How a drug is produced: the pharmacologist’s point of view

L. Berrino

Pharmacology Section “L. Donatelli” – Department of Experimental Medicine
Faculty of Medicine – II University of Naples

Drug production is a long process consisting of various steps, each with a well defined goal. Given the biological target, a specific candidate molecule has to be identified. A first basic pharmacological and biochemical screening allows to isolate among thousands molecules 20-30 leader compounds, namely the precursors of a real drug. As soon as chemical and physical features are defined, animal trials begin by testing acute and chronic toxicity; if a compound assigned to become a drug has shown a good efficacy and safety profile, clinical trials can start. Clinical trials are powerful tools to verify if novel drugs can be suitable for people; nevertheless, the relevance of a research can not justify a violation of human rights and dignity. After aberrant trials carried out in Nazi concentration camps the international scientific community has set up ethical rules for human trials: the Nuremberg Code (1949), in which is solemnly proclaimed that “subject’s voluntary consent is absolutely needful”, and the Declaration of Helsinki (1964, then updated in 2004), regulating the rights of humans involved in drug trials.

The European Union has also adopted a set of rules regulating trial correctness and standing for a formalization of the ethicity assessment ratified by the Declaration of Helsinki. In order to ensure respect of “Good Clinical Practice”, specific protective tools have been established, such as the Ethical Committees, the competent Authorities of the member Nations and the relative rules for personal data protection. In Italy no clinical trial can be performed unless the protocol has been evaluated and approved by an Ethical Committee. Ethical Committees have various duties: to assess protocols of clinical trials from scientific, ethical and feasibility points of view; to monitor study course; to promote information and training for physicians and patients; to give opinions and suggestions in case of specific requests; to verify the financial coverage of trial-related expenses; to warrant investigators’ rights to disseminate and publish their findings, regardless the sponsor’s opinion and in observance of the laws in force regarding privacy and copyright.

Within their many activities, Ethical Committees have often to answer to relevant and difficult questions, such as clinical trials with subjects unable to give effectively their consent (i.e. children, demented persons, psychiatric patients, etc.), or the use of placebo. In case of patients’ groups unable to give a consent, their inclusion in clinical trials must be done according to very narrow criteria and only after a written consent by the patient’s proxy, given together with the caring physician. As for as placebo ethics is concerned, on the other hand, according to the
Recommendations of the European agency for drug registration (EMA) and the statements of the Declaration of Helsinki, any clinical trial aiming at proving a treatment efficacy must ensure to patients the best available therapy. In this regard, remarkable questions for Ethical Committees rather often arise, such as the meaning of “the best available therapy”, or the definition of circumstances where the use of placebo is allowed.

At the core of discussion there is always and in any case the patient’s interest, which must prevail over that of science and society. Ethical codes, guidelines, informed consents are only a starting point, because the best warrant for an ethical research is the investigator’s ethical conscience. Ethics serving science, finally, represents an important stimulus for looking ahead, beyond data and postulates, to overcome them by finding out a new balance point.