BSL-3 standard.
- **Q:** Regarding storage vails in LN2: Is it possible to have cross-contamination? Should these samples be isolated from other ones?
- **A:** In general storage in LN2 carries a greater risk of contamination when compared to gas phase or dry storage.
- **Q:** What are the procedures to inactivate the virus? Is there any standardization on this? For example, for living PBMC? Or for preparing cells to be counted outside the biosafety cabin avoiding risk?
- **A:** We are not aware of such SOP but please refer to Chang et al. who described potential inactivation procedure in this paper https://www.ncbi.nlm.nih.gov/pubmed/32107119

Comment: Note that stabilisers typically used to stabilise stool for microbiome, virome analyses, inactivate viruses. Since the stool is not going to be used for virus isolation, but for viral RNA detection, such stabilisers are fit for purpose and procure safety.

- Q: What about patients' consensus to store and use the material? How should it be collected and when?
- **A:** If possible, follow local recommendations for informed consent. The study needs to be pre-accepted by a bioethical committee.
- **Q:** We have a research project collecting saliva for DNA extraction (OrageneDNA). I would assume it would fit within the BSL-2 due to the additive of the sample tube. Do you see any other risks?
- A: Please perform an individual risk assessment for your lab.
- **Q:** Some studies detect RNA of the virus in blood by PCR; is there any study that demonstrates that the virus is alive or potentially infectious in blood?
- A: Please see the publication https://jamanetwork.com/journals/jama/fullarticle/2762997
- Q: Is there any data around reinfection from biospecimens?
- A: Not to our knowledge. This is still under global investigation.
- **Q:** Are there any academic biobanks in Europe that have been 'repurposed' to assist in COVID-19 biobanking and diagnostic testing, etc.? If so, how did they have to boost their Risk Management plan and safety measures? Any examples?
- **A:** We have a list of biobanks that support COVID-19 research. Please refer to the link https://directory.bbmri-eric.eu/menu/main/app-molgenis-app-biobank-explorer/biobankexplorer
- Q: What is your experience with metabolite analyses of virus-inactivated samples?
- A: We have not found any publications on that issue yet.
- **Q:** I would like to ask your opinion about drying dried blood spots taken from patients that are suspected of having COVID-19 infection. Do we need to do this in a cabinet or can we dry the blood spot on the bench?
- **A:** We recommend to perform an individual risk assessment on the issue, and recommend to take enough pre-cautions.



- Q: Is there a need for routine testing for COVID-19 all samples in prospective collection?
- A: Serum and plasma samples could be tested in the future for IgM and IgG.
- Q: If you are not interested in COVID-19 specific research, and just want to proceed with former biobank processes (unintended use only): What additional measures have to be undertaken in times of COVID-19 when working in a BSL-2 facility? Why do we need additional risk assessment for SARS-CoV-2 e.g. compared to other risk class 3 microbes? Let's think for instance of lung cancer tissue asservation of negative and potentially positive patients.
- **A:** Please perform an individual risk assessment for your laboratory with regards to the biospecimen that is collected.
- **Q:** How should blood samples that may contain the virus be handled?
- A: Please follow WHO guidelines for laboratory testing.
- **Q:** If blood vials are stored in liquid nitrogen and if in the case that blood vials leak, can it aerosolize in the liquid nitrogen gas? If so, what would be recommended to best protect our researchers?
- A: As we proposed during our webinar, the LN tanks should be substituted by storage in a gas phase.
- Q: How long could the virus be active in a frozen plasma/serum at -80°C?
- A: We assume that the virus could possibly stay active for many months once frozen and stored at -80°C.
- Q: Do you think there is a greater risk if you use rubber stopper tubes than screw-cap tubes?
- **A:** Screw caps may be safer in handling and opening. But we have not performed validation of such methods. Please see recording of 7 April 2020.
- Q: How should surgical masks be decontaminated before reusing them (because of a lack of more masks)?
- A: Any possibility of reuse of disposable masks needs to verify with the entity's (hospital) recommendation.
- **Q:** With these samples that are hazardous wouldn't it make sense to freeze them first (especially feces) and then work with them as it minimizes exposure to the researchers. Frozen samples can be accessed without thawing through frozen sample aliquoting.
- A: We have not performed validation of such methods. Please see recording of 7 April 2020.
- **Q:** As long as N2L storage is discouraged just to avoid cross-contamination, which should be the guides to avoid cross-contamination in isopentane baths?
- A: We have not performed validation of such methods. Please see recording 7 April 2020.
- **Q:** BSL2 must not have an autoclave, which are the measures with waste to be transported to autoclave facility to another floor?
- **A:** Please refer to your health and safety authorities and requirements of your entity (hospital) regarding safe disposal of infectious waste.
- Q: Is the virus in feces still infectious?
- A: Yes, according to the published data.
- **Q:** Should we mark tubes or state in IT-system samples collected in a certain time frame. What should we consider the start point for possible infection?
- **A:** This is a valid idea. We suspect that the time when the patient 0 occurred in the country or the beginning of SARS-CoV-2 spread could be the starting point for marking the collection.



- **Q:** To manage the isolation of lymphocites (PBMC) you said that BSL-2 is enough? And what BSL do you recommend for culturing lymphocites for immunologic assays? And for cytometry or FACS?
- A: Please perform individual risk assessment and refer to your health and safety authorities.
- **Q:** How can we manage ELISA tests with sera of infected people? Would it be enough to inactivate before testing? At what temperature and how long?
- **A:** According to the literature, serum samples do contain very low amount of viral RNA and BSL-2 standard has been accepted by WHO for working with such samples.
- Q: Other publications (as an example: Peng, L., Liu, J., Xu, W., Luo, Q., Deng, K., Lin, B., and Gao, Z. (2020)) 2019 Novel Coronavirus can be detected in urine, blood, anal swabs and oropharyngeal swabs samples. medRxiv, 2020.2002.2021.20026179) claim that the virus is present in the urine? Can you comment?
- **A:** Current published data are not consistent. We found publication showing that urine does not contain active virus (https://jamanetwork.com/journals/jama/fullarticle/2762997), whereas yours demonstrates the opposite conclusion. We will concentrate on searching for more conclusive data.
- **Q:** Would deliberate research biobanking also be BSL-3?
- **A:** According to our current knowledge, biobanking does not have to be moved to BSL-3 standard unless you work with live virus.
- **Q:** We snap-freeze our fresh tissue and blood products in liquid nitrogen before transferring to -80 or vapor phase. Is there still risk of cross-contamination here? Sorry I should have said samples are contained within cryovials and then snap-frozen.
- A: Please perform an individual risk assessment. I understand the blood tubes are closed and then put into liquid nitrogen for freezing. In case the lid is screwed on the tube (according to the manufacturer's instructions) and later submerged into liquid nitrogen there is no cross contamination. It is more when the tubes are submerged for a longer time under liquid nitrogen the virus particles can diffuse from one to the other.
 - On top virologists in our institute (Erasmus MC) have stated that blood samples in the tube are not contagious in case of COVID-19.
 - It becomes also precarious when the lid is not sufficiently closed, and liquid nitrogen can penetrate into the tube. Cooling down causes a vacuum in the tube. These are the vials that can also explode when they are thawed. In case, and I am sure you do not, experience exploding tubes you are OK. The explosion as such can bring small particles in the air as aerosols.
 - The snap freezing term we use for tissues where the samples are frozen directly in pre-cooled isopentane and are then brought over to a precooled vial. After that the lid is closed and the sample kept in liquid nitrogen. There you have the possibility the virus can cause cross contamination to other samples. This is a completely different situation. On the other hand, we should take care when working with bio materials in general there could be infectious organisms in it, which are infectious and dangerous as COVID-19. Therefore, safety measures must always be in place when handling samples and when they are taken outside the vial you should always work at least for what I have now learned under BSL-2 conditions.
- **Q:** Please let us know about the storage of COVID-19 samples. Should we use separate LN2 tank?
- A: We do not recommend LN2 tank. Preservation and storage in dry phase seem to be a safer way.
- Q: Would you consider a halt in our biobanking activity, altogether? As virus load is the same in asymptomatic and symptomatic people and we don't know the incidence of the infection in general population, we biobankers need to adjust our protocols, training and risk management processes as if all donors are COVID-19 positive and so to upgrade our labs and practices to BSL-2 ... Is that feasible at all?



- **A:** We do not. Many biobanks from Europe already started collecting COVID-19 samples, following WHO guidelines for working with biological specimens. We assume that BSL-2 is enough when working with blood samples but we recommend performing risk analysis before biobanking such samples.
- Q: How should we manage blood samples?
- A: Please follow current WHO guidelines for clinical laboratories.
- **Q:** In blood donor centres we do not know if people are infected when samples are collected. Is there any evidence of high number of infections in these centres?
- A: Please have a look at Chang et al., Transfusion medicine reviews, 21th February 2020.
- Q: There is talk of virus inactivation buffers: is this compatible with blood sampling?
- A: We have not validated such methods.
- Q: We are starting the collection of COVID fecal samples in our biobank. I have some questions regarding this particular collection. Is there a standard protocol for the collection of fecal samples (in general)? Where can I find it? And for COVID fecal samples, is there a specific protocol for biobanking? It is known that the virus is present at high level in COVID fecal samples thus is it necessary to work in a BSL-3 laboratory?
- A: Please perform an individual risk assessment and refer to your health and safety authorities.
- **Q:** Is there a risk of cross-contamination between tubes conserved in the same box, particularly in liquid nitrogen tanks? Is there any recommendation to avoid risk (as we cannot really separate infected from the other, I thought to realize a disinfection of tubes prior to opening)?
- **A:** In general, we do not recommend storage in LN2, since there is a risk of contamination between samples.
- **Q:** I could not hear anyone talking about tissue samples e.g. lung biopsies; is there any known sampling/biobanking out in the world of this type of samples?
- **A:** We have concentrated on blood, urine and feces so far, but the storage of lung biopsies collected from COVID-19 suspected and confirmed patients requires special attention.
- Q: For tissue samples intended for paraffin embedding, will the formaldehyde fixation/alcohol dehydration/xylene procedure be considered as a good inactivation process of the SARS-CoV-2? (i.e. is there need for BSL-2 laboratory requirement for tissue sectioning?)
- A: In general, alcohol in the concentration > 60% inactivates the virus.
- **Q:** I would like to contact you as part of the creation of cancer-Covid19 collection. What are the technical recommendations? Is a PCR hood or a Sorbonne enough?
- A: Please perform an individual risk assessment and refer to your health and safety authorities.

EVA - GLOBAL

- **Q:** Does EVA GLOBAL have specific provisions for dual use viruses?
- A: Yes, we refer to the Australia Group objectives. The EVAg website (european-virus-archive.com) contains a link found in the Search function of the Home page, this provides a PDF guidance document which summarizes the regulations mandated by each country's authorities.

 In parallel with this guidance, EVA GLOBAL management follows a routine of screening and validating all requests to access our products, i.e. to ensure the end-user has the requisite facilities and expertise to receive and handle the product. Although the ultimate decision to supply rests with the owning

institute's PI, each product offered into the catalogue remains under the control of the member biobank.



Q: Are specific SOPs for the processing and handling of infected samples available?

A: No, we do not present such available documentation. Each member institute of EVA, as a publicly funded research body, will already have its own QMS (Quality Management System) arising from International Quality Standards as ISO17025; 15189 or 9001. Embedded within these QMSs will be SOPs controlling such processes and will be bespoke / unique to each institute's laboratory layout and function. One size does not fit all. As is the case with all Quality Standards, we do not insist on *how* partners carry out their lab management, but simply that they demonstrate *what* they do. Importantly, the key aspect that highlights EVA's raison d'être is what we do to collect, characterize, purify, evaluate, store and dispatch virus products.

Q: Does EVAg manage virus disease associated human specimens like serum or urine, or just the isolated virus?

A: No, EVA virus biobanks are managed separately to human tissue banks. Of course, many EVA labs are connected to hospitals (e.g. University of Ljubljana; Bernhard Nocht Institute, Hamburg; Le Charité, Berlin; Aix Marseille University) and have their own procedures for accessing human tissue under informed consent practices. So once the virus has been cultured from human material to create a Master Batch, this virus isolate is then used in a separate condition to the original human cellular material.

To complement the above, the EVA website has a range of information on products and services available, including access to specialist training at partners' labs. Institut Pasteur, Paris offers E-learning courses in biobanking for example, while other partners offer instruction in BSL3/4 biocontainment practice.

The Homepage provides a direct link to a list of 22 products / services under SARS CoV2 detection. The PORTAL link directs to the online web-based catalogue of viruses and derived products available free of charge to qualifying researchers. Click on the green Free Access Available link to read how to apply. Here you can find explanations of TNA (TransNational Access), our Selection Panel and the various processes necessary to engage with EVA GLOBAL.

EXPRESSION OF INTEREST – OPPORTUNITIES – UPDATES AND GENERAL INFO FROM PARTICIPANTS

I have consecutive series of 200 blood and serum samples from patients with PCR positive and negative coronavirus tests. It is important to circulate this information for scientists interested in utilizing those samples. (Angelo Paradiso)

GEN-COVID & reCOVID project collecting prospectively 2,000 COVID patients: https://tinyurl.com/ss5jfkb

Comment from Hungary: we isolated the virus, we have the genome, we are starting clinical trials and biobanking of COVID-19 patients' samples funded by the government.

Comment from Italy: BBMRI.it built up a <u>COVID-19 ELSI expert group</u> that is available to support research.

Comment from Italy: We have approved a COVID-19 Research Registry at the Fondazione IRCCS Policlinic Hospital in Milan.

In PG23 BB (Italy) there are: From September 2019 to December 2019 stored about 6000 plasma samples/month (= total 18,000 samples) + from January 2020 at today stored 4000 plasma samples/month (= total 12,000 samples).

Rapid serological test and pcr tests provide different information. In our hands, 200 samples rapid tests provide relevant information on immunology answers of single patients.



There is a German study on about 150 patients using Ab blood test. The test shows a 5% failure rate after the 10th day of infection and 2% after 15 day. In the first 10 days, because of the low titer of antibodies the failure rate is about 30%. So, patients with negative results need to go for a PCR or repeat the test after 10 days after suspicion of infection.

Could we have more precisions on the percentage of IgG positivity in asymptomatic patients during the crisis period, since this will be critical when it comes to the end of the crisis. Do other colleagues from Sienna have data?

The Italian SME VisMederi is doing IgG and IgM tests: montomoli@vismederi.com

See also this overview to antibody-tests: https://www.nature.com/articles/d41587-020-00010-2

How to ramp up Covid-19 mass testing immediately in the UK:

Please read this: https://www.ft.com/content/02a2bece-72b5-11ea-90ce-5fb6c07a27f2

Comment from Turkey: If you plan to organize another seminar, it would be great if you focus on "biobanking during outbreaks". It would be good if we can listen to previous experiences of different experts who were experienced on recent outbreaks (such as Ebola, Zika, etc. outbreaks), from the biobank perspective and talk about what has been learned from them.

ETHICAL AND LEGAL ISSUES

WEB CONFERENCE: COVID-19 AND ETHICAL, LEGAL & SOCIETAL ISSUES

24 April 2020 – 14-16 h CEST

Recording and Q&A available soon: https://www.bbmri-eric.eu/news-events/web-conference-covid-19-

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