Matchmaker Exchange Informed Consent Proposal

The following proposal for consenting patients for genomic matchmaking has been discussed with the Global Alliance for Genomics and Health (GA4GH) Regulatory and Ethics Working Group (REWG) members and the Consent Task Team. The need for patient consent to data sharing for clinical care or research depends on the probability of occurrence and seriousness of potential harm of re-identification in the matchmaking process. The first step of matchmaking involves a search being conducted by a data requester to establish the existence of similar patients in a collection of patient records. Once a discovery hit has occurred, it is typically then desirable for more detailed patient data to be exchanged between the data depositor and the data requester.

- **Level 1 (clinical setting)** - Undertaking matchmaking based on HPO terms and/or candidate gene names - consent to data sharing and queries is not required (but notification of the patient should be considered)
    - Broad phenotype description - as a disease name (OMIM or Orphanet e.g. Charcot-Marie-Tooth disease) or by using structured phenotypic terms (*e.g.* HPO terms). Clinical judgment should be used to assess the potential for re-identification and possible harm depending on the level of phenotypic detail provided.
    - HGNC approved gene names - for the suspected or candidate pathogenic loci.
    - Use of this level of information in data discovery would not require patient consent to data sharing and queries.
    - Subsequent exchange of this level of information between depositor and requester (i.e., data sharing) raises no additional consent risks.
    - Subsequent exchange of more detailed information between depositor and requester (i.e., data sharing) may require consent (see Level 2).
- **Level 2 (for research)** - Undertaking matchmaking based on unique or sensitive phenotypic information and/or DNA or protein sequence level information including genomic variant datasets - consent to data sharing required
    - Detailed phenotype description descriptions or sets of terms detailed enough to raise concern for uniquely identifying a patient or containing highly sensitive medical information. Pooling sources of data and removing some phenotype information based on its sensitivity could minimize the risk of possible re-identification.
    - Genomic variant dataset - including one or more variants (irrespective of suspected etiologic role), or related information such as variant class, amino-acid alteration, variant location, affected exon, etc.
    - Use of this level of information in data discovery implies a possible risk of re-identification and harm and such use requires appropriate patient consent to data sharing.
    - Subsequent exchange of this level of information between depositor and requester (i.e., data sharing) likewise requires consent.
    - However, consent for matchmaker discovery and subsequent sharing of level 2 data can be taken to have been given if consent exists for the data to be included in an open or registered access database whose declared purpose involves data sharing for purposes consistent with matchmaking.

Version: March 2015

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