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Clinical Genomics Consent - DRAFT

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Clinical Consent Clauses: Context and Use

As genome wide sequencing enters the clinic as part of routine diagnosis, health authorities may require an authorization for such testing in addition to the consent already provided by patients for medical care generally. While such integration of genetic tests into modern medical care supports personalized, precision medicine, obtaining an additional informed consent (authorization/permission) from patients in the clinical context poses several challenges. The most obvious one is that of providing the necessary information itself, to say nothing of both the timing and finding the time in the clinic. Ideally, information on the need for such a test and the meaning and type of results would be made clear prior to any intervention. There may also be a need for domain-specific scientific information particular to fetal genomic testing or whole tumor genomic profiling, for example. The reality is that most health care systems do not provide opportunities for detailed communication with the patient, especially in the hospital setting. At a minimum, prior educational materials/videos should be made available describing and distinguishing the typology of genomic tests including the

one proposed to the patient. In addition, the brief authorization form that will become part of the medical record should remind the patient, in summary point form, of the core elements of genomic testing in the health care setting.

These particular considerations have influenced the format and brevity of the proposed typology of examples of clinical genomic clauses presented by GA4GH. The clauses presented herein are each within categories and largely originate from those countries that are beginning to deploy such testing in their health care systems. To some extent, they largely resemble (albeit greatly shortened) those found in other GA4GH Consent Clauses tools. Some elements however, are different. For instance, the medical care environment mandates returning clinically actionable results. There is also the need to specifically require explicit permission for participation in ongoing research or for recontact for future research. In short, these adjustments reflect the fact that genomic testing decisions are taken at the same time as other clinical care ones. As genomic testing becomes a natural part of the clinical care pathway, authorization forms must be adapted to current medical practices and fit both the needs of the patient and healthcare providers'. Since consent has been given to clinical care and genomic tests will form part of the diagnostic pathway, we suggest labeling such a form an "authorization."

To date, the Consent Task Force of the Regulatory and Ethics Workstream (REWS) has prepared WGS template clauses for: genomic research, large scale initiatives (biobanking and population studies) and clinical genetic testing. A typology of clauses specific to familial testing, rare diseases and pediatrics has also been prepared. They all cross the categories listed above.

Table of Consent Clauses

Categories	Consent Clause(s)
About the Test	I understand that I will be undergoing genome-wide sequencing to possibly identify the genetic cause(s) and genomic variant(s) related to my condition.
	The purpose of this test is to identify variant(s) in gene(s) that has/have been found to be associated with my condition.
	The purpose of this test is to identify the genetic cause(s) of my health issues.

	This test examines a very large number of the genes in the body all at once. To do the test, [name of the institution] needs a small sample of DNA.
	The genetic test will attempt to identify the cause of a suspected disease by analyzing my genetic material (DNA) for an abnormal change (variant).
	I understand that the genetic material or DNA in my sample (blood, solid tissue, …) will be tested for a panel of genes, as indicated below.
	My DNA contains a lot of information that can be “seen” with genomic testing. This test is designed to show my healthcare providers information only about gene changes related to my condition. This information allows the hospital staff to better diagnose and treat patients with the same condition as me.
Types of Results	**Positive** or pathogenic, and may: - explain the cause of a genetic condition. - reveal carrier status for a genetic condition. - reveal a predisposition or an increased risk for developing signs and symptoms of a genetic condition in the future. - have implications for other family members. **Negative** or normal, and may: - reduce but not eliminate the possibility that a condition has a genetic basis. - reduce but not eliminate any predisposition or risk for developing signs and symptoms of a genetic condition in the future. - indicate that additional testing may be considered. **Uncertain**, and may: - indicate that additional testing may be considered for other family members to be informative. - remain uncertain for the foreseeable future.

	- be resolved over time. I should check with my healthcare provider every few years to see if there is more information about my genetic variant.
What is Reported	- Genetic variants that may have caused my signs and symptoms. - Genetic variants found in genes unrelated to my condition, but which may have an important impact on my health and have medical management implications, unless I decide that I do not want this information. - Genetic variants identified in family members and related to my signs and symptoms will be included in my report. Family members [will or will not] receive separate written reports.
What is not Reported	- Variants in genes that are not thought to affect my health. - Variants identified in research studies where association with diseases remains unclear. - Variants that predict an increased risk of a disease, but do not cause a disease by themselves. - Variants which are not thought to cause disease(s). - [...]
Uncertainty (Variant of Unknown Significance (VUS))	The results of my test may reveal genetic variation for which the significance is not yet known. I acknowledge that interpretation of my results may change over time as additional evidence is gathered. I also understand that this could change what my results mean for me and my treatment over time.
	The test may find one or more '*variants of unknown significance*' (VUS), which means that the impact of the variant cannot be determined today. The understanding of a VUS may change over time. Testing of family members and/or future research may help clarify a VUS.
	The significance of my results may be uncertain or unknown; meaning an identifiable variant is not (yet) relatable to a disease diagnosis.

Unexpected Information (Incidental Findings)	The results of my test may reveal a chance of a disease in the future that has nothing to do with why I am having this test. This may be found by chance. I may then need further tests to understand what this means for me. If these additional findings are to be looked for, I will be given more information about this.
	I am aware that in very rare cases, there may be incidental findings with significant health implications for me and my family and that my physician may be under an obligation to inform me even if I have chosen not to receive information about incidental findings.
	Findings not related to my condition may also be revealed. I will be informed of such findings if clinical treatment or prevention is available. These findings will also be put in my medical record.
	The results may identify clinically actionable and/or non-clinically actionable secondary findings, not related to the initial reason for my genetic test.
	It is possible that results not related to the purpose of my genetic test may also be revealed. Though the healthcare providers do not actively look for these results, they will return such results to me if treatment or prevention is currently available based on the information they currently have about my condition. I may choose not to be informed of these results, even if treatment or prevention is currently available.
	There is a small chance that incidental findings about my health that are not related to my diagnosis may be identified when genomic testing is carried out. I will be informed of these incidental findings only if an expert committee, in consultation with my doctor or genetic counsellor, determines that these findings could have a significant impact on my health care.
Limitations of Genomic Testing	This report will not provide medical advice. The genetic results will include information my healthcare provider can use in combination with professional knowledge and clinical information to determine what might be causing my symptoms, and the best medical course of action. I should not ignore any symptoms I

	experience or discontinue treatment based on the content of this report. In case of doubt, I should seek medical advice.
	GWS does not always lead to a definitive explanation for a person's medical condition. This is due to current limitations in medical knowledge and/or testing technologies. Since the interpretation of results cannot be made with certainty, the implications of the results of the test on my health may be difficult to establish.
	A negative genetic test does not rule out a diagnosis of, a predisposition towards, or the ability to pass on a genetic disease, but it does decrease the likelihood that the gene(s) that will be tested for are involved in the disease.
	Genomic test results are based on current knowledge, which may change in the future. My sample may be examined again in the future when additional genes are found to be associated with my condition or when new testing methods are introduced.
	Since the interpretation of results cannot be made with certainty, the implications of the results of the test on my health may be difficult to establish.
	I understand that only the family specific mutation(s) will be tested therefore the test will not reveal other possible mutations that may be present in the gene(s) tested.
	Information about genetic variants may change with time. [Name of institution] may contact my referring practitioner if it learns of new information that may affect my results.
	Genomic testing is not able to detect every genetic condition. A test for a specific genetic condition may not be able to find every genetic variant responsible for that condition. My provider may recommend more tests in the future.

	There may be possible sources of inaccuracy. Rarely, inaccurate results may occur for various reasons including, but not limited to: mislabeled samples, inaccurate reporting of clinical/medical information, rare technical errors, or unusual circumstances such as bone marrow transplantation or the presence of changes such as mosaicism (small percentage of cells that may or may not be detectable by the test).
	The testing process involves highly skilled technicians and advanced technology. Although the method is extremely reliable, as in any laboratory, there is a small possibility that the test will not work properly or an error may occur.
	It is possible that my test results will not provide any benefit. Much about genetics and its role in health is still not known.
	It is important to remember that genomic testing is not a general health test and will not identify all gene changes that could contribute to health problems that may develop in the future. My physician may determine that further/other DNA testing is necessary in addition to this test.
	A normal result does not completely rule out the possibility that I have a genetic condition.
	Reanalysis may occur in cases where there are uncertain results. [Name of the institution] will only reanalyze my genome/exome sequencing results if a healthcare provider requests it as part of follow-up care.
	No laboratory test is 100% accurate. - The genetic diagnosis may be incorrect. - My true diagnosis may not be discovered by this test. - I may receive uncertain results.

	Genomic testing has some limitations: - There are no guarantees that this test will find a cause for my condition(s). - Further testing or information sharing may be needed to verify the results. - Tests are based on current best-practice knowledge, and this knowledge may change in the future. - The implications of my results may change at a later time point. - Procedures are in place to review knowledge against patient data to identify opportunities for updated diagnoses.
	A cause for the condition may not be found for a number of reasons, including: - the variant(s) causing the condition cannot be found by the test; - the gene causing the condition was not tested; - the gene causing the condition is not yet known; - the quality of my DNA sample was not sufficient; - my clinical diagnosis is inaccurate; - my family medical history is inaccurate. [Name of the institution] is taking extensive measures to avoid errors and failed tests.
Family Implications	My test results may have implications for my biological family members.
	Because genetic testing can be performed as a family analysis, the same genetic variants that are identified in me may also be found in other family members that have given a sample for testing.
	Unexpected family relationships may be identified through genomic testing.
	I understand that the genetic material or DNA in my sample (blood, solid tissue) will be tested for the familial mutations or variants of unknown significance (VUS) associated with [condition].
	This test may reveal that the biological relationships in my family are not what they seem.

	In some families, genomic testing might discover non-paternity, or some other previously unknown information about family relationships, such as adoption.
	GWS results may reveal that biological relationships in a family are not as they were reported to the healthcare provider. This includes non-paternity/non-maternity and adoption (the stated father/mother of an individual is not the biological parent) and consanguinity (the parents of an individual are related by blood). As incorrect information about biological relationships and health status may prevent the accurate interpretation of GWS results, it may be necessary to report these findings to the healthcare provider who ordered my test.
	Biological samples or related clinical information from my biological parents and/or biological family members may be requested to help interpret my results.
	In the event that my family members are followed for the same condition, my test results or related clinical information, if available, could be used to help interpret their results, but my identity will not be revealed to them.
Discrimination Risks	All these results and findings may have an impact on my insurability or employment.
	Testing may possibly affect my ability to obtain some types of insurance.
	Genomic testing may result in life insurance, disability insurance and/or long-term care insurance discrimination that is not prohibited by law.
DNA Storage	Blood and DNA samples are normally discarded after [number of] days, following test completion, unless I provide the laboratory consent to store the DNA after testing is performed. Storing my sample may allow me to request testing in the future without having to obtain a new sample, or to participate in future research, should I wish to do so.

	I will be asked if the laboratory can store my DNA for future tests ordered by my healthcare provider. I should feel free to say yes or no. The laboratory may also use my stored DNA for a variety of reasons, including testing new equipment, research, or future tests ordered by my healthcare provider. For such purposes, I will be anonymized/not be identifiable.
	To perform additional clinical genomic testing related to my condition and to avoid providing a new sample, my sample will be kept and stored at the [insert name] laboratory for up to [number of] years.
	The laboratory will store any remaining sample(s) for [number of] years, and may discard those samples after [number of] years.
	Sample collected (blood/muscle/skin/other) may be sorted for an indefinite time and can be retested if future testing may be more informative.
	The sample will be stored in the laboratory for a minimum of [number of] years.
Data Storage	Data from my test will be stored to allow for possible future interpretation.
	The laboratory will store the test report for [number of] years.
	The information from genomic testing will be stored by the laboratory according to government regulation.
	The data from my genomic test will be securely stored so that it can be looked at again in the future if necessary.
	My results and genomic data will be stored securely in databases that meet local/international security standards and laboratory guidelines.

Data Sharing	To help with the interpretation of my test results, my anonymized genetic information may be deposited in public variant databases where it will be shared with other geneticists or physicians, in [country] and/or around the world. Because of the broad nature of this data sharing and its anonymization, it is unlikely that I will directly benefit from this sharing.
	I agree that the result may also be disclosed, if necessary, to help other family members, for the purpose of their counseling and diagnosis, without disclosing details about myself. [Yes] [No]
	I agree that my de-identified genetic data may be submitted to genome-wide depositories as part of a global effort to better understand the role of gene variations in disease and health. [Yes] [No]
	My de-identified genetic variant may be/will be deposited in public variant databases.
	To help with the interpretation of my test results, my de-identified genetic information may be shared with other geneticists or physicians, in [country] or around the world.
	A preference not to share my genomic data will not affect the medical care I receive.
	Sharing of my genetic data and related health information may aid in obtaining a diagnosis for myself and for others. However, this sharing may provide no direct benefit to myself or my family.
	Sharing of my genomic data and health information can advance scientific knowledge. This includes sharing gene variant information with large databases to help improve scientific and medical understanding e.g. by comparing my results to those of other people.
	I give my authorization to: - Share genetic sequencing data in coded form (eg, genomic testing) in restricted access databases in order to reach a diagnosis for my disease YES ☐ NO ☐

	- Share clinical data and family medical history in a coded manner in restricted access databases in order to reach a diagnosis for my disease YES ☐ NO ☐ - Share photographs or images in restricted access databases in order to reach a diagnosis for my disease YES ☐ NO ☐
Quality Control / Quality Assurance	The normal laboratory practice of [name of institution] is to store the DNA extracted from my sample even after my current testing is complete. My DNA might be used for future analysis and/or to ensure that other testing (for example that of family members) is of high quality (i.e., quality control).
	My sample, data and genetic information may be used for quality control (QC) and quality assurance (QA), internal validation, test improvement, and training purposes.
	My residual samples may be used for clinical laboratory validation.
Protection of Privacy	My privacy is very important to [name of the institution], and they will take all appropriate measures to protect my privacy. They do not share any information like address, name, date of birth, contact information, medical record number, or social security number. All personal identifying information is replaced with a unique code.
	My results, genomic data and identified sample, or the fact that I have had genomic testing, will not be used or disclosed outside of my care without my consent, unless required or allowed by law.
	The laboratory will securely store the information. It can only be accessed by specified personnel.
	The results will be available to health professionals involved in my care.
	The laboratory results of my genetic test, diagnosis and other health information will be de-identified (i.e., information that directly identifies me is permanently removed) before being submitted to national or international public databases.

	When my data is shared there are safeguards in place to help protect my privacy, such as: - Personal identifiers (information) will be removed (such as my name and address); - Security measures that help prevent unauthorised access or misuse. However, there is always a very small chance that I might be re-identified. There may be other privacy and confidentiality risks that [name of the institution] does not know about today or cannot predict.
	- The laboratory will report test results to the physician or health care provider who ordered the test. - The laboratory will not give test results to other individuals without my written permission. - The written report is expected to become part of my medical record. My health insurance provider or other parties may have legal access to this information.
	My results are confidential to the extent allowed by law. Those with legal access include, but are not limited to, healthcare providers involved in my care and my health insurance provider. My results will be included in my electronic medical record and will only be released to other medical professionals from an outside institution, family members, or other parties (e.g., insurance carriers, government and oversight agencies) with my written consent or because allowed by law.
Health Records	After the test is completed the written report will become part of the my permanent medical record
	My doctor or genetic counselor can speak with me about my results.
	I will be informed of any results related to my state of health.
	The results of this testing will be placed in my electronic medical record. My doctor or genetic counselor will discuss the results with me. Genetic counseling is also offered at [name of the institution] if I would like to use this service.

Handling of Results	I will be told the results by a doctor or a genetic counselor who will arrange appropriate follow up care, as necessary.
	My results will be given to my health care provider who will discuss them with me.
	My test results will be sent to the physician that ordered the test. I will speak with my physician if I would like a copy of the test results.
	The laboratory will make every attempt to report results as soon as possible, but cannot accept responsibility for delays.
	The sample, genomic results and test report will be handled according to applicable law and standard laboratory practice.
	Relevant clinical testing results will be given in person.
	I will be told the results by a doctor or a genetic counsellor who will arrange appropriate follow up care, as necessary.
Risks Associated with Genomic Testing	Whole exome sequencing may identify serious, untreatable genetic conditions. It may be distressing, both for me and my family. The detection of such a condition could also affect the health or health care needs of my siblings, children, or other close relatives. The doctor can arrange needed follow up, such as meeting with a genetic counselor, social worker, spiritual care services, or a psychologist.
	This test requires DNA most often provided from a sample of [identify type of sample]. [Include potential side effects relating to the collection of sample]
	Learning about my test results might cause anxiety and psychological stress, which include alteration of self-image, increased anxiety and guilt, familial stress related to identification of other at-risk family

	members, as well as difficulty obtaining life and/or disability insurance or employment, and the detection of misattributed parentage.
In Case of Death	In the event of my death, my results can be released to: [insert name and contact info].
Recontact	I may be recontacted for the following reasons: - Additional samples may be requested. - I may be asked to complete survey(s) regarding my understanding and experience of genomic testing, costs associated with living with my condition.
	The opportunity to participate in research that may or may not be related to my reason for undergoing genomic testing may arise. These research opportunities may or may not provide any direct benefit to my health or treatment. All research will be approved by regulatory and ethical boards prior to being conducted.
	After testing is completed, there may be research studies that I may be eligible for and may be of interest. The laboratory may share my contact information with researchers who have a research study with appropriate ethics approval and for which I may be eligible for participation. [Yes] [No]
	Understanding of genetic variants is rapidly advancing, meaning that some of the changes [name of the institution] find in my genome might be better understood in the future. [Name of the institution] recommends that I keep in contact with my healthcare provider on an annual basis to learn of any new developments in genetics and to provide any updates to my personal or family history.
	The laboratory may contact my physician should new information become available about the findings of this test that could affect my medical care.

	[No recontact needed:] I agree to my DNA sample and clinical information being used for ethics approved research related to [condition].
	My doctor may inform me of clinical trials associated with my condition: [Yes] [No]
	Due to the rapid advancement of knowledge in genetics, it is possible that the understanding and interpretation of my results may change over time. Therefore, I will keep in touch with my physician.
	Significant advances in society have been made as a result of research involving humans. I wish to be recontacted to be invited to participate in ethics-approved research, for which I may be eligible: [Yes] [No]
	The [name of the institution] conducts research about inherited genetic disease. I would like to be contacted to know about research studies in which I may be able to participate: [Yes] [No]
	After my treatment has ended, if there is new knowledge about my genetic analysis with health implications for me, I agree to be recontacted: [Yes] [No]
	The opportunity to participate in research that may or may not be related to my reason for undergoing genomic testing may arise. All research will be approved by regulatory and ethical boards prior to being conducted. I am willing to be contacted about/participate in future research opportunities: [Yes] [No] This will entail the sharing of my personal contact information (e.g. name and email).
Withdrawal/Change of Mind/Right not to Know (Unperceived Risk)	In the case that I refuse to take the test, I should consult with my healthcare provider for possible alternatives, and implications for diagnosis and treatment.
	I am free to withdraw at any time prior to taking the test without any impact on my future health care.
	If I change my mind, I can choose not to be told about the result.

	I am aware that I can terminate the examination at any time without giving reasons and/or abstain from the notification of the results. In this case the findings remain with the above mentioned institute.
	I can change my mind about having genomic testing or being told the results. I can cancel the test at any time before the laboratory finishes the test.
Destruction of DNA/Data	I request my sample(s) be destroyed after the required storage time: [Yes] [No].
	I have the right to request the destruction of all test/examination results not already known to me.