H3AFRICA REPORT ON INFORMED CONSENT AND COMMERCIALISATION

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BACKGROUND

Over the past decade, there has been an acceleration in genomics research, its application to biomedical technologies, and its translation into healthcare products and services. These advances are critical to realizing the potential of genomics research for facilitating improved health and disease prevention, diagnosis, and treatment. Despite its tremendous opportunities, the dynamic and increasingly global landscape of genomic research commercialisation has been accompanied by a variety of ethical challenges and concerns pertaining to researchers, healthcare professionals, patients, research participants, families, communities, academic institutions, industries, and governments [1-6].

Recent reports of alleged unauthorized use of DNA samples from hundreds of African people to develop a DNA chip [7] has reignited discourse on the meanings, implications, and impacts of commercialisation, benefit sharing, and appropriate consent in genetics and genomics research. They have also spurred introspection within the field and have amplified attention to protocols and procedures for consenting participants into large-scale global projects that are likely to generate commercial resources or products.

The Human Heredity and Health in Africa (H3Africa) Initiative was established in 2012 and facilitates fundamental research into diseases on the African continent while also developing infrastructure, resources, training, and ethical guidelines to support a sustainable African research enterprise. The H3Africa Consortium consists of 51 African projects that include population-based genomic studies of common, non-communicable disorders such as heart and renal disease, as well as communicable diseases such as tuberculosis. These studies are led by African scientists, with and for Africans, and use genetic, clinical, and epidemiologic methods to identify hereditary and environmental contributions to health and disease. To establish a foundation for African scientists to continue this essential work into the future, the consortium also supports many crucial capacity building elements, such as: ethical, legal, and social implications research; training and capacity building for bioinformatics; capacity for biobanking; and coordination and networking.

In light of the vast amount of genetic diversity in African populations, H3Africa provides an unparalleled research resource for the benefit of people in Africa and across the globe. Thus, the sharing of data is a guiding principle for H3Africa, and the translation of research findings to commercial products, resources, and services is consistent with its mission. Driven by a commitment to transparency and accountability, the H3Africa leadership convened a panel of experts (authors) to review the research ethics processes and practices being employed in the H3Africa Consortium projects with the aim of identifying gaps and making recommendations for improvements going forward with regard to commercialisation. Specifically, the panel was asked to review H3Africa consent documents and talk with key members of the Consortium, including members of the Ethics Working Group, to determine how H3Africa Consortium projects have implemented informed consent procedures for studies involving biobanking and the sharing of data and/or biospecimens.

NATURE AND SCOPE OF THE REPORT

This report reflects the panel's response to the charge. In organizing the report, it seemed important to lead with a typology of commercialisation to facilitate framing of the findings and recommendations. Gleanings from communications with a variety of Consortium members helped provide context for the entire project, particularly the interpretation of findings from the consent review process. Careful examination of H3A guidelines and policies pertaining to data and biospecimen access was a foundational and critical element of the work. The review of the consent and assent forms, information sheets, and other research documents submitted by a subset of H3Africa investigators is the heart of the report. It drives the summary and recommendations, informed by other components of the report.

We note that this report focuses on ethical questions concerning use and commercialisation of data and/or biospecimens. While there are also many legal issues raised by commercialisation from genomics research (e.g. conflict of interest, intellectual property rights), there is substantial diversity in the legal aspects of commercialisation that are largely dependent on policies and laws set by institutions, organizations, and countries. Rigorous examination of these issues on a global scale, such as in H3Africa, is beyond the scope of this report.

Similarly, we acknowledge the complexities surrounding commercialisation in relation to legacy collections. However, given that the majority of the current H3Africa projects are utilizing new samples and data, we are not addressing previous collections in this report. Over time, the topic will become more relevant to H3Africa, and the outcome of this report can be a useful guide in developing mechanisms to address it.

THE MEANING OF COMMERCIALISATION: TOWARDS A TYPOLOGY

'Commercialisation' is open to interpretation in different ways, which leads to potential divergence in understandings when the term appears in a consent form. Looking at the Word Salad in Figure 1 provides an illustration of the number of related concepts that may be involved. One caveat: this shows related concepts in the English language, but it is not necessarily the case that all cultures will understand commercialisation in the same way and for some the concept may be inseparable from the idea of money changing hands. Conversations with H3Africa members have informed us that this is the case in some participant communities. At one extreme the very idea of commercialisation may produce a reaction akin to a phobia, as when it is considered to involve making profits for a party or parties, likely at the expense of others (where the loss involved can take various forms, not only financial but possibly affecting someone's, or a group's, sense of identity). Hence it may be associated with the concept of *exploitation*. Certainly, it is not hard to find examples of situations where this has occurred, historically (see e.g., [8, 9]). At the other end of the spectrum, commercialisation may be regarded as a necessary means towards producing a public good. Drugs and vaccines, for example, which are essential for public health (as in the context of the COVID pandemic) require investment in research and clinical trials as a prerequisite for public benefit. Indeed, research that does not lead to translation into clinical practice might well be regarded as at least partly a failure. In

between these two ends of the spectrum there are contested areas, e.g., over the distribution of benefits, and some of these have been the subject of legal cases. Such cases (e.g. the John Moore cell case in the United States) are evidence that the relationship between commercialisation and the human body has had a fraught history [10].

Figure 1

There have been long-standing debates about topics such as the marketing of body tissues and body parts, and about the proper allocation of value arising from the conduct of research on bodily tissues. As far back as Immanuel Kant, it was clear that parts of the body should not be sold [11]. My body is not a possession: it is *me*. The conclusion of this line of thought was that it is wrong to sell even a tooth [12]. However, we may regard this argument today, it is clear that selling counts as one possible type of commercialisation and may be one that readily springs to mind when the concept is under consideration.

While selling may be an obvious mode of commercialisation, however, in the sometimes long and winding pathways from research to product development, there are others to be considered. Much may depend in these debates, on how bodily parts and tissues are regarded, and how *different* ones (e.g. blood) can be thought of as having more or less importance. Also, the identity of the different parties involved, and the balance of power between them, may affect how we regard commercial transactions.

In thinking, therefore, about the meaning and ethics of commercialisation, it may be helpful to develop a typology (see Table 1). The table sets out factors to take into account in thinking about the acceptability and desirability of a particular instance of commercialisation. The table can be used for any individual case that is proposed in relation to a research population.

Table 1: Commercialisation Typology

	Modifying Factors								
Types of Commercial Engagement	Object to be commercialized (e.g, samples, data)	Source (e.g, individuals, groups, populations	Identity of commercial entity	Consent	Community engagement	End use and users	Potential harms/ concerns	Potential benefits	Role of intermediaries (e.g., governance structures)
Partnership									
Clinical Translation/ Product Development									
Research by Commercial Entity									
Investment in Infrastructure									
Buying and Selling									

The vertical columns in the typology describe different modes of commercialisation. So, the first question is, exactly what type of commercial engagement is proposed? Is it a partnership, as, for example, when a University research group enters a partnership with a commercial partner in order to do research leading to a product such as a vaccine? Or would the commercial arrangement be best described as giving a commercial entity a potential monopoly, in relation to the ownership of the results of research?

On the other hand, is the proposed commercial engagement an arrangement to allow *access* to samples for research purposes, or to sell to a company samples collected from a population?

Another possibility is a situation that might best be described as one in which a commercial company is offering to invest in infrastructure for research or future health care – for example by financing laboratories or treatment facilities. If so, issues arise about what conditions might be attached.

The type of engagement in the vertical column is only the first step in an assessment. The horizontal columns illustrate various *modifiers* of potential commercial engagement. For example, it might be relevant not just to consider the involvement of commerce, but to discuss what *type* of company is involved. Not all companies are (whether justifiably or not in particular cases) regarded in the same light, reputationally speaking. There may be a

question as to whether the ethos and aims of a commercial entity are compatible with the purposes of h3africa, for example.

In the context of research involving human participants who donate samples, in particular, the type of sample or data collected, what consent has been given, if any (and what does it say about commercialisation) and whether there has been community engagement, are all highly significant modifiers. There is also a question about what role has been or will be played by intermediaries such as ethics committees and/or committees with a remit to decide on questions of access, especially where consent appears to be silent on the issue of commercialisation.

Another set of questions includes the consequences in the longer term. These include issues of end use. Who will the end users be who will use any product arising from the commercialisation process: the source population and/or others? What are the potential harms and losses that may accrue to the source population? And what benefits? In particular, what arrangements, if any, are to be made for benefit-sharing? Some themes cut across all these questions and have therefore not been included as separate items in the typology. These include intellectual property arrangements and questions of conflicts of interest. Intellectual property is a feature of both benefit-sharing and ownership: it is something to be considered in partnership arrangements. There are also questions about who is in a position to claim intellectual property and there may be complicated questions of potential conflict of interest for researchers working in educational organisations such as Universities.

The typology does not give weighting to the cells, but there are some guiding principles to take into consideration about priorities:

- First, there is a need to have regard to the context in which the assessment is to be carried out. While this typology could be used in different settings, in the present context there is an overriding need to ensure that any instance of commercialisation is not in conflict with the purposes and aims of h3africa.
- Second, specific consent to commercialise (or not) is widely acknowledged to override other considerations. Difficulties arise when consent is either lacking – e.g., in a legacy collection - or unclear.

In order to demonstrate how the typology can be used, we are including a case study that was prepared by and for members of H3Africa (see Box 1). It would be possible and perhaps necessary to go into considerable detail in discussions of different cells in relation to consideration of real world cases - for example, discussion of any commercial entity involved might give rise to debate about its aims and mission statement - but our treatment is designed to illustrate, briefly, the sequence of different steps involved.

Box 1: Cervical Cancer Research Network (CCRN) Case Study

Prepared by Victoria Nembaware, Nchangwi Synita Munung and Godfrey Tangwa for H3Africa

The CCRN study recruits women who have been diagnosed with cervical cancer in hospitals and clinics and collects blood samples from them for genetic and biochemical analyses. Samples from the data, as well as the genotypic and phenotypic data from the project, will be shared with other researchers.

While conducting community engagement for the project, Sr. Ruth and her team meet 32-year old Banji, enrolled into the study 2 years ago. Banji is very happy to see Sr. Ruth and requests to have a conversation with her. Banji has three requests for Sr. Ruth:

a) Could Sr. Ruth, please, assist in making sure she (Banji) receives her treatment faster? Banji is on the waiting list to see the Oncology specialist. She is looking forward to starting a family with Rogers.
b) Could Sr. Ruth, please, assist in helping her sisters to be screened for cervical cancer? Banji's older sister passed away a few months ago from cervical cancer complications. Banji also has two younger sisters that are in need of screening but the procedure in the public healthcare system takes too long.
c) Her partner, Rogers, had also signed up for a smoking study (Sr. Ruth was recruiting) and he is keen to find out any results that could help him as he is still struggling to quit smoking.
d) Banji had recently joined a new church in the hope that they might provide a cure for her condition through a miracle. The church forbids the sharing and storing of any bodily fluids, specimens or even data; so she would like all her materials to be returned to her as soon as possible so that the prophet could pray over them before destroying.

Sr. Ruth goes back to the office and asks Matthew and Dr. Kune to check for Banji's and Rogers' results and samples. They realize that both Banji and Rogers are carriers of the Sickle Cell Disease. In the meantime, Dr. Kune meets Professor Tabo to discuss his career plan. Having worked hard in academia over the past years and yet unable to secure a full time position, owing to lack of first and last authorship of manuscripts; he has started the process of registering a diagnostic company in Zambia. He plans to use samples and data from the CCRN since he worked closely with Matthew on this project. Professor Tabo requests for some time to think through this since it has implications for Intellectual Property and Commercialization and he cannot quite remember if all the sites signed an identical consent form and what the implications are for data sharing (as per H3Africa guidelines) if a diagnostic company were created?

Meanwhile, Prof. Gregory calls Prof. Tabo to inform him that he has a Post-doctoral Fellow in the USA who has secured his own funding and has a novel idea and would like to use the CCRN data that Matthew had worked on. They are also thinking of starting a for-profit direct-to-consumer (DTC) genetic testing company, and are of the opinion that the data from the CCRN will be a useful resource for the company. He then invites Prof. Tabo, Dr. Kune and Matthew to review the work after completion and says that they could gain middle authorship should they make appropriate contributions to the manuscript. They could also become shareholders in the DTC genetic testing company.

Dr. Kune is excited at all these new developments and asks Matthew to present their plans to the Steering Committee of the H3Africa Consortium. The Steering Committee asks Mathew to present their project ideas to the Ethics Working Group, so they could advise accordingly and says that an application should also be sent to the H3Africa Data and Biospecimen Access Committee.

Personae

Professor Tabo works at the National University of Zambia. He has been studying cervical cancer for three decades and is the lead investigator of the Cervical Cancer Research Network (CCRN). He has an H3Africa research grant to research on genetic predisposition to cervical cancer. The project enrolled research participants form Malawi, Nigeria, the Democratic Republic of Congo (DRC) and Zambia. **Dr Kune** is a co-investigator on the CCRN research project. He is also based at the University of Zambia and is a trusted collaborator of Prof Tabo. **Sr. Ruth** is a Senior research nurse and the coordinator of the research project. She also conducts Community Engagement activities. **Matthew** is a CCRN Post-doctoral researcher. He has invented a novel diagnostic tool for predicting the likelihood of an individual getting cervical cancer. This test is specific for the population under study. A pre-print of the publication of this novel tool has been released. While Matthew has training in laboratory and bioinformatics analyses, he is interested in ethics. **Professor Gregory** is a long-term collaborator of Prof. Tabo, based in the United States of America. Matthew had visited Prof. Gregory's laboratory for mentorship and training. Mathew had developed the diagnostic tool for early detection of cervical cancer while on this visit. Copies of his data are in Prof Gregory's laboratory.

Analysis of the CCRN Case Study

This case study (see Box 1) raises a number of issues apart from those of commercialisation, but for present purposes only the latter will be considered. Using the typology, the first thing to be considered is what instances of commercialisation are involved, before proceeding to look at the modifying factors.

Type of commercialisation. Two different companies are considered.

(1) The diagnostic company in Zambia: A diagnostic company is to be set up. In the vertical column, this could include ticking the clinical translation box, if the aim is to offer a service. It could also involve ticking the infrastructure box, as the company is to be located in Zambia. Professor Tabo realises there are also issues of intellectual property involved.

(2) The for-profit direct-to-consumer company: The type of commercialisation involved here could be described as selling, i.e. selling a service to anyone who will pay. It does not fit into the category of offering a clinical service. As in the case of the Zambian company, issues of intellectual property are involved.

Object to be commercialized. Turning to the horizontal rows, which include modifying factors for both types of company, the first question is what is the object of commercialisation. The project involves collecting blood samples along with genotypic and phenotypic data.

Source population. The samples in the CCRN project have been collected from women who have been diagnosed with cervical cancer. They are therefore people who are in a vulnerable situation. The participants have been drawn from Malawi, Nigeria, the Democratic Republic of Congo (DRC) and Zambia.

Identity of commercial entity. The diagnostic company will be located in Zambia, being established by Dr. Kune, who plans to use samples and data from the CCRN project, on which he has been a co-investigator. It is made clear, however, that it is Matthew who has invented the diagnostic tool. It is also said that the test is specific for the population under study. Questions arise as to how the company will make a profit from this, and the extent to which it will be possible to branch out beyond this in the future.

The DTC company is the idea of Professor Gregory, who is located in the United States. He has a postdoc who has a ‘novel idea’ and they would like to use the CCRN data as a resource for this company.

Consent. To what extent has consent been acquired from the source population? The issue is raised as to whether all the participants have signed an identical consent form. The consent also needs to be checked to see precisely what language, if any, is used in relation to commercialisation possibilities. It is known that at least one participant has requested return of her samples.

Community engagement. It is made clear that community engagement has taken place but there is little detail on this. It is not stated, for example, whether the issue of commercialisation was addressed at this stage. This needs to be checked.

End use and users. We are told that the diagnostic company will be located in Zambia and that the test is specific to the sample population, but that population is drawn from multiple countries. To what extent will those countries have access to the same testing opportunities?

The DTC company aims to offer a for-profit service, presumably to anyone who will pay. It is not made clear what the 'novel idea' is.

Potential harms/concerns. There are clearly issues of equity and justice to address. All the sample donors are women, whereas the people who stand to benefit from the companies, it seems, are men. There are also issues of power to address in relation to intellectual property. Matthew, who has developed the diagnostic test, is a postdoc, but his development of the test benefited, apparently, during a visit to Professor Gregory's laboratory in the United States.

Potential benefits. In the light of the fact that some people stand to benefit financially from the commercialisation of the collected samples and data, the question of benefits to the source population need to be considered. If commercialisation was addressed in the informed consent and/or community engagement process, was it made clear that the research participants would not receive a share of any potential profits? If not, what other mechanisms of benefit-sharing might have been addressed?

In relation to the company in Zambia, the diagnostic text itself is of potential benefit to future members of the population, but it is not clear that this was envisaged beforehand.

In the case of the DTC company, Professor Tabo, Dr. Kune and Matthew are offered shares in the company, but there is no mention of benefit-sharing with the sample source population.

Role of intermediaries and governance structures. In the case of h3africa, there are policies and structures which provide an extra layer of protection over and above the consent forms themselves. Professor Tabo thinks about the h3africa guidelines: the overriding aim of h3africa is to bring benefit to African populations. While the first company is to be located in Zambia and will directly provide a service there, the DTC company will not.

The role of the Data and Biospecimen Access Committee (DBAC) is also mentioned, which will consider requests for access.

<u>Conclusions from Case Study Analysis</u>

Using the typology does not generate a precise conclusion as would a mathematical formula, but it makes clear which areas are very problematic.We suggest that access to African samples for the DTC company in the United States is ruled out on the grounds of lack of benefit to African populations and potential exploitation of the sample population, although not enough detail is known about the content of the informed consent.

As regards the company in Zambia, here a better case can be made for benefit to the source population(s), although once again, the informed consent needs to be checked and the precise terms on which the diagnostic company will operate should be further investigated, for a proper ethical assessment.

This is in line with the overall position that the paramount considerations are that any commercialisation should be in line both with the informed consent given and with the principles on which H3Africa is based.

CONVERSATIONS WITH KEY H3AFRICA CONSORTIUM MEMBERS

As part of our data-gathering process, we had a variety of conversations with several groups and individuals integrally involved with the H3Africa initiative. One author participated in a dialogue on commercialisation at the planning session for the H3Africa consortium meeting that was slated to be held in Kenya in March 2020. This author also participated in an Ethics webinar that engaged multiple H3Africa project investigators and team members. Subsequently, we were invited to a meeting of the H3Africa Ethics Working Group where a considerable amount of time was devoted to the topic of commercialisation. On multiple occasions, including during the fall 2020 virtual H3Africa Consortium meeting, we briefed the Independent Expert Committee (IEC), Steering Committee, and funders on our progress and received invaluable input. Throughout the project, we also consulted with the Coordinating Center PI and other critical individuals to request other materials or gain more in-depth understanding of various topics or questions that arose during our work.

Through these insightful exchanges, we received first-hand knowledge about perspectives of the informants, activities on the ground in implementing the H3Africa projects, as well as the breadth and depth of issues to be explored. We have incorporated this feedback to the extent possible and as it fits within the scope of our charge. We believe this has enhanced the quality and, hopefully, the utility of the report.

H3AFRICA DOCUMENTS RELEVANT TO DATA AND BIOSPECIMEN ACCESS

We have reviewed several documents developed by the H3Africa Consortium that pertain to the report. The H3Africa Data and Biospecimen Access Committee Guidelines (http://biorepository.h3africa.org) outlines the process for review of requests from researchers for access to biospecimens collected and data generated by the H3Africa Consortium. The Committee is composed of nine voting members with diverse professional backgrounds with scientific, bioethics and data expertise. The H3Africa DBAC maintains detailed records of those who have been given access to biospecimens and datasets; this ensures programmatic oversight. Related documents reviewed include the H3Africa Data Biospecimen Request Form, H3Africa Data Access Agreement, and the H3Africa Consortium Data Sharing, Access and Release Policy which was updated in December, 2019. We also reviewed the H3Africa Biorepository Biospecimen Release Material Agreement (BRMTA) which documents the transfer of biological material from the H3Africa Host Biorepository to the recipient scientists and their institution.

Our assessment of these documents reveals the substantial effort expended by the H3Africa Consortium to safeguard and appropriately share biospecimens and data from H3Africa research participants. We expect that this report, commissioned by the

Consortium, will facilitate continuation of these efforts, leading to specific H3Africa guidance concerning commercialisation.

INFORMED CONSENT: DATA SHARING AND DATA USE

Informed consent and voluntary participation are recognized as essential to ethical conduct in the implementation of scientific research. Informed consent is based upon the ethical principle of respect for persons for both individuals and the communities within which they live. There are three key elements of the consent process: communication of information about the purpose and procedures of a study, comprehension of this information, and voluntary participation on the part of the individual being recruited to a study or their surrogate. Ideally, the consent process rests on several assumptions. First, that information about a study shared by investigators uses language and concepts that are understood by participants. Second, that potential participants are able to comprehend the information they are given. Third, that participants or their surrogates have the ability to voluntarily consent to joining a study. Practical issues faced by investigators in the field may diminish the possibility of achieving this ideal process (such as language difficulties associated with the use of complicated scientific concepts).

There is now a growing literature on applications of the informed consent process in middle and low-resource contexts and specifically, on consent processes for genomic research implemented in African settings.[13-24] Additional issues associated with informed consent for genomic research include the establishment of and governance for biobanks [25-33] and, in some cases, the creation of immortalized cell lines. [34, 32] The H3Africa Guideline for Informed Consent (https://h3africa.org/), developed by the H3Africa Ethics and Regulatory Group, describes challenges surrounding the implementation of informed consent for genomic research, highlighting a range of issues faced by investigators in the design and implementation of genomic studies. For example, The H3Africa Guideline for Informed Consent (https://h3africa.org/) calls attention to concerns that arise over literacy skills, questions associated with who has decisional authority to provide consent, and variability in national policies that may impact the implementation of informed consent for genomic research. The H3Africa Guideline for Informed Consent (https://h3africa.org/) also emphasizes the importance of conducting community engagement in developing processes for informed consent for genomic research.[35, 36]

Processes for implementing Informed consent are represented by a number of different approaches. In some cases, participants are asked one time to provide a signature indicating their voluntary agreement to join a study. Models for a dynamic consent process emphasize the importance of an ongoing engagement with participants throughout a study, periodically revisiting informed consent. In the context of genomic research, another approach to informed consent is represented by tiered-consent in which potential participants are offered choices about the storage, use and sharing of specimens and data.[37, 20] Broad consent, in which potential participants give their permission to share stored genetic material with other investigators for future unspecified research, represents an additional approach to the informed consent process.[38] The H3Africa Guideline for Informed Consent (https://h3africa.org/) suggests that broad consent is preferred for

genomic research in African settings. While broad consent reduces some of the complexities associated with tiered consent, challenges remain including the possibility of diminished autonomy and the reduction of participants being allowed to indicate their particular choices. [39-41]

REVIEW OF H3AFRICA CONSENT DOCUMENTS

In an effort to better understand information communicated to potential participants in H3Africa projects involving data sharing, storage and future use of genetic information, we reviewed the informed consent documents of a sub-set of 18 projects. Our analysis includes an assessment of the specific language used in the consent documents to provide information about data sharing, data use, future use, and references to commercialisation of genetic samples.

As shown in Table 2 below, a total of 38 informed consent documents associated with the 18 projects were reviewed: 26 adult consent forms; 8 child assent forms; and 4 information sheets. More than half of the 26 adult consent forms (n=15, 58%) included checkboxes for participants to indicate their understanding of, or willingness to agree to a range of actions including, for example, storage of genetic material and in some cases other data, agreement to share data for future use, and transfer of the data to researchers out of the country for further analysis. Three of the 26 adult consent forms included checkboxes to allow data to be shared and used by researchers in any field, or a specific field. Two of the 8 child assent forms included checkboxes for allowing data storage, future use of samples, and biobanking. The four information sheets reviewed provided detailed information on study goals, procedures, data sharing and future use of data.

Table 2: Consent Forms: Number and Types of Consent Forms

Projects	Number of Forms	Adult Consent	Child Assent	Information Sheet
1	1	X Checkbox sample sharing, future use		
2	2	X X		
3	1	X		
4	3	X X Parent for child	X	
5	2	X Checkbox data sharing researchers any field, allow samples sent abroad		X
6	1	X		
7	3	X Parent/caregiver consent, checkbox allow storage, re-use of samples and data, share with researchers in any field, transfer out of country, photos X Parent for child consent, checkbox stored without identifiers, sharing samples and data with investigators in any field, samples sent out of country, photos		X

Projects	Number	Adult Consent	Child Assent	Information Sheet
8	5	X Checkbox allow samples stored, future use X Ebola survivor study consent form, checkbox allow samples stored, future use X Lassa fever consent form, checkbox allow samples stored, future use	X Assent, Sierra Leone X Assent, Edo State	
9	6	X Parent/guardian consent adolescent enrollment X Parent/guardian consent, checkbox storage, future use X Consent, enrolment Phase V:Antiretroviral Therapy X Consent, specimen storage, Phase V: Antiretroviral therapy, checkbox storage, future use	X Adolescent consent enrollment X Adolescent consent, checkbox storage, future use	
10	1	X Checkbox future use		
11	2	X Checkbox biobanking	X Checkbox biobanking	
12	1	X		
13	3	X Checkbox data sharing, future use in specific field, and research in any field X Parent consent for child	X	
14	1	X With checkbox DNA tests, data storage, data sharing, data sent out of country, new studies reviewed by ethics committee, no direct benefits from study		
15	2	X Checkbox understand DNA tests, approved by ethics committee, DNA and information may be used, DNA sent out of country, data storage, new studies reviewed by ethics committee, no direct benefit from study, may withdraw any time		X
16	1	X		
17	1	X Parent and child consent combined		
18	3	X Checkbox for DNA, data storage, data sharing	X	X
18 Projects	**38 Forms**	**26 Adult Consent**	**8 Child Assent**	**4 Info Sheets**

Table 3 describes the types of samples collected that investigators would share with other researchers, agencies, and corporations. The exact language included in the informed consent documents is listed. The term “unspecified” is used to represent general language without specific information. Twelve (67%) of the 18 projects suggested that unspecified samples would be shared. Thirteen (72%) of the 18 projects specified that blood would be shared and 14 projects (78%) indicated that DNA or genetic material (e.g., saliva, urine, nose swabs, biological samples) would be shared. Three (17%) of the 18 projects specified that tissue, such as biopsies, would be shared. The majority of the 18 projects (n=14, 78%) specified that health information would be shared (e.g., unspecified information, medical or health histories, lab tests, questionnaires, body measurements, photos).

Table 3: Consent Forms: Types of Samples Shared

Projects	Unspecified Samples	Blood	DNA, Genetic Material	Tissue	Health Information
1	X	X	X		X unspecified
2		X		X biopsy	X unspecified
3	X				
4		X	X saliva, urine	X biopsy	X unspecified
5	X		X human, bacteria, DNA		X unspecified
6		X	X		X health history, lab tests
7	X		X		X unspecified
8		X	X urine, saliva		X unspecified
9	X	X	X biological samples (vaginal swabs), urine		X unspecified
10	X		X	X biopsy	X medical history, lab tests
11	X	X	X saliva, urine, sputum		X health history, lab tests
12		X	X		
13		X			X unspecified
14		X	X		
15		X	X urine		X questionnaires, test results, body measurements
16		X			X health history, lab tests
17		X	X urine, nose swabs		X unspecified, lab tests
18			X DNA, saliva		X unspecified, photos
Total 18 100%)	**12 (67%)**	**13 (72%)**	**14 (78%)**	**3 (17%)**	**14 (78%)**

As shown in Table 4, consent documents for all eighteen projects indicated that samples would be shared with unspecified researchers, scientists or investigators. Thirteen (72%) of the 18 projects indicated that samples would be shared internationally with researchers out of the country. Seven (39%) of the projects said that samples may be shared with entities such as universities, laboratories or hospitals. Six (33%) of the projects indicated that samples would be shared with the European Genome/Phenome Archive, dbGap, or NIH/GWAS. Two (11%) of the 18 projects indicated that samples might be shared with governmental agencies. Three (17%) of the 18 projects pointed out that samples could be shared with unspecified companies, and three (17%) projects indicated that samples could be shared with drug companies.

Table 4: Consent Forms: Sample Sharing with Individuals, Institutions, Agencies, Corporations

Projects	Unspecified Researchers Scientists Investigators	Out of Country Researchers Scientists Investigators	Universities Laboratories Hospitals	European Genome Phenome Archive dbGAP NIH/ GWAS	Government Agencies	Unspecified Companies	Drug Companies
1	X	X	X				
2	X			X		X	
3	X	X					
4	X						
5	X	X	X				
6	X	X	X		X	X	
7	X						
8	X	X		X			
9	X		X	X			
10	X	X	X	X			X
11	X	X	X	X	X	X	X
12	X						
13	X	X	X	X			X
14	X	X					
15	X	X					
16	X	X					
17	X	X					
18	X	X					
	18 (100%	**13 (72%)**	**7 (39%)**	**6 (33%)**	**2 (11%)**	**3 (17%)**	**3 (17%)**

Table 5 describes the language in the consent forms that designate how the samples collected during the study would be used in the future. All of the adult consent forms and information sheets for the 18 projects specified that the samples would be used in future research. The consent forms and information sheets for seven (39%) of the 18 projects suggested that the samples could be used to develop drugs or other products and one project indicated that the samples could be used to develop vaccines. In describing the future use of samples, four (22%) of the consent forms for the 18 projects used the word "commercialisation" and one project indicated that future use could include sharing

samples with “companies that make and sell medicine.” The term “commercialisation” was not defined in the documents when it was used.

Table 5: Consent Forms: Future Use of Samples

Projects	Research	Drug and Product Development	Vaccines	Commercialisation
1	X			
2	X			
3	X			X “commercialisation”
4	X			
5	X			
6	X	X		X “commercialisation”
7	X			
8	X	X		X “commercialisation”
9	X		X	
10	X	X		
11	X	X		X “companies that make and sell medicines”
12	X	X		
13	X	X		
14	X			
15	X			
16	X			
17	X	X		
18	X			
18 (100%)	**18 (100%)**	**7 (39%)**	**1 (5%)**	**4 (22%)**

Table 6 identified the number of consent forms associated with the 18 projects that explicitly promised not to sell DNA samples or indicated that profits from drug or product development would not be shared with study participants. Six (33%) of the consent forms for the 18 sub-set of projects reviewed said explicitly that DNA samples would not be sold and six (33%) indicated that profits would not be shared with the participants. As shown in Table 6, five of the 18 projects indicated both a promise not to sell samples in addition to stating that profits from drugs or other products would not be shared with participants.

Table 6: Consent Forms: Promise Not to Sell Samples, Profits from Drug/Product Development Will Not Be Shared with Participants

Projects	Promise not to sell samples	Profits from drug/product development will not be shared with participants
1		
2		
3		X
4		
5		
6	X	X
7		

Projects	Promise not to sell samples	Profits from drug/product development will not be shared with participants
8		
9		
10	X	X
11	X	X
12		
13	X	X
14		
15		
16	X	
17	X	X
18		
Total 18 (100%)	**6 (33%)**	**6 (33%)**

SUMMARY

Here we summarize findings from our conceptual and empirical work that inform our recommendations to H3Africa for identifying and addressing ethical issues regarding commercialisation.

The commercialisation typology we provide for genomic research samples and data highlights the complex range of meanings associated with "commerce." Types of commercialisation are modified by myriad factors including, for example, the types of samples to be shared, whether or not consent was obtained, the end-users of the samples, and the potential benefits or risks. We have illustrated that rather than a polarity, issues surrounding commercialisation fall along a continuum between exploitation and shared benefit. A common understanding of commercialisation is that it implies buying and selling. The benefits and risks associated with buying and selling depend upon what is being "bought" and what is being "sold" and the context within which these transactions take place. The case study we present serves a practical guide for exploring and addressing this and other aspects of commercialisation.

Our analysis of the informed consent documents included with the sub-set of 18 H3Africa projects involving data sharing, data storage and future use of samples, suggest clarity about sharing genetic samples. All of the projects reviewed, for example, indicated that samples would be shared with other researchers, scientists, or investigators. However, less than half of the 18 projects indicated specifically on consent forms that genetic samples would not be sold, and that participants would not share in the profits from drug or product development. Moreover, only four of the eighteen projects used the term "commercialisation" or language that implies commercialisation (e.g., "companies that make and sell medicines).

Investigators conducting genomic research are often unable to offer potential participants specific information concerning with whom samples or data will be shared. Nor is it always possible to be specific about the nature of product or drug development and how

products/drugs will be marketed. Therefore, in the development of consent documents for genomic research, investigators use more general language to describe with whom data will be shared--researchers, universities, or corporations. Our findings are consistent with this approach.

RECOMMENDATIONS

The following recommendations are based on: what is known (or not known) about the global landscape of commercialisation; the commercialisation typology we have provided; and our qualitative and quantitative findings regarding current H3Africa practices.

1) There is a need for standardized language for concepts such as selling and profiting in relation to commercialisation. This would facilitate consistency in communication and understanding among the various stakeholders.

2) Consent forms need to be more explicit about researchers not selling samples and participants not profiting. Given the possibilities for misunderstandings associated with the use of commercialisation within the context of genomics research, it is important that investigators employ direct language about whether or not genomic samples and other data will be sold, and whether or not participants will profit from the development of drugs or other products.

3) Investigators should refrain from using the term ‘commercialisation’ without specificity in consent forms and other communications with communities and study participants. For clarity, they should include examples, such as drug development, vaccine, or test development.

4) The process of community engagement for studies involving the sharing of biospecimens and/or data, should include conversation about commercialisation. A researcher might not be able to provide explicit details to community members or potential research participants about the future use of their samples or data to develop commercial products. However, it is important to discuss the possibility, meanings, and implications of commercialisation in the local language and to dispel perceptions of literal buying and selling of their samples and data.

5) More empirical research is needed on perspectives of diverse stakeholders - e.g. researchers, funding organizations, biotech companies, clinicians, potential participants - regarding commercialisation. To optimize the generalizability and value of these studies, they should include researchers from multiple disciplines, utilize qualitative and quantitative methods, and represent local, national, and global contexts.

6) A global framework is needed to guide commercialisation processes. This could be generated through structured discourse among an international and interdisciplinary group of scholars about conceptualizations of commercialisation, equity,

vulnerability, etc. H3Africa could be a catalyst for a global symposium that would facilitate this discourse and lead to the development of the framework.

7) A separate report is needed to identify and address the legal implications of commercialisation, such as intellectual property and conflict of interest. As mentioned previously, these are related and important issues, but are outside the scope of the current report. Beyond consent, at a minimum, proper legal agreements with partner institutions and companies are needed. A report on legal implications does not need to be commissioned by H3Africa; H3A could partner with other interested organizations on this effort.

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