EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 May 2016

Submission of comments on 'ICH guideline E18 on genomic sampling and management of genomic data ' (EMA/CHMP/ICH/11623/2016)

Comments from:

Name of organisation or individual
ACRO (Association of Clinical Research Organizations)

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	The Association of Clinical Research Organizations (ACRO) represents the world's leading, global clinical research organizations (CROs). Our member companies provide a wide range of specialized services across the entire spectrum of development for new drugs, biologics and medical devices – from discovery, pre-clinical, proof of concept and first-in-man studies through post-approval and pharmacovigilance research. With more than 110,000 employees engaged in research activities around the world (including more than 30,000 in Europe), ACRO advances clinical outsourcing to improve the quality, efficiency and safety of biomedical research. Each year, ACRO member companies conduct more than 9,000 clinical trials involving nearly two million research participants in 142 countries. On average, each of our member companies works with more than 500 research sponsors annually. ACRO welcomes and supports the draft ICH E18 guideline on genomic sampling and management of genomic data. In particular, given the rapid pace of developments within the field of genomic testing, ACRO welcomes the inherent flexibility of the draft guideline in recognising that: • Genomic research may be conducted during or	

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	after a clinical study and therefore may not be pre-specified in the clinical trial protocol; • With appropriate consent, genomic samples may be stored beyond a drug development programme to enable re-use and/or future use; • Informed consent for the collection and use of genomic samples may permit broad analysis of the samples regardless of the timing of analysis; • The use of single coding of genomic samples is an appropriate means of maintaining confidentiality; • A subject's desire or consent to receive or not to receive genomic information should be respected. Because the draft guideline issued for comment by the European Medicines Agency (EMA) was reformatted from the original ICH draft -- resulting in changes to the line numbers -- ACRO has included both the "ICH" (meaning the original ICH draft guideline) line numbers and the "EMA" (meaning the reformatted document published by the EMA) line numbers so that ACRO's comments may be linked back to either draft document.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
ICH 61 – 63 and 67 - 68 EMA 67 - 69 and 73 - 75		Comment: In order to ensure clarity about how samples may be used, ACRO suggests including a requirement to add to the protocol and, consequently, the informed consent information, the range of potential pre-defined genomic testing or broad analysis of the samples, and its objectives. Proposed change (if any): Include a requirement to add to the protocol and informed consent information the range of potential pre-defined genomic testing or broad analysis of the samples, and its objectives.	
ICH 72 -73 EMA 78 - 79		Comment: The draft statement does not refer specifically to retention of samples, which, as a long-term requirement, is distinct from routine storage. Proposed change (if any): Revise the sentence to read: “The focus is on the general principles of collection, processing, transport, storage, retention and disposition of genomic samples or data, within the scope of an informed consent.”	
ICH 83 - 86 EMA 88 - 91		Comment: ACRO strongly supports the statement that “genomic sample acquisition is strongly encouraged in all phases of clinical development. Moreover, the quality of clinical research is dependent upon unbiased systematic collection and analysis of samples, ideally, from all subjects in	

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		order to fully represent the study population." However, ACRO notes that research ethics committees/independent review boards frequently require (a) that an informed consent form separate from that for the main clinical trial is used to obtain consent for genomic testing, and (b) that a subject may consent to participate in other aspects of a clinical trial while refusing consent for genomic testing. ACRO recognises that, as a regulatory guideline, ICH E18 (rightly) does not address ethical aspects of genomic sampling and analysis but, given the importance of unbiased systematic collection and analysis of samples to the scientific validity and integrity of clinical trials, ACRO recommends that ICH and its member organisations accompany publication of the final guideline with outreach efforts to research ethics committees and to international bodies responsible for establishing global ethical standards in clinical research (e.g., the World Medical Association, the Council for International Organizations of Medical Sciences, etc.) in order to ensure widespread recognition of the scientific principles involved and to help facilitate a situation where they can be followed. Proposed change (if any):	
ICH 240 - 243 EMA 234 - 237		Comment: Following the list of factors for which sample inventory should be monitored and curated, the draft guideline states "Reconciliation of all samples relative to the aforementioned aspects should be performed prior to the use	

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		of each sample." It is ACRO's view that procedures should be in place to ensure all samples are curated appropriately and to ensure destruction of samples at the end of the retention period stated in the informed consent information or when a subject withdraws consent. Consequently, ACRO recommends that prior to use of each sample, it is necessary only to reconcile that sample, rather than all samples, relative to the aforementioned aspects. Proposed change (if any): Revise the statement "Reconciliation of all samples relative to the aforementioned aspects should be performed prior to the use of each sample" to read "Reconciliation of each sample relative to the aforementioned aspects should be performed prior to the use of that sample."	
ICH 259 - 261 EMA 251 - 253		Comment: ACRO supports the view that "Under exploratory settings, genomic data can be generated using research grade reagents and instruments that may not have been validated to support clinical use." However, to avoid confusion, ACRO recommends that the term "exploratory settings" is more accurately defined as it may be open to subjective interpretation. For consistency with the definition given in the ICH E8 (general considerations for clinical trials) guideline, ACRO recommends replacing the text "Under exploratory settings" with "In therapeutic exploratory clinical trials".	

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		Proposed change (if any): Replace the text “Under exploratory settings” with “In therapeutic exploratory clinical trials”.	
ICH 261 - 263 EMA 253 - 255		Comment: ACRO supports the statement “When genomic data are to be used for clinical decision making, appropriate level of assay validation should be considered in accordance with local regulations and policies.” ACRO recommends that this should also apply when genomic data are used to support regulatory decision making. Proposed change (if any): Revise the statement “When genomic data are to be used for clinical decision making” to read “When genomic data are to be used for clinical decision making or to support regulatory decisions….”	
ICH 276 - 289 EMA 266 - 278		Comment: ACRO recommends including a statement regarding traceability of samples. There is a need to ensure traceability of samples to a specific location, so as ensure appropriate actions can be taken in the event a subject withdraws consent for current or future testing of their samples. Proposed change (if any): Reference the need to ensure traceability of samples to a specific location, so as ensure appropriate actions can be taken in the event a subject withdraws consent for current or future testing of their samples.	

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ICH 294 - 295 EMA 282 - 285		Comment: ACRO agrees that "Appropriate security measures using coding schemata and restriction of access should be implemented at each step of analysis and storage" and recommends that these measures should also apply during sample collection and transport. Proposed change (if any): Revise the statement "…..analysis and storage" to read "…..sample collection, transport, analysis and storage."	
ICH 316 - 330 EMA 302 - 315		Comment: One might infer from the statement on ICH Lines 317-318 and EMA Lines 303-304 that the subject may choose to *provide* consent for the *clinical study* while *withholding* consent for *genomic research*: "Consent for genomic research may be either included in the consent for the clinical study or obtained separately." ACRO is concerned that this presentation of consent for genomic research as 'optional' and 'separate' is contrary to the important scientific principles articulated earlier in the draft guidance on ICH Lines 84-86 and EMA Lines 89-91, which states: "Moreover, the quality of genomic research is dependent upon unbiased systematic collection and analysis of samples, ideally, from all subjects in order to fully represent the study	

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		population." In addition, ACRO notes that the position that consent for genomic research is optional and separate may actually conflict with the requirements of the protocol. Comment: ACRO strongly supports the view that the identification of common and essential elements for a globally acceptable informed consent for genomic sampling would greatly enable genomic research. Recognising that, as a regulatory guideline, ICH E18 (rightly) does not address ethical aspects of genomic sampling and analysis, ACRO recommends ICH and its member organisations to reach out to international bodies responsible for establishing global ethical standards in clinical research (e.g., the World Medical Association, the Council for International Organizations of Medical Sciences, etc.) in order to stimulate the development of such an approach. In addition, ACRO makes the following suggestions: ACRO recommends including a statement regarding enduring consent to address all future research, including potential commercial use of the genomic sample. ACRO recommends including a statement as to how the	

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		sample will be handled in the event the subject withdraws consent – sample destroyed/returned. ACRO recommends including a statement clarifying that, in the event of the death of the subject, samples from that subject may continue to be used and analysed in accordance with the informed consent signed by that subject. Proposed change (if any):	
		ACRO thanks the ICH Secretariat for the opportunity to submit comments on the "ICH guideline E18 on genomic sampling and management of genomic data." Please do not hesitate to contact us if we can provide additional information (knoonan@acrohealth.org or +1 202 464 9340).	

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