March 12, 2021 Rule No. 2-9

C-CAT Policy for Secondary Data Utilization (“Policy”)

1. Purpose

The Center for Cancer Genomics and Advanced Therapeutics (“C-CAT”) is a department organized within the National Cancer Center Japan (“NCC”), based on the national policy of Japanese Government, to accomplish optimal utilization of the information obtained through collection, analyses and proffer of information of cancer genomic medicine all over Japan for the purpose of servicing and generating novel medical care. C-CAT promotes the utilization of data of both clinical information and genomic information accumulated in C-CAT (collectively "C-CAT Data"). C-CAT Data are utilized in two ways: (1) primary utilization, in which data are shared with Hospitals for Cancer Genomic Medicine (refer to the definition in following paragraph) for improving medical practice and insurance medical care, and (2) secondary utilization for research and development by third-party organizations to use C-CAT Data under authorization of C-CAT.

This Policy defines requisite matters for fair and smooth secondary utilization of information of cancer genomic medicine collected by and stored at C-CAT in collaboration with Designated Core Hospitals for Cancer Genomic Medicine, Designated Hospitals for Cancer Genomic Medicine, and Cooperative Hospitals for Cancer Genomic Medicine (collectively "Hospitals for Cancer Genomic Medicine") in Japan.

2. Definitions

(1) **Cancer Knowledge DataBase** (“**CKDB**”) means database built to interpret the results of genome analyses and give clinical significance. C-CAT documents investigation results (“C-CAT Findings”) using CKDB for each patient based on the results of genome analyses sent from Clinical Laboratories and Test Facilities, and sends C-CAT Findings to Hospitals for Cancer Genomic Medicine.

(2) **Cancer Genomics Repository** (“**Repository Database**”) means database of genomic and clinical information of cancer patients collected from Hospitals for Cancer Genomic Medicine. Part of data sets are offered through C-CAT to third parties for secondary utilization such as research and development of new therapeutics, diagnostics or medical care services.

(3) **Designated Core Hospitals for Cancer Genomic Medicine (“Designated Core Hospitals”)** means such medical institutions in Japan that are qualified by the Minister of Health, Labor and Welfare of Japan as prepared with advanced faculties for leading cancer genomic medicine in Japan to build up a system that enables Japanese citizens to receive cancer genomic medicine everywhere in Japan. Their key roles are as follows to:

- Conduct quality assured genomic testing (allowed to be outsourced.)
- Provide interpretation of test results (by Expert Panel as defined in (6) in this Section 2)

・Conduct and support genetic counseling
・Conduct clinical trials, make patient referral and registration for clinical trials
・Appropriately collect, manage and register clinical information (registration at C-CAT)
・promote human resources development relating to cancer genomic medicine

(4) **Cooperative Hospitals for Cancer Genomic Medicine ("Cooperative Hospitals")** means such hospitals in Japan that work with Designated Core Hospitals or Designated Hospitals to provide medical care based on the results of comprehensive genome profiling test. Furthermore, subject to confirmation by Designated Core Hospitals or Designated Hospitals regarding the fulfillment of requisite maintenance guidelines by any candidate medical institution, such medical institution being notified by Designated Core Hospitals or Designated Hospitals as its partner institution to the Minister of Health, Labour and Welfare of Japan and then announced as such publicly. Cooperative Hospitals assume the role to provide, by means of ordering and conducting comprehensive genomic profiling tests, patients referral to clinical trials at its affiliated Designated Core Hospitals or Designated Hospitals, and adequate genomic medicine to their patients.

(5) **Designated Hospitals for Cancer Genomic Medicine** ("**Designated Hospitals**") means medical institutions in Japan that are qualified as eligible to achieve by itself complete cancer genomic medicine based on the following requirements:
・Genomic testing and Expert Panel equivalent to those of Designated Core Hospitals.
・Medical care provision system equivalent to that of **Designated Core Hospitals**
・Human resources development, clinical trials, advanced medicine, etc. equivalent to those of Cooperative Hospitals

(6) **Expert Panel** means a multi-disciplinary panel (Molecular Tumor Board) organized at each Designated Core Hospitals or Designated Hospitals to medically interpret the results of comprehensive genome profiling test.

(7) **Clinical Laboratories and Testing Facilities** mean private organizations in Japan that undertake insurance-reimbursed comprehensive genome profiling test and other testing services outsourced by Hospitals of Cancer Genomic Medicine.

(8) **C-CAT Data Licensing** means disclosure, provision, or licensing of C-CAT Data to third parties for the purpose of secondary utilization.

3. Secondary data utilization

(1) C-CAT's rights on handling of C-CAT Data

・C-CAT may, with the approval of the C-CAT Data Utilization Review Board, grant a C-CAT Data Licensing.

・If a C-CAT Data licensee breaches this Policy, C-CAT shall be entitled to, among others:

announce the name of such licensee, suspend the C-CAT Data Licensing, reject new license applications, seek an injunctive relief, and claim for damages against the licensee.

(2) Requirements for C-CAT Data Licensing

・Approval of a research plan by the research ethics committee (REC) and head of the applying institution (if a research plan is subject to the ethicalguidelines)

・Approval by the C-CAT Data Utilization Review Board

・Execution of an agreement with C-CAT on C-CAT Data Licensing ("C-CAT Data License Agreement"), and payment of the utilization fee

(3) Data available under the C-CAT Data Licensing are set forth in Attachment 1.

(4) Restrictions for C-CAT Data Licensing

・C-CAT grants C-CAT Data Licensing for the applications aiming at academic researches or the development of pharmaceuticals. Examples of permissible purpose of utilization include, marketing research, creating clinical trials/research plans, running safety research, identifying new therapeutic targets, and conducting research and development of treatment approaches.

・C-CAT prohibits C-CAT Data licensees from offering, selling or reselling relevant data to any third parties, provided, however, that the licensees may provide the data to its affiliate or outsourcee company on the condition the licensee imposes same confidentiality obligations under this Policy and C-CAT Data License Agreement on the said affiliate or outsourcee company.

・C-CAT does not grant a C-CAT Data Licensing if a prospective C-CAT Data licensee is found out to be a part of, or related with anti-social forces, or if the C-CAT Data Utilization Review Board considers that there is a serious concern that the business activities of the affiliated organization of the prospective licensee may negatively affect the peoples' health. Also, if the foregoing concern becomes apparent with existing C-CAT Data licensee, C-CAT shall suspend such C-CAT Data Licensing.

・Furthermore, C-CAT Data licensees are strictly prohibited from such prohibited use as stipulated in a C-CAT Data License Agreement (including without limitation, rebuilding, reverse-engineering, disassembling, or decompiling of all or a part of products/analysis programs used for generating C-CAT Data).

4. C-CAT Data Utilization Review Board

(1) C-CAT establishes the C-CAT Data Utilization Review Board ("CDURB") to ensure the impartiality of C-CAT Data licensing to third parties. 50% or more of the members of the CDURB shall be individuals of both genders outside of the NCC. The secretariat of the CDURB is placed within C-CAT.

(2) Members of the CDURB are subject to adequate COI management under the NCC's COI management policy and owe a duty to maintain the confidentiality of information learned while

performing their role.

(3) Individuals that wish to use C-CAT Data shall submit the following documents to C-CAT for review by the CDURB:

・C-CAT Data use application form (defined separately)

・Research plan (if applicable)

・Result Notice of REC's review (if a research plan is subject to the ethical guidelines)

(4) The CDURB examines the following matters to decide whether to grant a C-CAT Data license:

・Applicant‘s use of C-CAT Data is intended for academic research or pharmaceutical development.

・Data are not used to: identify blood relatives; confirm the presence/absence of blood relation; or howsoever potentially harm an individual, small group, or community.

・A research plan is scientifically valid, and the scope of data use is valid.

・Applicant has sufficient experience or capability to execute a research plan.

・Applicant’s employer organization has adequate research facilities and an information management program in place including data storage and disposal.

・Any other matters deemed required by members of the CDURB

(5) Users of C-CAT Data must not use C-CAT Data for any purpose other than that authorized by the CDURB.

5. Intellectual Property Rights

(1) With respect to C-CAT Data, no rights, including intellectual property rights, are transferred or licensed to users unless explicitly stated in this Policy and a C-CAT Data License Agreement.

(2) Intellectual property and intellectual property rights arising from the use of C-CAT Data belong to a user who has created such intellectual property and is granted intellectual property rights.

6. Fees

C-CAT Data utilization fees are set forth in Attachments 2 and 3.

7. Publication and reporting

(1) C-CAT Data users may publish the results of research using C-CAT Data

(2) Notwithstanding the foregoing provision (1), users are not allowed to report the following genomic information of C-CAT Data in their paper for publication which covers use of the data and research results (“Papers”):

(a) Original sequence data (FASTQ/BAM, etc.)

(b) List of the entire mutations in an individual (VCF/XML, etc.)

(3) C-CAT Data users may include patients' clinical information of C-CAT Data in Papers to the extent

required to present results.

(4) When executing C-CAT Data License Agreement, CDURB examines a C-CAT Data user in connection with publication of Papers using C-CAT Data. However, even after the execution of C-CAT Data License Agreement, users must carefully monitor potential risks of identification of personal information, and must report any such potential risks and discuss with the CDURB before publication of Papers.

(5) C-CAT Data users must submit an annual report to C-CAT that includes the C-CAT Data use status and the list of titles of published Papers of research results. The deadline of the annual report submission is within 60 days after the date of expiration or termination, or renewal date of the agreement.

8. Confidentiality

(1) In relation with sub-section 4-(3), C-CAT treats as confidential any content of documents provided by applicants and information explicitly marked as confidential when disclosed by them, and saves for a reasonable period of time.

(2) C-CAT Data licensees shall keep information related to C-CAT Data in confidence and must not disclose or offer such information to any third parties. However, within the scope of purpose permitted by the CDURB a user may disclose information to an analytics service provider on the condition that such provider is bound by the same confidentiality obligations of the user.

(3) In handling C-CAT Data, C-CAT Data licensees must take reasonable security measures to protect data from the risks of unauthorized access, losses, destruction, and leakage.

(4) C-CAT Data licensees shall appoint a manager who is responsible for C-CAT Data management and notify C-CAT identity of the appointed manager. C-CAT Data licensees shall notify C-CAT in the event of the change of such manager without delay.

9. Disclosure

Notwithstanding the provisions of foregoing Section 8, C-CAT may disclose the names and other basic information of C-CAT Data licensees.

10. Disclaimer

C-CAT Data users shall indemnify and hold C-CAT and NCC harmless from any and all claims from third parties regardless of whether direct or indirect damages arising from use of the C-CAT Data. Users shall not preclude C-CAT and NCC from exercising their right to claim recourse for a third party's claim for damages arising from C-CAT Data use.

Supplementary provisions

(Effective date)

This Policy comes into effect as of March 12, 2021.

Supplementary provisions (2021 No. 34-2)

(Effective date)

This Policy comes into effect as of November 18, 2021.

Attachment 1　Genomic and Clinical Information Made Available under C-CAT Data Licensing

<Genomic Information>

Genomic information 1: Genetic alterations mentioned in test results (included in C-CAT Findings);

Genomic information 2: FASTQ or BAM files provided by testing companies

VCF files recreated on C-CAT platform are also available.

<Clinical Information>

Basic information	Hospital ID*, sex, age, registration ID*
Sample information	Genomic test classification, Genomic test category, tumor cell content, sampling date, sampling method, sampling site
Background information	Pathological diagnosis, smoking history, alcohol drinking history, ECOG PS, multiple primaries in single organ, multiple primaries in different organs, family history (presence/relationship, cancer type, age of onset)
Cancer information	Metastasis at registration, genetic test results for specific type of cancer (*EGFR, ALK, ROS1, HER2, KRAS, NRAS, BRAF, gBRCA1/2, etc.*)
Pre-EP regimen information	Treatment line, purpose, regimen, drug name, start/end dates of administration, best overall response, adverse events of Grade 3 or higher (if present, provide the name of adverse event)
Post-EP regimen information	Date of EP, treatment policy, treatment line, , regimen, drug name, dosage and administration, body height, body weight, start/end dates of administration, best overall response, adverse event of Grade 3 or higher (if present, provide the name off adverse event)
Outcome	Outcome, last follow-up date, date of death, cause of death

＊Approval by the C-CAT Data Utilization Review Board is required for using hospital ID and/or registration ID.

Attachment 2　C-CAT Research-Use Portal site Utilization Fee

Annual Utilization Fee	7.8 million yen (including consumption tax)
Utilizations	view and download data of all cases registered in C-CAT

<Genomic Information>

Genomic information 1: Genetic mutations mentioned in test results (mutations included in C-CAT Findings)

<Clinical Information>

Same as that described in Attachment 1

Attachment 3　Fees for Academia in Japan

Hospitals for Cancer Genomic Medicine shall have free access to C-CAT Research-Use Portal site as they play key roles to help C-CAT collect, manage, and promote the utilization of information of cancer genomic medicine. Such roles include adding data to C-CAT after unifying the names of agents and correcting errors in their own data. (For-profit companies that participate in joint research are required to pay the fee.)

Unlike commercial pharmaceutical development, research by academia is not-for-profit clinical research on rare cancers and mutations and academic research for generating novel ideas and businesses. Academic research is conducted for various purposes and at diverse levels. Free availability of C-CAT Research-Use Portal site to promote research shall be limited to AMED research, research programs that have been awarded grants by the Minister of Health, Labour and Welfare of Japan and Ministry of Education, Culture, Sports, Science and Technology of Japan, and other projects selected by the Japanese government based on certain directions and evaluation criteria. (For-profit companies that participate in joint research are required to pay the fee.)