The Lung Cancer Cohort Consortium (LC3) Access Policy

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1. Introduction

1.1. Mission statement and scientific mandate

The mission of the Lung Cancer Cohort Consortium (LC3) is to facilitate and carry out collaborative research on lung cancer risk and aetiology. The LC3 is committed to facilitating the use of LC3 data by the wider research community for research within its scientific mandate, including:

- Research on the aetiology of lung cancer incidence and survival
- Research on lung cancer risk assessment, early detection, and screening
- Research on tobacco exposure and tobacco-related health outcomes

1.2. Purpose and scope of the Policy

The LC3 Access Policy ("the Policy") outlines how the use of data gathered and generated by the LC3 is governed, and the principles and procedures according to which the use of LC3 data may be granted and accessed.

2. Definitions

The capitalized terms and expressions used in the Policy are defined below or in other sections, and the meaning is the same whether used in singular or plural.

The Lung Cancer Cohort Consortium (LC3 consortium, or LC3): The group of prospective cohort studies who have contributed data and/or samples to LC3 studies and the LC3 database.

LC3 Resources: Biospecimens gathered within the LC3 Consortium and/or Data from LC3 Study Participants, as defined hereafter.

LC3 Member Cohort (Cohort): Prospective cohort study that has contributed individual-level data to the centralized LC3 database (see Appendix A).

LC3 Principal Investigator (LC3 PI): Each Cohort is represented within the LC3 Consortium by a designated scientist, typically affiliated with the research institute that coordinates that Cohort (see Appendix A).

LC3 Steering Committee (LC3 SC): The entire group of LC3 PIs.

LC3 Access Committee (LC3 AC): Five designated LC3 PIs responsible for pre-screening requests to use LC3 Resources.

LC3 Coordinating Centre (LC3 CC): The institute responsible for coordinating the LC3 activities and hosting the LC3 Database. As of January 2022, the International Agency for Research on Cancer (IARC), the cancer research agency of the World Health Organization (WHO) is the designated LC3 CC.

LC3 Study Participants (Study Participants): Individuals who were recruited in one of the Member Cohorts of the LC3 consortium.

LC3 Biospecimens: The biospecimens that have been gathered from Study Participants. These may include human tissues, cells, biological fluids and derived products such as DNA,

plasma or serum, and associated sample annotations and quality metrics. Such associated data may also qualify as Personal Data to the extent it may identify, either directly or indirectly, a Study Participant.

LC3 Data: The data available within the LC3 database held at the LC3 CC, and/or data generated from the use of LC3 Resources. These include the de-identified individual-level data collected from the Study Participants at baseline or during the follow-up ("Study Data"); and the biological data or variables derived from the use of LC3 Biospecimens and/or LC3 Data, including all laboratory results such as, e.g., genotyping results, results of biochemical analysis, etc. ("Derived Data"), all of which may qualify as "Personal Data".

Personal Data: Any information relating to an identified or identifiable natural person (for the purpose of this Policy, "natural person" refers to "Study Participant"); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person. Personal Data may also be referred to as "Person-Identifiable Data".

Research Applicant: A scientist affiliated with a public, academic, or non-profit research institution/organization based in any country, who is applying for access to LC3 Resources for the purpose of consistent with the LC3 scientific mandate.

Approved Investigator: An investigator who has received the necessary approvals and has been granted access to LC3 Resources for the purpose of conducting an LC3 study. For the purpose of this Policy, all obligations applying to the Approved Investigator, in particular in relation to the use of LC3 Resources, shall also apply to ***Approved Users*** who shall be under the direct supervision and responsibility of the Approved Investigator.

Research Results: All scientific results obtained from the use of LC3 Resources within an approved research project.

LC3 Data Use Agreement (DUA): The agreement established between IARC and the Approved Investigator's institute, to lay out the terms and conditions under which access is provided to LC3 Resources. These must be signed by the Approved Investigator and, if applicable, the Approved Users, as well as an authorized legal representative of the Approved Investigator's institute.

The LC3 Access Policy (Policy): The present LC3 Access Policy, including its appendices and other referenced LC3 forms and documents.

3. Governance of the Lung Cancer Cohort Consortium

3.1. The LC3 and the LC3 Member Cohorts

The LC3 was formed in 2010 to carry out collaborative research on questions related to lung cancer risk and aetiology. The LC3 involves 25 Cohorts (Appendix A) from various geographical locations, currently including North America, Europe, Asia, The Middle East, and Oceania. Each Cohort is represented within the LC3 by a designated LC3 PI, who acts as the scientific liaison between their home institution and the LC3 Coordinating Centre. The International Agency for Research on Cancer (IARC/WHO) has coordinated the LC3 consortium since its inception and currently acts as the LC3 Coordinating Centre. The contributions from the Cohorts to the LC3 consortium, including how LC3 Resources can be used, are governed through a series of Material Transfer Agreements (MTAs), Data Transfer

Agreements (DTAs), and Collaborative Research Agreements (CRAs) that have been established between each Cohort and IARC/WHO.

The LC3 Member Cohorts, LC3 PIs and home institutes are listed in Appendix A.

3.2. Principles applied to access LC3 data

Access to LC3 Data, including any Personal Data in the LC3 Database, are governed by the research institutes of the LC3 PIs. Research Applicants external to the LC3 Consortium can submit a request to access LC3 Data which will be evaluated by the LC3 Access Committee to ensure that the proposal falls within the LC3 scientific mandate, the scientific relevance and feasibility of the proposed analysis, and the potential overlap with other ongoing analyses within LC3. Following approval from the LC3 Access Committee, the Cohorts from which data are requested can choose to participate in the proposed analysis through their designated LC3 PI by either an opt-in or opt-out process, as stipulated in their respective MTA/DTA. LC3 Data can only be accessed remotely, and Approved Investigators and their Approved Users are obliged to follow the LC3 authorship rules (see 7.1) on any publication arising from the use of LC3 Data.

3.3. The LC3 Coordinating Centre and custodian of LC3 Resources

The International Agency for Research on Cancer (IARC/WHO) is the cancer research agency of the World Health Organization (WHO), a Specialized Agency of the United Nations, headquartered in Lyon, France. As an intergovernmental institution/organization of the UN System, IARC/WHO operates within a particular legal and regulatory framework, under the general principles of public international law and the applicable international treaties and conventions. To ensure the independent exercise of its functions and fulfilment of its public health mandate, it enjoys privileges and immunities under international law, and is subject to IARC/WHO's rules, regulations, and policies, as adopted by its governing bodies.

Accordingly, IARC/WHO has the obligation to ensure the highest ethical and professional standards are adhered to in any of its research activities, including any LC3 study facilitated by IARC/WHO (e.g., through the use of the central LC3 Database). This includes, without being limited to, matters related to research with human biological material, and data protection and privacy related matters. For such matters, in addition to its governing bodies and the IARC/WHO regulatory framework, IARC/WHO seeks guidance from the IARC Ethics Committee and the IARC Data Protection Officer (DPO) as appropriate.

IARC/WHO has served as LC3 Coordinating Centre since its inception, and has acted and continues to act as the host and custodian of the LC3 Resources. IARC/WHO is represented within LC3 by two IARC scientists who are supported by other IARC staff actively involved within LC3, including a data manager and an administrative assistant.

4. Ethical principles and data protection regulations

4.1. Ethical principles

As a general principle, any research performed with the use of/access to LC3 Resources must comply with internationally recognized ethical standards and must be ethically and scientifically reviewed and approved by an appropriate independent board or committee.

In participating in a proposed analysis (either through opt-in or opt-out process), the LC3 PI confirms that the proposed analysis complies with their respective IRB approvals, or whether additional IRB clearance is required. In addition, any study using LC3 Data must be approved by the IARC Ethics Committee (IEC). The IEC is composed mainly of external independent

members with diverse expertise and backgrounds, with representation from both IARC and WHO. The current IEC composition and mandate, as well as information on submission procedure, reference guidelines and useful resources are available on the IEC website: https://ethics.iarc.fr/.

It is the Research Applicant's responsibility to ensure compliance with applicable laws, rules, regulations, research governance and ethical guidelines, or other regulatory requirements that may apply to the proposed research and use of the LC3 Resources.

Data protection and privacy principles

As an overarching principle, LC3 Resources remain the property of the respective LC3 Cohorts/home institutes, as the originating source, and have been entrusted to IARC as custodian. LC3 Data held at IARC are de-identified.

IARC, as LC3 Data custodian, in collaboration and close consultation with relevant bodies such as the LC3 SC, the IEC, and/or the IARC DPO:

- ensures the compliance of LC3 Data storage, use, processing and/or transfer, with the applicable data governance framework; and
- determines the means and purposes of the data processing in compliance with applicable policies and regulations.

In connection therewith, IARC ensures that Personal Data included in the LC3 Database:

- are processed fairly, for legitimate purposes and in a transparent manner in relation to the Study Participants;
- have been collected by the LC3 Cohorts for specified, explicit and legitimate purposes and will not be further processed in a manner that is incompatible with those purposes;
- are adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed;
- are kept accurate and, where applicable, up to date; and
- are stored and processed in a manner that ensures appropriate security of the Personal Data.

Further restrictions may be imposed based on specific regulatory requirements applicable to individual LC3 Cohorts that have provided the LC3 Data to IARC.

Approved Investigators are expected to adhere to the highest standards of data protection, confidentiality and privacy principles. This implies protecting and respecting the Study Participants' anonymity and consent at all times. Under no circumstances may Approved Investigators reverse-engineer Personal Data or attempt in any way to identify Study Participants.

IARC also acknowledges that Approved Investigators and their respective institutions may be subject to national data protection legislations, including where applicable the General Data Protection Regulation of the European Union (GDPR) or other similar data protection regulations.

For the avoidance of doubt, by virtue of their privileges and immunities under national and international law, WHO and IARC are not subject to EU (incl. the General Data Protection Regulation, GDPR) and/or any national data protection legislation. Notwithstanding the foregoing, ensuring the appropriate protection of Personal Data is of the outmost importance

to WHO and IARC. To this effect, IARC/WHO complies with the "Personal Data Protection and Privacy Principles for UN System Organizations", UN-HCLM 2018 (the "UN Principles"), and IARC/WHO's regulatory framework including *inter alia* the IARC/WHO Data Protection Policy. The aforementioned UN Principles are in line with the general principles of the GDPR.

The IARC DPO (dpo@iarc.fr) is available to provide advice and guidance to IARC and the LC3 Cohorts, as well as the Approved Investigators. The IARC DPO is also available as a contact point for Study Participants.

4.2. Remote access to LC3 Data

IARC has established a high-performance secure platform (the "LC3 Analytical Hub") to serve as centralized repository for all LC3 Data. The LC3 Analytical Hub is subject to clearly defined procedures to ensure adequate controls and the highest level of protection and security of the data hosted therein, in accordance with the IARC/WHO regulatory framework.

By providing remote access to de-identified data via the LC3 Analytical Hub, IARC aims to address data protection and privacy concerns, and to avoid physical transfer of LC3 Data. Accordingly, where the Research Applicant requests access to LC3 Data for the purpose of a proposed research project, access is granted remotely via the LC3 Analytical Hub. Access remains subject to the research project being approved by the LC3 Access Committee and individual LC3 PIs, and the relevant bilateral agreement being signed between IARC and the Approved Investigator/Approved Investigator's institution. Physical transfer of LC3 Data to Research Applicants will not be facilitated by IARC.

5. Proposing an LC3 Project and the process for data access

5.1. Proposal submission

Researchers who are interested in accessing the LC3 Data are invited to contact the LC3 CC on LC3@iarc.fr to find out whether the proposed research is feasible using the data that have been harmonized within the LC3 Database. Access requires submission of the LC3 Data Access Proposal which includes information about the investigator's team; the background, aims, and methods of the proposed project; the cohorts and variables requested; and the project timeline. The completed proposal should be sent to LC3@iarc.fr.

5.2. Proposal assessment process

Submitted data access proposals are reviewed by the LC3 Access Committee, which includes 5 LC3 members with representation from the LC3 Coordinating Centre and the participating Cohorts. Proposals are assessed for scientific relevance, appropriateness of the LC3 Data, overlap with existing initiatives, and whether the proposed research falls within the scope of the LC3 scientific mandate. The LC3 Access Committee will meet on an ad-hoc basis, as required, and will return a decision on a data access request within 2 months of submission at most. The LC3 CC holds a permanent seat on the LC3 AC, while the other 4 members will rotate among the LC3 PIs approximately every 2-3 years, according to interest and willingness to participate.

For proposals that are approved by the LC3 Access Committee, each Cohort has the option to participate in the proposed analysis on an individual basis, but is also able to decline participation/usage of their LC3 Data. The LC3 Coordinating Centre distributes approved proposals to the Cohorts who are requested to participate in the project. The Cohorts, through their designated LC3 PI, subsequently have 30 days to agree to participate in a given analysis, either through an opt-in or opt-out process (based on their own preference and as agreed upon

in the respective MTA/DTA, see Appendix A). A reminder is sent 23 days after the initial proposal circulation. After 31 days following the initial circulation of a proposed analysis, the LC3 Coordinating Centre considers Cohorts who have either *i)* explicitly agreed to participate in the analysis or *ii)* remained silent and contribute to the LC3 Analytical Hub through an opt-out process, as participants in the proposed analysis. Remaining Cohorts are considered by the LC3 Coordinating Centre as non-participants to the proposed analysis, including Cohorts who have either *iii)* explicitly opted-out to the proposed analysis, or *iv)* remained silent and contribute to the LC3 Analytical Hub through an opt-in process.

5.3. Access to data following approval of a proposal

Following the approval of a data access proposal, a Data Use Agreement (DUA) will be signed between the LC3 CC and the institution of the Approved Investigator/Approved User who will analyse the data. The DUA establishes principles and boundaries for use of the LC3 Data, and expressly prohibits the analyst from making any attempt to download the data or re-identify Study Participants. The terms and conditions stipulated in the DUA are non-negotiable.

Once the DUA is established, the LC3 CC will prepare a database for access by the analyst. The database will only include data from Cohorts who participate in the specific analysis and will only include the variables requested by the Approved Investigator in their data access proposal. The database will be made accessible remotely to the Approved User/Investigator via the RStudio Pro environment (it is currently not possible to use a statistical software other than R). The Approved User/Investigator will have the ability to save analysis output on the server, and the database administrator at the LC3 CC will facilitate later transfer of output to the Approved User/Investigator upon verification that it does not contain any individual-level information.

5.4. During the study

Formal progress reports are not required, but the LC3 Access Committee reserves the right to request updates for progress of specific projects. In cases where projects are not progressing, and other investigators have requested to pursue the same topic, the LC3 Access Committee reserves the right to terminate access after a probationary period of 3 months. LC3 Cohorts also retain the right to request, in exceptional cases, that their data be removed from a particular project up until the point when a manuscript has been submitted.

5.5. End of the study

DUAs are established for 3 years. Access to the LC3 Data is terminated after (a) publication of the final manuscript from the project or (b) 3 years, whichever is earlier. In cases when investigators require more than 3 years to complete their analysis, it is possible to extend the DUA.

5.6. Special requirements for specific Cohorts

Some Cohorts have special requirements to access or publish their data. It is the responsibility of the Approved Investigators/Approved Users to comply with these special requirements, as follows:

Cohort	**Requirement**
CLUE	Each analyst must sign a data use agreement (DUA) for the Maryland Cancer Registry before accessing CLUE data and submit it to the LC3 PI for CLUE. All manuscripts must be approved by the MCR; this process is handled by the LC3 PI.

WHI	Investigators must submit a paper proposal and must have manuscripts approved by the WHI P&P Committee. Paper proposals are requested for record keeping but are not required for review and approval unless the lead author is a WHI investigator.

6. Access Limitations

Access to the LC3 Data is restricted to 'bona fide' researchers/Approved Investigators/Approved Users, who are affiliated with academic, non-profit, or governmental research institutions, and who have no links to the tobacco or arms industries. The LC3 Coordinating Centre cannot grant access to LC3 Data to commercial entities and/or for commercial purposes, including development of patents.

Access to LC3 Data may be denied for various reasons. The following list, while not exhaustive, provides examples:

- The proposed research project falls outside the LC3 scientific mandate (see 1.1).
- The proposed research project overlaps with ongoing or planned projects/analyses leading to unnecessary duplication of work and waste of resources;
- The scientific quality of the proposed research project is considered inadequate;
- The LC3 Data are not suitable to answer the proposed research question;
- There are ethical or legal issues with the proposal, including, for example, when the proposed use of the LC3 Resources is not compatible with the original informed consent of the Study Participants, or if the proposal is non-compliant with the applicable data protection regulations;
- The proposed research project is not compatible with the goals of public health;
- The proposed research project is considered not in compliance with the general guiding principles of this Policy – LC3 is committed to respecting and protecting the rights, privacy, and consent of its Study Participants at all times.

As a general principle, the LC3 Access Committee and the LC3 Cohorts reserve the right to reject access requests and appropriate feedback will normally be provided in such cases. The respective home institutes of the LC3 Cohorts have the ultimate authority over the provision and/or use of LC3 Resources originating from their respective LC3 Cohorts, and may individually refuse the use of their data for specific research projects.

7. Publication of Research Results, authorship and intellectual property rights

7.1. Publication

As a general and prevailing principle, the Approved Investigator is expected to disseminate the Research Results to the public through appropriate means, most importantly through peer-reviewed scientific publications. To this end, the Research Results should be submitted for peer-reviewed publication in timely manner, i.e., within 3 years after receiving access to the LC3 Data, or otherwise as agreed upon with the LC3 Access Committee and LC3 Cohorts.

Any research conducted by an Approved Investigator using LC3 Data is by definition conducted in collaboration with the LC3 PIs as the originating sources. Accordingly, any publication arising from the use of LC3 Data should include co-authors from the LC3

Cohorts in accordance with the recommendations from the International Committee of Medical Journal Editors (ICMJE). This will typically involve 1 or 2 co-authors from each LC3 Cohort from which data were used, and each LC3 PI is responsible for evaluating whether their co-authors comply with the ICMJE authorship guidelines. The LC3 Cohorts may also include any text in the Acknowledgment section of the manuscript to highlight the contribution of funders or individuals. Publications should also include 1-3 co-authors from the LC3 CC, depending on the level of involvement in the analysis. Some Cohorts have additional procedures for approval of manuscripts prior to submission which must be followed as requested by the Cohort representatives. Approved Investigators should anticipate that additional time (minimum 1 month) will be required for completion of these processes between initial circulation to co-authors and submission to a peer-reviewed journal.

7.2. Use of Research Results and intellectual property

The ownership of the LC3 Resources, including Derived Data to the extent such data fall under property rights, remains with the respective originating LC3 Cohorts/institutes with general custody being entrusted to the LC3 CC. As LC3 CC and custodian, IARC does not have the authority to share or provide access to LC3 Resources for purposes other than **non-commercial, research and academic purposes**, in accordance with the LC3 mission and general principles (see 1.2 and 4.1).

In line with the above, the LC3 Resources should not be used for gain or commercial profit or benefit, nor for or in connection with the filing of patents or similar intellectual property protection. Likewise, the Approved Investigator should not seek to obtain any such intellectual property protection in respect of any Derived Data arising from the use of LC3 Resources.

Exceptionally, where further development and exploitation of the Research Results are judged essential or potentially highly beneficial for public health purposes, IARC as custodian of LC3 Resources should be contacted for further discussion. As a general and fundamental principle, it would need to be clearly demonstrated that such outputs will be developed in a manner that would best deliver health benefit and wider public good, and would not be exploited in a manner that is divergent or contrary to that goal. Should the case arise, any industrial or commercial exploitation of Research Results would remain subject to prior approval of IARC, the LC3 Cohorts and home institutes, and a separate agreement to be established and negotiated in good faith between the parties concerned.

7.3. Access to data generated with NIH funding

In accordance with the NIH Data Sharing Policy, access can be requested to a dataset containing data generated within the LC3 consortium using funding from the INTEGRAL project (U19 CA203654). This dataset includes proteomics measurements generated within specific cohorts and case-control status. The purpose must be for non-commercial research related to lung cancer. Requested use of this dataset will not be refused due to the nature of the research question (provided it is related to lung cancer), overlap with ongoing or planned projects, or the proposed methodological approach. Publications resulting from analyses of this dataset are not subject to the requirement to include LC3 investigators as co-authors.

8. Documentation

1. IARC/WHO Data Protection Policy: https://www.iarc.who.int/wp-content/uploads/2021/10/IARC-Data-Protection-Policy_Sept2021.pdf
2. LC3 Access Policy (current document): https://www.iarc.who.int/wp-content/uploads/2021/12/LC3_Access_Policy.pdf.

3. LC3 Data Access Proposal: https://www.iarc.who.int/wp-content/uploads/2024/04/LC3-data-access-proposal-and-COI-v4.0.docx
4. LC3 Data Use Agreement (DUA): Available for Approved Investigators

Appendix A: Participating Cohorts in the Lung Cancer Cohort Consortium

Cohort	Acronym	Institute	LC3 PI
Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study	ATBC	US National Cancer Institute	Stephanie Weinstein
Campaign Against Cancer and Stroke	CLUE	Johns Hopkins Bloomberg School of Public Health	Kala Visvanathan
Canadian Study of Diet, Lifestyle, and Health	CSDLH	Albert Einstein College of Medicine	Tom Rohan
Cancer Prevention Study – II	CPS-II	American Cancer Society	Ying Wang
European Prospective Investigation into Cancer and nutrition	EPIC	IARC	Mattias Johansson
Generations Study	GS	Institute of Cancer Research, Royal Cancer Hospital	Richard Houlston
Golestan Cohort Study	GCS	IARC / Tehran University of Medical Sciences	Reza Malekzadeh, Mahdi Sheikh
Health Professionals Follow-up Study	HPFS	Harvard T.H. Chan School of Public Health	Hong Zhang
Melbourne Collaborative Cohort Study	MCCS	Cancer Council Victoria	Roger Milne, Julie Bassett
Multiethnic Cohort Study	MEC	University of Hawai'i	Loic Le Marchand
New York University Women's Health Study	NYUWHS	New York University School of Medicine	Alan Arslan
NIH-AARP Diet and Health Study	AARP	US National Cancer Institute	Linda Liao

Northern Sweden Health and Disease Study	NSHDS	Umea University	Kjell Grankvist, Mikael Johansson
Nurses' Health Study	NHS	Brigham and Women's Hospital	Hong Zhang
Physicians' Health Study	PHS	Brigham and Women's Hospital	Howie Sesso
Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial	PLCO	US National Cancer Institute	Neal Freedman, Wen-Yi Huang
Shanghai Cohort Study	SCS	University of Pittsburgh	Jian Min Yuan
Shanghai Men's Health Study	SMHS	Vanderbilt University Medical Center	Xiao Ou Shu
Shanghai Women's Health Study	SWHS	Vanderbilt University Medical Center	Wei Zhang
Singapore Chinese Health Study	SCHS	University of Pittsburgh	Jian Min Yuan
Southern Community Cohort Study	SCCS	Vanderbilt University Medical Center	Qiuyin Cai
Trøndelag Health Study	HUNT	Norwegian University of Science and Technology	Arnulf Langhammer
VITamins And Lifestyle Study	VITAL	Fred Hutchinson Cancer Center	Emily White
Women's Health Initiative	WHI	Fred Hutchinson Cancer Center	Lesley Tinker, Chu Chen

Women’s Health Study	WHS	Brigham and Women's Hospital	Howie Sesso