Comments of the German Biobank Node/ bbmri.de on the Article 29 Working Party Guidelines

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Comments on The Article 29 Working Party Guidelines on Consent under Regulation 2016/679 (wp259) and on the Guidelines on Transparency under Regulation 2016/679 (wp260)

The guideline explicitly refers to **medical research** and should offer paths and solutions to facilitate research for the sake of our patients. Therefore, some basic assumptions of the Art. 29 WP Guidelines cannot remain unchallenged.
In particular, some key points need to be addressed in the light of the current challenges and opportunities medical research has to face today:

1. **How biomedical research is nowadays carried out?**

Unfortunately, the currently proposed guidelines seem to assume research scenarios and research methods, that belong to the past…
Healthcare and biomedical research including clinical trials have always been closely linked. However, in the current era of precision medicine, the same methods and resources are used for the identification of individual therapeutic treatment options in many disease-areas, particularly in cancer. Vice versa, the data obtained or derived from the clinical course of patients are feeding biomedical research data bases as a basis for the progress, *inter alia* serving to develop and/or optimize individualized treatment options.

Many European and global collaborations aiming at exchange of research data have been funded and promoted by the EU. Disease-specific or more general research and infrastructure networks have been set-up and research resources including biomedical databases have been established. All these infrastructures depend heavily on the **lawfulness of data re-use and data exchange**.
Real world data are more and more required to demonstrate long-term effects of drugs and therapies (outcomes-based healthcare) by EMA and FDA. Healthcare providers and patients have realized

that traditional clinical trials represent only a very limited part of the truth: Study-populations are highly selected and often do not represent real world settings. In addition, only sparse data are available on the long-term well-being and quality of life of study participants, if only data collected during a specific trial are taken into account. The pharmaceutical industry currently counteracts such obvious drawbacks by changing the setting of clinical trials: study programs (series of clinical trials with one drug or several members of a drug-family) or umbrella studies (with drugs targeting different paths, alone or in combination) etc. are initiated in order to prolong observation intervals and/or to switch more rapidly to promising treatment regimes.
Data protection is considered the main hurdle in making progress in various fields of biomedical research. Often data from various sources are needed to gain medical/scientific knowledge, but in many cases restricted underlying (e.g., mostly study-specific) consents make it impossible to conduct cross-border research or to widen the disease-area(s) addressed by biomedical research.
Currently huge amounts of so-called legacy data are gathering dust in archives and remain unused due to the legal uncertainty instead of being leveraged for the sake of progress in research. Legal uncertainty causing bureaucratic burden and endless negotiations with various partners is always mentioned, if a survey asks, what the roadblocks for research projects are. The currently proposed Art. 29 WP-Guidelines will not be helpful in reducing this burden and thus will not contribute to facilitate medical research: As the Art. 29 WP-Guideline explicitly states, that “swapping” between different legal grounds for data processing is forbidden, a researcher has to choose the appropriate legal basis for his project in advance. As a result, it could even be risky to ask research participants for consent, if he/she could use another legal gateway. The decision, which legal ground to choose, often needs the involvement of a lawyer and causes red tape without benefit for research participants. Asking them for consent should always be a good choice as long as it is made clear in the consent process, that other legal grounds for using the data for research might exist and that withdrawal of consent therefore may have limited effect.

2. Data re-use is ethically required

Data re-use is an **ethical requirement** in order to avoid unnecessary repetition of the same studies/ examinations and/or analyses (and recapture duplicate data). The ignorance and non-use of available medical or diagnostic knowledge may lead to inadequate patient care which may even bring harm to the patients. Access to this information (e.g., on new diagnostic methods, the appropriate dosage of a drug or potential (late) adverse events) without unnecessary data protection restraints is essentially required. How could we explain to parents of a child who has been harmed by a drug that has been classified not harmful in clinical trials but later on harmful in observational registries/long term surveys? This still happens too often due to a lack of data availability.

Effective pharmacovigilance requires access to as much clinical and research data as possible. Pharmacovigilance is a permanent process and its typical assumption is: we do not know, what we are looking for, otherwise we would have prevented it.

3. How to keep research participants being involved?

In biomedical research, health data and human biological materials are generally pseudonymized and - for good reasons - very rarely anonymized: on the one hand, in reality it is often hardly possible to anonymize data in a fashion that they are still useful for future research, and on the other by employing various anonymization tools data may be de-identified to an extent, that the result bears the risk of generating false positive or negative results and/or associations (genetic data). And most important, anonymization generally hinders the addition of important clinical/diagnostic follow-up data to a same case, thus hindering a potential gain in medical/scientific knowledge.

In general, it is not desirable to anonymize research data from a patient's perspective because any feed-back of incidental/unsolicited findings or any re-contact is impossible, including advances in drug-therapy, diagnostic methods etc. Deleting the identity of patients in a database is the opposite of keeping them involved in medical progress. First, it hinders the collection of additional health data including current health problems/ newly acquired diseases/ risk factors. Ethically even more important is the exclusion of anonymized donors/patients from potential therapeutic/diagnostic benefits gained from clinical studies/medical research including novel diagnostic methods/parameters. In the end, anonymization cuts all direct information on progress in medical research.

4. Useful communication with patients instead of fulfilling formal requirements

Research plans and even research aims are mostly extremely complex and hardly explainable to research/study participants in the granularity, the Guideline seems to require. Therefore, **independent ethics committees** have been installed to additionally protect individuals.
Patients and healthy volunteers are very often research oriented and wish their data to be used in order to advance the progress in medical research and treatment. Many of them are not interested in being overly and/or systematically re-contacted and confronted with complex research information. The tendency in designing ICFs therefore is, to make the text as concise as possible using lay language. Otherwise, people feel bad while signing a consent that keeps being mysterious or unclear to 60-80%.
Forcing people to learn or actively participate in things or processes, they are not interested in, is a burden for both the patient and the clinical researcher. In addition, there is often a lack in time or (medical/scientific) education of next-door patients/donors to fully understand the scope and/or procedures of clinical/medical research. Instead, (medical) research institutions, clinical data bases and/or clinical biobanks should make detailed information on their research aims, current stage and results of their research (topics) publicly available, so that the general public and/or the research- or study-participant himself can take notice/get the desired information(s) whenever they wish.

In general, such details should not be a mandatory part of an ICF, but should rather be offered to those, who really want to get informed on particular research issues. An ICF should rather contain the means and procedures, how such information can be accessed.

The same way should be taken regarding future research and data re-use. **Research participants should be allowed to give their consent in a rather broad manner** as long as they get more detailed information on demand. This would ensure the fundamental right of research participants/donors to withdraw their consent a soon as they feel uncomfortable with biomedical research using their data and/or biomaterials and wish no further involvement. There is no need in order to accomplish the principle "data control by the data subject" to force participants/donors - against their will and conviction - to decide repeatedly on each and every single (betimes complex) research step with often varying granularity dependent on the nature of this step.

Appropriate communication with **research participants/donors** means to explain the risks and benefits of dedicating sensible health data to biomedical research databases/clinical biobanks and to respect their wishes. This comprises to provide as much information as they would like to obtain and not bother them with "you have to understand" obligations (which generates a feeling of being responsible for something, they are often not capable to decide on). The responsibility for the proper use – of course, taking reasonable expectations of participants/donors into account – the integrity and protection of the health data/ biosamples lies with the researcher and cannot *via* consent be imposed on the research participant/donor. Appropriate governance and safeguards (including an involvement of independent ethics committees) as well as information on request should therefore replace an **overflow of mandatory information** (e.g., in an ICF) and an **"obligatory" over-collection of re-consents** (including dynamic options), which are mostly considered mere formalities then real patient/donor-protection or -involvement.

5. **Missing obligatory involvement of independent ethics committees as key custodians for individuals/patients participating in medical research.**

In line with the proposed Art. 29 WP-Guidelines the purpose of the collection, storage and intended use of (health) data and/or human biological materials by a medical research project, (biomedical) research data base and/or clinical biobank should be – in general - specified as exactly as possible. Such purposes might be, e.g., the conduct of a particular clinical study, or research focused on a specific disease (i.e. lung cancer) or on well defined disease-entities (e.g., cardio-vascular diseases or brain disorders).
On the other hand, biomedical research data bases and clinical biobanks must be prepared to satisfy **future medical questions** and meet future challenges in public health by **permitting broad use of health data and human biological materials**, including cross-border exchange and cross disease-area(s) use of data and/or biomaterials. The ethical framework should enable biomedical data-bases/ clinical biobanks to fulfil their key missions based on the arguments (i) **opening new vistas for medical research,** and (ii) **supporting optimization of public health care**.

However, as a pre-condition for the legal validity of a donor's broad consent the unpredictability of future use of his/her data and/or biological materials must be compensated by appropriate measures and procedures. In this regard, **independent ethics committees** are of paramount relevance for both (i) the assessment of a (biomedical) research data base or a clinical biobank itself (during set up and

operation), and (ii) the assessment of individual biomedical research projects later on requesting "broad consent" health data/biosamples as a general pre-condition for the release and delivery of such data/samples. **This important role and task of independent ethics committees as key custodians for individuals/patients participating in medical research has been fully neglected by the proposed Art. 29 WP-Guidelines and must be added therein!**

In addition, in case of broader consent(s) independent ethics committees will check whether patients/donors have been informed in an understandable manner and unambiguously on the broad scope of the future use of his/her health data and/or biological materials including the option of cross-border or disease-overlapping medical research.

However, in line with the proposed Art. 29 WP-Guidelines (even under the conditions of a broad consent) the donor should be given the possibility to exclude certain research fields and/or procedures from the future use of donated health data and/or biological materials at least to some extent, preferably during the **initial** consenting procedure, thereby securing and documenting the donor's wishes from the very beginning of his/her data or bio-sample donation on.
This fact fits, but is not at all identical, to a so-called dynamic consent, which is **almost impossible to achieve for clinical data warehouses/biobanks having access only to pseudonymized data and biomaterials**. From a logistical point of view such attempts are far away from every day practice/ feasibility for biomedical research data bases and/or clinical biobanks hosting data and materials from several hundred thousand or millions of pseudonymized donors: This is almost due to the fact that each modification of consent requires an involvement of the respective local data custodians/ protection officers which appears logistically not feasible on a case by case-basis.