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## Letter to the Editor

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# Reflections on changes in biomedical research ethics

The impetus for the following subjective comments on ethical principles in experimental research were the complaints in the lobby discussions concerning both increases in excessive red-tape, used as preconditions for the implementation of inventive ideas in experimental fields of science, and some negative experiences in the evaluation of research projects. The present author belongs to the generation of scientists whose activities in pharmacological and toxicological laboratories have lasted more than half a century and who remember well the times when the moral qualities of the scientist were considered a spontaneous feature of his or her character, when the scientist was considered a person whose compulsive gifts and inclinations of his character prompted him to make research the mission of his or her whole life. The atmosphere of openness and trustworthiness between colleagues was considered the most natural self-regulation. Those who betrayed these principles and were misled to pseudoscientific staggering used to be excommunicated by the gravity of verified advances in knowledge and marked by a subsequent stigma of inexplicable untrustworthiness. The sufficient formal expression of this natural condition was the Latin graduation pledge spoken on touching the university insignia. The formulation of the graduate's university pledge has not changed much and in most universities it is still in Latin, yet the hierarchy of values is what has changed substantially. The changes towards neoliberal ideology connected with the tendencies to simplify human efforts and activities according to the rule of economic indices have been reflected in the moral principles of the individual and thus also in the values of the relationships between people. The loosening of stereotypes therefore draws social groupings towards ever increasing delimitation of legislative codifications as precise as possible for every shade in the activities. It has resulted in the ever increasing number of new accreditation preconditions, which define every single professional activity, followed by Parkinson-like creeping trends of bureaucratic dictatorship. Sciences are thus found in the situation when even the very best inventive idea which is to be verified experimentally is limited by a guardianship of detailed regulations and an interrelated funnel of financial costs for verifying anything (even data which have been verified many times before). For the majority of bio-medically oriented researchers who seriously consider science to be a service for mankind, the moral barriers based on rules generally declared for all sciences and on the binding

exceptionality of experiments on living creatures, have nevertheless remained natural and self-evident. The essence of this exceptionality is that research that aims at the human being, i.e. the representative of the biological species which includes also the experimenter and the subjects as well as the object of investigation, involves systems with limited methodical availability (resulting from ethic strictures) and this with only relative exactness of holistic data obtained. But I do not argue against "clearly formulated and sensible rules". Progress does not profit, however, from unbalanced formalism without taking account of feedbacks. Due to the bureaucratic machinery, particularly in biological experiments using animal models we face such illogical situations that it is relatively easier to perform a clinical study on a human being than a preparatory preclinical experiment on a laboratory animal. The reality is that for a clinical experiment it is sufficient to obtain the consent of the appropriate state normative institution and the permission of the regional ethical committee, which are final. On the other hand, an animal experiment is subject to a series of permissions (particularly in the Czech Republic where the recommendations of the legislation of the European Union are sometimes applied to an exaggerated degree): the "animal ethical professional" committee → the ministerial committee (according to the incorporation of the research institute in the particular ministry) → the national committee (which submits the documents concerning an animal experiment to the European Centre) and, in addition, parallel constant supervision of the veterinary service over the research institute carrying out the experiment. It results in various application forms, columns, stamps, and ladders of officials in charge, most of whom have only theoretical notions concerning the biological experiment. This system suppresses or even misses the link of "the personal moral of the scientist" (based on his/her very nature) with the "inner moral of the research team" (as the most effective control mechanism in the experimental activity itself).

A more general evaluation of the degree of functioning or not functioning of the systemic feedbacks under the given social conditions is a task for political scientists. A more dominant position of the feedback regulator in particularly defined normative problems, especially those connected with discoveries in biology, should perhaps be taken – with a certain degree of platitude – by those who are directly carrying out the given type of research. The answer to the question "why the voices from scientific communities about the standards of their own work are not heard too

much by those who have the legislative power" is certainly multi-factorial (including interdisciplinary and political interactions). One of these recognised causes are evidently the very features of the characters of most researchers (which are due to the fact that they decided to devote their whole life to science) which prevent them to hurry to the slant slopes of politicians. The low social commitment of experimentally oriented scientists exerts a negative impact on the awareness of elected representatives (quite many of whom are gradually transformed into professional politicians), mostly possessing the motivational tendency "to quench only the immediate fires", or the tendency to underrate the indispensability of science (in particular basic research, not immediately usable) as the foundation for progress in civilisation. Their moods and actions are, of course, under the fire of arguments both from the party of differently informed and biased social groups (i.e. those who elect the politicians) and those who produce the largest share of "public opinion", and that under the influence of heedless mass media with a varying degree of plausible seriousness. The innermost part of the scientific community itself should be provoked to systematically produce a flow of information of balanced arguments concerning the moral authorisation for experimental performance of a biological – in a stricter sense biomedical – research project. The precondition for balanced argumentation should be respect for the variability of opinions and ideology, at least according to the population groups which prevail in society. Credibility of these efforts should be underpinned not only by differently formulated information targeted outside the scientific community but also by opposing critical reflection on the awareness and systematic work in the research teams.

The complexity of the level of argumentation targeted outside the research groups results from the great number of opinions of the lay public. This should at least concern specific formulations addressing those who are aware of the complexity and difficult understanding of the essence of scientific knowledge in contrast to usually relative simplicity of pseudoscientific assertions. It is that segment of the society which is willing to take into consideration the contradictions between the explosions of uncritical, sensation-loving populism on the one hand and sober patient investigation of the principles governing the phenomena and their causalities on the other hand. The level of argumentation, which concerns the substantiation of biological experiments for the populist movements of "protectors of anything" is incomparably more complex. The difficulty of these adequately targeted attempts of formulation stems from the fact that there are groups with whom the polemic usually ends obliquely and without solution, and that due to their uncritically fanatical personal or group efforts to come to the limelight. The activists of these associations with their simplified thinking, which does not allow for other than their own criteria, use even extreme forms, violent destruction of laboratories, their equipment, and irreplaceable documentation. They carry out the so-called "liberation of laboratory animals", often genetically modified and unable to survive in nature. Endless polemical discussions with these groups sometimes slide into "pseudo-philosophising"

between anthropocentric and biocentric opinions declaring the equal or unequal value of all forms and manifestations of life, whether to refuse the developed food chains, and whether to intervene into the natural regulation of populations. In spite of the uselessness of polemics with this social sub-category, the democratic necessity is not only "not to lump everything together" but to repeat again and again the most rational and sober argumentative substantiation that an experiment using test tubes is not adequate to reflect whole-organism regulations.

At first sight (but not in detail), the simplest are the levels of thoughts which should be targeted inside the research community itself, i.e. at those persons whose lives' substance became the biological experiment. Most of these persons in their investigation subconsciously use their personal relation to all living matter, their respect to the miracle of life, and try to consciously judge the legitimacy of each partial experiment and substantiation of working procedures. However, there is an open question whether every person who feels to be well-qualified for this type of research and whether all persons who became chiefs of such research teams possess enough "research skill" to accept, without reservation, the well-trying hierarchy of working research methodologies and subdue their habits to it. The primary ethical foundation of the biological experiment should be the interrelation of the level of the research problems under investigation with the level of researchers. Due to the progress and the related ever more complex research technologies, the contemporary biological experiment (which began at least half a century ago) is impossible without interdisciplinary team cooperation. It is thus the balance of the composition and quality of the research team which is decisive, i.e. the level of investigative efforts reached by its members. When judging the readiness of action of the research team, it is not unsubstantial that maturation to achieve an independent experimental creative level (including a personal formulation of the problem, methodical management of its solution, and adequate interpretation of results) has its individually different length of development:

- from the stage when what was devised and commissioned by a more experienced team is being examined,
- via the stages of prevalently analytical and descriptive character,
- via the period of more narrow interpretations
- to the formation of more broadly combined interpretations, which should result in further more principal inventive stepping-stones or prognostic thoughts.

The level of researchers should be assessed by their conscious distance from "pseudoscience" as an offence against science. The contemporary promotional explosion of irrational and pseudo-rational theories (particularly in therapy, for example "the would-be therapeutic miracles"), popularised by a number of superficial and sensation-seeking mass media, underlines the topicality of the

conscious unsympathetic approach of the research team to pseudoscientific inklings. These should not be formal declaratory clichés but rather the whole atmosphere of the research project, its design of implementation and the content of interpretation. One of the criteria for the evaluation of the level achieved by the team can be the quality of written working papers, recently required by various organising agencies, which are to substantiate the requirements addressed to the funding agencies. It is sometimes difficult to disclose the pseudoscientific aspect in the given formulations. Their characteristic features include ideas deprived of the context of the actual knowledge, ideas which prevent objectively checked verification, lay approach (naivety) and subjective "ego", stressing exaggerated secrecy (refusal of team cooperation) being afraid of theft of the idea (i.e. refusing the principle that from the standpoint of human progress it is not important who discovered a new item of knowledge but that the decisive element is that it was discovered by somebody at a given stage). Pseudoscientific approach can be revealed according to:

- the degree of generality of definitions: the less concrete and bombastic the formulations with superficial gobbledegook, the greater the suspicion of amateurism,
- the manifestations of graded subjectivism without self-correction (formulations may be clear and seemingly persuasive but without any discussion of the alternatives),
- argumentation supported only by dominant opinion clichés without considering possible doubts, without attempting auto-opposition of the formulated hypothesis,
- a lack of a methodical system (with a haphazard collection of disposable tests).

The quality of the composition of the research team is the logical starting point of the extent of the proposal ("what is to be investigated") and the profundity of its examination ("how to investigate it"). In the sub-question of "what is to be investigated", the balance and research maturity of the team is evidenced by its resourcefulness, capability of inventive formulation of the problem (the hypothesis concerning the relationships between the phenomena), the art of combining and estimating the objectives of the research (while keeping to the principle "to define the objectives and conditions, not results") either in the static concept (by describing the relations), or in a dynamic one (analysing the mechanism of relationships), or in a prognostic one (by estimating the broader connection of relationships). In the sub-question of "how to investigate it, how to verify the idea", the following sequence is to be accepted: literature

search → formulation of the project → experimental stage → utilisation of the results. The complexity of the composition of the individual sub-items is sometimes however less systematically elaborated. An example can be a less evident platitude of a compilatory confrontation from the aspect of the hypothesis itself on the one hand, and on the other hand the compilatory confrontational aspect of possible methodical approaches (including the questions of usability of alternative techniques as one of the ethical methodological principles). Similarly, a varying balance and detailed elaboration of the written proposal of the "design" of the study is not uncommon; it should include the stages of investigation (examination of the principal question, parallel questions and their presumable modifications), time links, economic and resultant technical-methodical arrangement (including the ways of verification of methodological validity and reproducibility), presumed techniques of evaluation of the findings (including estimation of intra-individual and inter-individual variability of experimental sets and estimation of how many probable experimental repetitions will be needed given by *a priori* principles of balance between the degree of statistical probabilities and ethical requirements), as well as presupposed interpretational reflections (for further direction of investigation?, for implementation in practice?, for the development of a broader theory?). Similarly, it is a matter of course that the subsequent experimental stages of implementation are based on the elaborated design. Systematic checking of the individual research procedures is however not always kept in such a way that only one variable is being changed (or a minimum of exactly identified variables). The intersection of several independent verifications is obtained by respecting the exactness and consistency of terms (as one of the starting points for subsequent adequate interpretations).

The summarising conclusion is based on the sub-text implying the necessary linkage between the agreed ethical rules of the biological experiment and the personal subjectivity of the researcher or the research team:

The generally declared ethical standards cannot schematise the moral feeling of the researcher, his or her estimation of the limits for the selection of alternative methodological approaches and the level of his or her relationship to any living creature and the resultant quality of action towards the individuality of the experimental subject. It is therefore the primary responsibility of the experimenter how sensitively he or she will consider the methodological combinations from computer simulations via tissue cultures to the *in vivo* experiments in such a way that a new item of knowledge would be as comprehensive as possible and within the framework of "the ethical principles respecting any form of life", protecting the human volunteer, the patient, or experimental animal, i.e. living creatures as he or she actually is.

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