

## Comments relating to the CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects

February 2016

Guideline	Specific comment to the consultation	Observations, notable text, impacts, etc.
1: Social Value	None	<ul style="list-style-type: none"> <li>• Science must be of potential public/social benefit.</li> <li>• Respect and concern for the rights and welfare of the individual participants is vital – including informed consent, transparency, control of risks, justice and fairness.</li> <li>• <b>Staff must be competent and have had appropriate ethics education and training.</b></li> <li>• Scientific rigor and quality are vital for research to generate results that can be relied upon for decision making.</li> <li>• Protocols must contain specified ethics content.</li> </ul>
3: Equitable distribution of benefits and burdens in the selection of groups of participants in research	None	<ul style="list-style-type: none"> <li>• <b>“Groups and communities that are invited to participate in research must be selected for scientific reasons and not because they are easy to recruit given their compromised social or economic position or their ease of manipulability.”</b> (lines 213-216)</li> <li>• “Groups that are unlikely to benefit from the knowledge to be gained in the research must not bear a disproportionate share of the risks and burdens of research participation.” (lines 218-219)</li> <li>• <b>“In other cases, impoverished groups have been overused because of their willingness to serve as subjects in exchange for relatively small stipends, because of their desire to access medical care, or because research hospitals are often located in places where members of the lowest socioeconomic classes reside.”</b> (lines 264-267)</li> </ul>
4: Potential	None	<ul style="list-style-type: none"> <li>• <b>“For research interventions or procedures</b></li> </ul>

<p><b>benefits and risks of research</b></p>		<p><b>that offer no potential benefits to participants, the risks must be appropriate in relation to the social value of the knowledge to be gained</b> (expected benefits to society from the generalizable knowledge).” (lines 294-297)</p> <ul style="list-style-type: none"> <li>• “In general, when it is not possible or feasible to obtain the informed consent of participants, research interventions or procedures that offer no potential benefits must pose no more than minimal risks.” (lines 298-300)</li> </ul>
<p><b>7: Community engagement</b></p>	<p>This is a laudable requirement. However, it seems too prescriptive and may not be appropriate or feasible in many instances. For example, there are some practicable difficulties in implementing this provision in the context of biobanks:</p> <ul style="list-style-type: none"> <li>• Biobanks may not have sufficient resources for an adequate outreach programme.</li> <li>• Biobanks may be remote from the participants, where biobank samples are acquired from routine clinical activities.</li> <li>• Biobanks may have no need for an ongoing relationship with participants for research-related purposes.</li> <li>• It may be difficult or impossible for the biobank to locate participants to maintain engagement on an ongoing basis.</li> <li>• Researchers who use biobank resources are at least one-step further removed from the donors.</li> </ul> <p>However, we accept that community engagement is the socially responsible, transparent and accountable way to involve participants in research, where it can be achieved.</p> <p>In particular, we support the suggestion in the commentary that community engagement can enhance the study in</p>	<ul style="list-style-type: none"> <li>• <b>“Researchers, sponsors and relevant institutions should engage potential participants and communities in a meaningful participatory process that involves them in an early and sustained manner in the design, development, implementation, and monitoring of research, and in the distribution of its results.”</b> (lines 793-786)</li> <li>• “Community engagement should be an ongoing process, with an established forum for communication between researchers and community members. This can facilitate the creation of educational materials, planning the necessary logistical arrangements for the conduct of the research, and providing information about the health beliefs, cultural norms, and practices of the community.” (lines 831-834)</li> <li>• <b>“Community members can assist in the development of the informed consent process and documents to ensure that they are understandable and appropriate for potential participants.”</b> (lines 837-838)</li> </ul>

	<p>practical ways, for example, by informing the design of logistical arrangements for conducting the study or developing informed consent appropriate to potential participants.</p>	
<p><b>9: Individual Informed Consent</b></p>	<p>We support the primacy of participation following individual informed consent and accept this should be the preferred <i>modus operandi</i> for research wherever practical. However, we also support the provision for waiving or modifying individual informed consent where justified, with the proviso that there is approval of a research ethics committee to do so.</p> <p>In research using stored biological samples, for example in a diagnostic archive that then makes the samples available as a unique “research biobank” resource, consent is often not in place and could be impracticable or sometimes impossible to obtain. Therefore, the provision for a waiver of consent under research ethics committee approval is a vital and valuable enabler for legitimate research.</p> <p>We also support the provision for waiving the need for individual consent for the use of data in health registries under certain conditions.</p> <p>The guidelines states that “Appendix 2 includes the details of the relevant information that must be provided, as well as possible supplementary information.” (Lines 978 – 979). However, we could not find “Appendix 2” anywhere in the text. Nonetheless, it is too prescriptive for these guidelines to stipulate all of the details that must be provided in the informed consent, as different national laws and ethics committees may have their own requirements for the content of the informed consent.</p>	<ul style="list-style-type: none"> <li>• “Before being enrolled in health-related research, potential participants must provide their voluntary, informed consent. Informed consent should be understood as a process. <b>Waiving or modifying individual informed consent requires justification, and must in all cases be explicitly approved by a research ethics committee.</b>” (lines 937-940)</li> <li>• “<b>In long-term studies, researchers must ensure at pre-determined intervals that each participant is willing to continue study participation, even if there no changes in the design or objectives of the research.</b>” (lines 954-956)</li> <li>• “<b>The principal researcher has a duty that cannot be delegated to ensure that all personnel obtaining informed consent for a study comply with this guideline.</b>” (lines 957-958)</li> <li>• “Informed consent is a process. The start of this process requires providing relevant information to a potential participant, ensuring that the person has adequately understood the material facts and has decided or refused to participate without having been subjected to coercion, undue influence, or deception.” (lines 961-964)</li> <li>• “The information must be provided in ordinary language understandable by the potential participant.” (line 968)</li> <li>• “Appendix 2 includes the details of relevant information that must be provided, as well as possible supplementary information.” (lines 978-979)</li> <li>• “An oral presentation of information or the use of appropriate audiovisual aids, including pictographs and summary tables,</li> </ul>

	<p>The guideline requires that researchers performing long-term studies ensure at <b>pre-determined intervals that each participant is willing to continue study participation, even if there are no changes in the design or objectives of the research.</b> However, this requirement may be problematic for long term epidemiological studies using specimens. Participants may be difficult to locate, and failure to include them in the ongoing study could compromise the scientific validity of the study. Furthermore, the rationale for this requirement is unclear. Instead, participants should be informed at the time of initial consent that they may withdraw at any time from the study, and be given the information required to do so.</p> <p>The requirement for oral presentation of information or the use of appropriate audio-visual aids to supplement written consent seems too prescriptive. The guideline should not preclude the use of written consent alone or other approaches such as oral consent alone in appropriate circumstances as may be determined by an ethics review committee.</p>	<p>must supplement written consent documents.” (lines 982 -984)</p> <ul style="list-style-type: none"> <li>• “Consent may be indicated in a number of ways. The participant may express consent orally, or sign a consent form. As a general rule, the participant must sign a consent form, or, where the individual lacks decisional capacity, a legal guardian or other duly authorized representative must do so.” (lines 994-997)</li> <li>• “Informed consent must be obtained by a member of the research team. <b>Delegation of obtaining consent, for instance to a research nurse or another member of the research team, is allowed as long as the person who obtains consent is qualified to obtain consent and has prior experience in obtaining consent.</b> The principal researcher is responsible for ensuring that all personnel working on the project comply with this guideline.” (lines 1061-1065)</li> <li>• “<b>Information leaflets must be short and preferably not exceed two or three pages. The information must be clear and readable and presented using any evidence-based methods. Someone with basic education must be able to understand the leaflet.</b>” (lines 1066-1068)</li> <li>• “The requirement to obtain informed consent for research on data in health-related registries may be waived, provided the conditions in guideline 10 are met.” (lines 1072-1074)</li> </ul>
<p><b>10: Modifications and waivers of informed consent</b></p>	<p>In research using stored biological samples, for example in a diagnostic archive that then makes the samples available as a unique “research biobank” resource, consent is often not in place and could be impracticable or sometimes impossible to obtain. Therefore, the provision for a waiver of consent under research ethics committee approval is a vital and valuable enabler for legitimate ethically justified research.</p>	<ul style="list-style-type: none"> <li>• “<b>Researchers must not initiate research involving humans without obtaining each participant’s individual informed consent or that of a legally authorized representative, unless researchers have received explicit approval to do so from a research ethics committee.</b> “ (lines 1083-1085)</li> <li>• “A research ethics committee may approve</li> </ul>

	<p>The need for a formal waiver of consent from an ethics committee is an important safeguard to prevent unrestricted uses of samples that have been rendered anonymous as a mechanism to avoid ethical oversight.</p> <p>However, the decision as to whether a study is of “important social value” could be difficult in practice and is rather subjective.</p>	<p>a modification or waiver of informed consent to research if:</p> <ul style="list-style-type: none"> <li>* the research would not be feasible or practicable to carry out without the waiver or modification; and</li> <li>* the research has important social value; and</li> <li>* the research poses no more than minimal risks to participants when research interventions or procedures offer participants no potential benefits.” (lines 1090-1098)</li> </ul> <ul style="list-style-type: none"> <li>• “These three conditions must also be met even when a study involves personally identifiable data or biological specimens, meaning that the data or specimens carry a person’s name <b>or are linked by a code to a person.</b> ” (lines 1158-1160)</li> <li>• “In addition, <b>the three conditions for waiving informed consent must be met when data or biological specimens are not personally identifiable and the research has important social value.</b> In this situation, the individuals concerned are unknown to the researcher and hence cannot be contacted to obtain informed consent. Moreover, because the data or specimens are not personally identifiable, the risks to those individuals are no greater than minimal.” (lines 1163-1167)</li> <li>• “Waivers must be granted only in cases where a modification of the informed consent process is not possible, or would not offer participants sufficient information to make a meaningful decision about participation.” (lines 1113-1115)</li> </ul>
<p><b>11: Use of stored</b></p>	<p>The scope of this provision is not clear. If specimens and related data are completely</p>	<ul style="list-style-type: none"> <li>• “When specimens are collected for <b>research purposes, either specific</b></li> </ul>

<p><b>biological materials and related data</b></p>	<p>anonymized (no link is kept to participant identities) or coded (identifying information removed), do they still fall within the scope? It may not be reasonable to apply all of the requirements of this section to specimens and related data that are completely anonymized or coded.</p> <p>We welcome the recognition of the validity of both models of 1) specific informed consent and 2) broad informed consent for unspecified future use. In the context of banks of stored biological samples, broad informed consent with proper governance oversight is an extremely important measure to allow for legitimate ethical research in the absence of specific informed consent.</p> <p>In relation to “residual tissue” uses in research, we also welcome the additional possibility of an informed opt-out consent model. We agree with the 3 provisos for the legitimacy of this model.</p> <p>While we support the ability for a participant to withdraw their data (or discontinue use of data), it is often not possible to retrieve data once it has been distributed. Furthermore, withdrawal of a participant’s data could jeopardize the scientific validity of the study. It is precisely for this reason that the FDA in the US does not permit participants to withdraw their data from a clinical trial if such data has already been analysed.</p> <p>In relation to “low resource settings”, what exactly constitutes such a setting? Would this imply that samples collected, for example, in the context of an international clinical trial and stored in a country other than the country of origin should be returned to the country of origin? When</p>	<p><b>informed consent for a particular use or broad informed consent for unspecified future use must be obtained from the source. Such broad informed consent relies on proper governance and management of the biobank.”</b> (lines 1197-1200)</p> <ul style="list-style-type: none"> <li>• “When human biological materials are <b>left over after clinical diagnosis or treatment (so-called residual tissue)</b> and are stored for future research, a <b>specific or broad informed consent may be used or may be substituted by an informed opt-out procedure</b>. This means that the material is stored and used for research unless the person from whom it originates explicitly objects. <b>The informed opt-out procedure has to fulfil the following conditions: 1) patients need to be aware of its existence; 2) sufficient information needs to be provided; 3) patients need to be told that they can withdraw their data; and 4) a genuine possibility to object has to be offered.</b>” (lines 1201-1207)</li> <li>• “When researchers seek to use stored materials collected for past research, clinical or other purposes without having obtained informed consent for their future use for research, <b>the research ethics committee may waive consent</b> if: 1) the research would not be feasible or practicable to carry out without the waiver; and 2) the research has important social value; and 3) the research poses no more than minimal risks to participants when research interventions or procedures offer participants no potential benefits.” (lines 1208-1213)</li> <li>• “When researchers use coded material that is stored in a biobank the key to <b>the code must remain with the custodian of</b></li> </ul>
---	--	--

	<p>and in which contexts should such return take place?</p> <p>In relation to the research uses of human biological material and related data, it is stated that the “protocol for every study ... must be submitted to a research ethics committee.” This is a laudable aim, which is not always possible in practice. For example, not all research organisations have access to ethics committees willing to or capable of reviewing protocols using human biological materials, especially where such samples are anonymous or where identities are shielded from the research users. In the absence of access to an independent ethics committee, would an internal ethics review body within the biobank or the research organisation be valid?</p> <p>In relation to the guidance on “<i>Anonymization or coding</i>”, we do not agree that “researchers can only use anonymized or coded material”. There are many instances in which a person who is the custodian of the bank is also the clinician with knowledge of the donors and the researchers who will use the samples. In some circumstances it is advantageous, for example for longitudinal clinical outcome data collection associated with the samples, for the identities of the donors to be known to the researchers. However, in such circumstances we would agree that consent to the use of <i>identified</i> samples and data would be necessary and for strong governance oversight to be in place.</p> <p>In relation to return of research results and incidental findings, we dispute the statement that “<i>There is an emerging consensus that at least some subsets of (genetic) research findings must be returned to individual donors if they wish so.</i>” Instead</p>	<p><b>the biobank.”</b> (lines 1214-1215)</p> <ul style="list-style-type: none"> <li>• “<b>Biobanks can only collect biological materials and related data from low resource settings in collaboration with local health authorities.</b> The governance structure of such biobanks must have representation of the original setting. <b>If the specimen and data are stored outside the original setting, there must be provisions to return all materials to the setting concerned and share possible results and benefits</b> (see guidelines 3, 7 and 8).” (lines 1216-1220)</li> <li>• “Since it is impossible to obtain specific informed consent at the time the material is collected, because the precise nature of the research is typically unknown, <b>an acceptable alternative to specific informed consent for future research use is broad informed consent.</b>” (lines 1228-1230)</li> <li>• “<b>The protocol for every study using stored human biological materials and related data must be submitted to a research ethics committee,</b> which must ensure that the proposed use of the materials falls within the scope agreed to by the donor if he or she has given specific or broad informed consent for future research. If the proposed use falls outside the authorized scope of research, re-consent is necessary. Research ethics committees may waive consent for research with historical materials...” (lines 1254-1259)</li> <li>• “<b>Broad informed consent describes the range of future uses in research for which consent is given.</b> This broad informed consent should specify: the conditions and duration of storage; who will manage access to the materials; the foreseeable</li> </ul>
--	--	--

	<p>we would say that there is no consensus although there are growing voices both for and against the obligation to return research findings. However, we support the assertion that a clear statement during the consent process about which information, if any, will be returned is a good measure. We also agree that <i>“information of uncertain scientific validity or meaning would not qualify for communication to the participant”</i>.</p> <p>In relation to <i>“Children and adolescents and biobanks”</i>, we understand the ethical viewpoint that minors should be given the option to consent or withdraw consent for themselves upon reaching the age of majority. However, this is currently not done often, as in practical terms, it can be difficult to achieve for many of the same reasons that modification to/re-consent is not practical. For example, 1) it can be an administrative challenge to track which samples in a biobank this will apply to and when; 2) the biobank may have no practical method of knowing the whereabouts of and re-contacting affected donors and; 3) children may not themselves be aware that samples are in storage, so may be confronted with a challenging scenario.</p> <p>The option of offering an <i>“informed opt-out system”</i> could be subject to the same practical considerations. For these reasons, the requirement to seek new consent when a child reaches the age of majority should be able to be waived by the research ethics committee when the criteria for waiver of consent have been met.</p>	<p>uses of the materials, whether limited to an already fully defined study or extending to a number of wholly or partially undefined studies; and the intended goal of such use, whether only for research, basic or applied, or also for commercial purposes, and the possibility of unsolicited findings and how they will be dealt with. The research ethics committee must ensure that the proposed collections, the storage protocol, and the consent procedure meet these specifications.” (lines 1267-1274)</p> <ul style="list-style-type: none"> <li>• <i>“Anonymization or coding.</i> Biological material that is stored in biobanks must be anonymised or coded. When researchers use coded materials from biobanks in later studies, the key to the code must remain with the custodian of the biobank. Thus researchers can only use anonymized or coded material.” (lines 1307-1310)</li> <li>• <i>“Return of results and disclosure of (un)solicited findings. .... the informed consent must clearly stipulate what return of information—if any—derived from analysis of the materials is foreseen, should the participant so wish.</i> There is an emerging consensus that at least some subsets of (genetic) research findings must be returned to individual donors if they wish so. .... Tiered consent, i.e. working with packages or ‘tiers’ of information, gives donors a range of choices and allows them to choose some options over others to give them greater control over the use of their biological materials. In general, life-saving information and data of immediate clinical utility involving a significant health problem must be offered for disclosure, whereas information of uncertain scientific validity or meaning would not qualify for</li> </ul>
--	--	--

		<p>communication to the participant.” (lines 1311-1322)</p> <ul style="list-style-type: none"> <li>• <i>“Children and adolescents and biobanks. Children and adolescents who reach the age of maturity must be given the opportunity to give broad informed consent to continue the storage and use of their collected material and data, and they must at this point also be able to withdraw their consent for future research. An informed opt-out system, in which persons are explicitly approached and alerted to their right to withdraw, could also be acceptable.”</i> (lines 1323-1327)</li> </ul>
<p><b>12: Use of health-related data in research</b></p>	<p>The scope of this provision is not clear. If data are completely anonymized (no link is kept to participant identities) or coded (identifying information removed), do they still fall within the scope? It may not be reasonable to apply all of the requirements of this section to data that are completely anonymized or coded. The scope of this provision is not clear. If data are completely anonymized (no link is kept to identifying), do they still fall within the scope? It is not reasonable to apply all of the requirements of this section to data that are completely anonymized. We note that even the draft EU Data Protection Regulation does not impose requirements that are completely anonymized.</p> <p>In relation to the use of data collected in the context of routine clinical care, why <b>must</b> an informed opt-out procedure be used? We recommend that this text be aligned with the similar provision for the use of human biological samples left-over after clinical diagnosis or treatment (so-called residual tissue) – that “a <b>specific or broad informed consent may be used or may be substituted by an informed opt-out</b></p>	<ul style="list-style-type: none"> <li>• “When data are used that were collected in the context of routine clinical care, an informed opt-out procedure must be used.” (lines 1340-1341)</li> <li>• “Researchers are only allowed to use anonymized or coded health-related data. The key to the code must remain with the custodian of the databank.” (lines 1355-1356)</li> <li>• <i>“Research ethics committees and storing health-related data. The protocol for every study using collected data must be submitted to a research ethics committee, which must ensure that the proposed use of the data falls within the scope specifically agreed to by the participant. If not, re-consent is necessary.”</i> (lines 1388-1391)</li> <li>• <i>“Confidentiality. An important aspect of storing health-related data is the confidentiality between researcher and patient. .... During the process of obtaining informed consent, the researcher must inform the potential patients about the safeguards that will be</i></li> </ul>

<p><b>procedure.”</b> We see no reason why specific or informed consent would be unacceptable in the context of use of data.</p> <p>In relation to the ability of researchers to use identified data, identical considerations to those raised in response to Guideline 11 apply. Namely <i>“There are many instances in which a person who is the custodian of the data is also the clinician with knowledge of the donors and the researchers who will use the samples. In some circumstances it is advantageous, for example for longitudinal clinical outcome data collection associated with the samples, for the identities of the donors to be known to the researchers. However, in such circumstances we would agree that consent to the use of identified samples and data would be necessary and for strong governance oversight to be in place”</i>. This is recognised in the Commentary, where the commentary seems to be at odds with the text of the actual Guideline.</p> <p>In relation to the need for the protocol of every study using data to be submitted to a research ethics committee – similar to the considerations raised under comments to Guideline 11, not all researchers using collected data have access to an independent ethics committee for such a review and in some jurisdictions, research based on existing or collected health data or registries are legally exempt from ethics committee review.</p> <p>The use of the word “explicit” when referring to consent in lines 1454 – 1456 suggests that broad consent or notification would not be acceptable for collection and storage of data. We recommend deleting the word “explicit” in this section. Similarly, we suggest deleting the word “explicit” in</p>	<p><b>taken to protect confidentiality as well as their limitations.”</b> (lines 1396-1402)</p> <ul style="list-style-type: none"> <li>• <b>“When project plans require personal identifiers to remain on records used for a study, researchers must explain to research ethics committees why this is necessary and how confidentiality will be protected. It can be acceptable to store personally identifiable data to enhance their value for future research; by implication, efforts to de-identify data in order to safeguard confidentiality and the resulting trade-offs in the scientific value of the given data need to be carefully balanced.”</b> (lines 1406-1411)</li> <li>• <b>“Archived data.</b> When existing data, collected and stored without an explicit consent process, offer important and otherwise unobtainable information, a research ethics committee needs to decide whether the use of such data is justified in the absence of explicit consent.” (line 1454 -1456)</li> </ul>
--	---

<p><b>13: Reimbursement and compensation for research participants</b></p>	<p>line 1468.</p> <p>The Guideline and Commentary in relation to compensation for participation in research raise some concerns.</p> <p>Whilst we agree that reimbursement of reasonable direct and indirect expenses should be the norm, where the study/institution has the resources to do so, levels of compensation that are appropriate versus unacceptable can be very difficult in practice to determine. Therefore, compensation for participation should be permissible but not mandatory.</p> <p>Additionally, in relation to the donation of biological samples, this guideline could be interpreted as at odds with other guidelines or laws in some jurisdictions that prohibit the sale or profit from a part of the human body. Any compensation for donation of a human biological sample risks crossing the thin line into the sale for profit of a part of the donor’s body. This presents a particular risk for vulnerable donors, who may experience undue inducement or exploitation with the offer of even low levels of compensation for the donation of biological samples.</p>	<ul style="list-style-type: none"> <li>• “Research participants must be <b>reasonably reimbursed for direct and indirect expenses</b> incurred during the research, such as travel costs and lost earnings, <b>and compensated reasonably for inconvenience and time spent. Compensation can be monetary or non-monetary.</b> The latter might include free health services unrelated to the research, medical insurance, educational materials, or other benefits. <b>Compensation must not be so large as to induce potential participants to consent to participate in the research against their better judgment ("undue inducement"). A local research ethics committee must approve reimbursement and compensation for research participants.</b> Concerns about undue inducement must not preclude the study of monetary or material incentives as a potential way of promoting healthy behaviors.” (lines 1505-1514)</li> <li>• “<i>Appropriate compensation. Participants must also be reasonably compensated for their inconvenience and time spent participating in research.</i> Compensation can be monetary or non-monetary and may include, for example, health services unrelated to the research, medical insurance, educational materials, counseling, or food supplies. Especially when the research poses low risks, <b>providing compensation for participating usually does not raise concerns about undue inducement.</b>” (lines 1527-1531)</li> <li>• “<i>Unacceptable compensation. Monetary or in kind compensation for research participants must not be so large as to persuade them to volunteer against their better judgment or deeply held beliefs</i></li> </ul>
--	--	--

		<p><b>(“undue inducement”).</b> It can be difficult to evaluate whether an undue inducement exists, in part because the compensation that makes someone volunteer against their better judgment <b>depends on their personal situation.</b> An unemployed person or a student may view compensation differently from an employed person.” (lines 1532-1537)</p>
<p><b>16: Research involving individuals who are not capable of giving informed consent</b></p>	<p>None</p>	<ul style="list-style-type: none"> <li>• “Before undertaking research with individuals who are incapable of giving informed consent, the researcher and the research ethics committee must ensure that: <ul style="list-style-type: none"> <li>* <b>a legally authorized representative of the person who is incapable of giving informed consent has given permission</b> and this permission takes account of the participant’s previously formed preferences and values; and</li> <li>* the assent of each subject has been obtained to the extent of that person's capacity, after having been provided with adequate information about the research at the level of the subject’s capacity for understanding this information” (lines 1720-1727)</li> </ul> </li> </ul>
<p><b>17: Research involving children and adolescents</b></p>	<p>This guidelines should permit a waiver of the requirement for parental permission and the child’s assent under certain circumstances using the Waiver Criteria stipulated in Guideline 10. For example, a waiver of this requirement should be permissible when approved by a research ethics committee for the use of residual archived specimens from children that are collected during the course of routine care.</p> <p>It is not clear why the term “age of maturity” is used throughout these guidelines. We recommend that the term</p>	<ul style="list-style-type: none"> <li>• “Before undertaking research involving children and adolescents, the researcher and the research ethics committee must ensure that: <ul style="list-style-type: none"> <li>○ a parent or a legally authorized representative of the child or adolescent has given permission.</li> <li>○ the agreement (assent) of the child or adolescent has been obtained in keeping with the child’s/adolescent’s capacity after having been provided with adequate information about the research tailored to the child’s/adolescent’s maturity.</li> </ul> </li> </ul> <p>If children reach the legal age of maturity</p>

	<p>“age of majority” be used instead, as we believe it is a more meaningful and more frequently used term, particularly in national and local law.</p> <p>In relation to the requirement to seek the consent of a child whose biological material is being used for research or is stored in a biobank for future research at the time that the child reaches the legal age of majority, the comments made in response to Guideline 11 apply. Namely:  <i>“In relation to “Children and adolescents and biobanks”, we understand the ethical viewpoint that minors should be given the option to consent or withdraw consent for themselves upon reaching the age of majority. However, this is currently not done often, as in practical terms, it can be difficult to achieve for many of the same reasons that modification to/re-consent is not practical. For example, 1) it can be an administrative challenge to track which samples in a biobank this will apply to and when; 2) the biobank may have no practical method of knowing the whereabouts of and re-contacting affected donors and; 3) children may not themselves be aware that samples are in storage, so may be confronted with a challenging scenario. The option of offering an “informed opt-out system” could be subject to the same practical considerations.”</i></p> <p>For these reasons, the requirement to seek new consent when a child reaches the age of majority should be able to be waived by the research ethics committee when the criteria for waiver of consent have been met.</p>	<p>during the research, their consent to continued participation must be obtained.” (lines 1849-1858)</p>
<p><b>23: Requirements for establishing research ethics</b></p>	<p>As stated in relation to Guidelines 11 &amp; 12, not all researchers studying stored human biological samples have access to an independent ethics committee.</p>	<p><b>“All proposals to conduct health-related research involving humans must be submitted to a research ethics committee to review their ethical acceptability, unless there are</b></p>

<p><b>committees and their review of protocols</b></p>	<p>To what extent is the formation of an internal review body within a biobank or research institution an adequate alternative where no independent ethics committee is available for research studies of biological samples and related data?</p>	<p><b>exemptions as specified by applicable law or regulations.</b> The researcher must obtain approval or clearance by such a committee before beginning the research. ” (lines 2477-2480)</p> <p>“Committee members must be duly qualified and regularly update their knowledge of ethical aspects of health-related research. <b>Research ethics committees must have mechanisms to ensure independence of their operations.</b> ” (lines 2489-2491)</p> <p><i>“Conflicts of interests from research ethics committee members. <b>Research ethics committees must have mechanisms to ensure the independence of their operations.</b>”</i> (lines 2557-2558)</p>
--	--	---