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EUROPEAN ATOMIC ENERGY COMMUNITY - EURATOM

EURATOM'S BIOLOGY PROGRAMME 1961-1964 REPORT AND PERSPECTIVES

by

R.K. APPLEYARD

1964

Directorate General for Research and Training
Biology Division

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— framework and methods of action;
— policy;
— practical development of programmes.

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1 — FRAMEWORK AND METHODS OF ACTION

1.1 Scope

The mission of Euratom, the European Atomic Energy Community, as laid down in 1957 by its constitutive Treaty, is "to contribute to the raising of the standard of living in the Member States and to the development of exchanges with other countries by creating the conditions necessary for the speedy establishment and growth of nuclear industries". This the Community is to achieve largely by appropriate research and development.

In the case of biological research, the Annex of the Treaty stated more precisely what the founders of the Community had in mind : the application of nuclear techniques to biological sciences, agriculture and medicine, and research directed toward the assessment and mitigation of the harmful effects of nuclear and ionizing radiations. Accordingly, it is these tasks that the Biology Division of Euratom has tackled. They are characterized by their broad scope and by their contribution of an essential term to the human and social equation in which both the profit and pain from nuclear energy must finally be entered

1.2 Resources

In Euratom's first five-year programme, which ran from 1958 - 1962 and for which a total sum of 215.10^6 U.A. [1] was provided, credits of 3.10^6 U.A. were earmarked for biological research and in practice remained available for the last two years of the period. In the second five-year programme, about 16.10^6 U.A. were earmarked for the biology division out of a total of about 425.10^6 U.A. or somewhat over three and a half percent of the total, a fraction not very different from that prevailing in other nuclear authorities. The Biology Division was also authorized to increase its personnel to 100 by the end of 1967. Of these, the majority will be professional research staff.

Like all Euratom staff, permanent members of the Division have a civil service type of protection in their positions and their effective salary remains invariant wherever they work. The present staff of the Division are listed in Appendix 1 to this report.

1.3 Organization

The Division is run by a Headquarters group consisting of the Director with one administrative and three scientific deputies, located in Brussels. It is immediately responsible to the Director-General of Research and Training, who is in his turn responsible to the Euratom Commission. The Commission receives its funds from a Council of Ministers, reports both to that Council

[1]) The unit of currency used throughout this paper is the European Monetary Agreement Unit of Account (U.A.), equivalent to 1 United States dollar.

and to the European Parliament and is juridically subject to a Court of Justice, the remaining principal organ of the Community.

The Constitution of Euratom requires that its Commission be advised in scientific and technical matters by a Scientific and Technical Committee whose members are appointed as individuals by the Council of Ministers with the advice of the Commission. The Council of Ministers and the Commission are also jointly advised by a Consultative Committee for Nuclear Research. The members of this Committee are representatives of their respective Governments and of the Commission and have so far met under the chairmanship of the President of the Commission.

In the particular area of biology, the Commission and the Biology Division are further advised by a more specialized Advisory Committee for Biology whose members are appointed by the Commission. It is pertinent here to pay a warm tribute to the members of this Committee, listed in Appendix 2. They have not only counselled the Commission and the Director of the Division on many questions but have undertaken individual and collective examination and discussion of some hundred ore more research proposals in the last three years, often under difficult conditions of timing and language.

Within Euratom, the Division's activities are linked to those of two other Departments with which it cooperates closely but which do not themselves execute research as their primary function : the Medical Service and the Health and Safety Directorate; and it is very closely linked, through a common Director, with the Commission's research programmes on labelled molecules and the production and use of radioisotopes.

In the world at large, it is a comparative newcomer to a field long laboured spasmodically by university and hospital scientists, and now tenanted by large, well-established research programmes outside the Community : in particular those mounted by the Atomic Energy Commission in the United States of America and the Medical Research Council and the Agricultural Research Council in the United Kingdom. It is a field in which, within the Community, the national nuclear authorities who are Euratom's partners are also making considerable and rapidly increasing efforts.

The organizational situation of the Division is shown in diagrammatic form in figure 1.

1.4 Methods

1.4.1 *Direct Research*

It has been laid down by the Council of Ministers of the Community that the work of the Division during the period 1963 - 1967 shall be carried out primarily by contract. Nevertheless, particular radiological problems may at any time arise from the Commission's own nuclear research activities. The Division has therefore found it essential to maintain its own biological group at the principal nuclear establishment of Euratom at Ispra in Northern Italy. This group is organized into three sections which work respectively on movement of radionuclides in the environment of the Centre, on the location and possible effects of potentially harmful products including radioactive isotopes and on the development of cellular techniques of particular value in hazard assessment. The group is completed by technical measurement and administrative support units, which can be minimal in size because of the direct support received from the Centre itself. The biology group at Ispra was started in May 1962. It now numbers twelve research workers and will be built up to about eighteen in the course of Euratom's second five-year programme. Since December 1963 it has occupied the new building constructed for it within the establishment.

1.4.2 *Contractual Research*

In the contractual field the Division has employed both the conventional research contract and the association contract.

1.4.2.1 Association Contracts

In an association contract Euratom and a partner attack a particular problem jointly, in the fullest sense of the word : there is joint finance, a mixed research group drawn from the staff of both associates, a joint management Committee. This type of partnership, introduced originally for very large scale reactor projects, has proved to have considerable advantages for the main projects of Euratom biology : it gives to many Institutes and persons a real place and interest in the programme as associates rather than just contractors; it fosters communication and flexibility through the ubiquitous presence of Euratom staff; and by the consistent inclusion in the management Committees of these associations of senior directors of other laboratories it forms direct, responsible and effective crosslinks not otherwise attainable. Since it is continuously involved in the immediate management of all these associations, the Headquarters group of the Biology Division retains direct and close contact with the various fields of research and a capacity to introduce, modify or terminate individual projects rapidly.

1.4.2.2 Research Contracts

Euratom's research contracts resemble those of other organizations but are true contracts to buy research and by no means just subsidies. Formally they are allocated on the competitive basis of proposals submitted in response to a public invitation [1]) to collaborate in a particular area. In practice, the feature limiting research contracts in nuclear biology is the shortage of individuals with worthwhile original ideas and the capacity to carry them out. Proposals for contracts are examined at three levels : by the staff of the Biology Division; by three or four (sometimes more) individual referees highly specialized in the field, of whom the majority are not even from the country of origin of the proposal and often one not even from the Community; and in the more general setting by the Division's Advisory Committee mentioned in paragraph 1.3.

The Division has tried through its research contracts to encourage not only original ideas but new growing points of research activity and enhanced responsibilities among younger research workers. However, it has at the same time placed considerable emphasis upon contributory contracts in which a financial counter-contribution to its projects is made by national, university or other institutional authorities. This ensures a certain local interest in the project and usually guarantees that there is a real increase in financial support rather than a mere switch from the single-nation to the six-nation bank account.

2 — POLICY

2.1 General considerations

In its broad lines, the role which must be filled by the Division is clear if one considers the general distribution of effort in the world of nuclear biology. Only very rough estimates and measures of this effort exist, but such as they are they indicate that for the period 1960-61 in

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[1]) Such announcements are published from time to time by the Euratom Commission in the "Journal des Communautés Européennes".

America the United States Atomic Energy Commission alone expended 50-60.10^6 U.A. and maintained at least 1,200 [1]) fully qualified research scientists; the United Kingdom, through its Medical Research Council's unit at Harwell and relevant work elsewhere, expended at least 2-4.10^6 U.A. [1]) and the six countries of the European Communities together fielded an effort of some 15-18.10^6 U.A. [1]) and some 900 [1]) fully qualified research scientists. The addition of the Euratom programme could therefore :

— represent a reasonable supplement to the Community effort,

— give emphasis to certain areas by the exercice of its own, distinctive scientific policy and

— contribute to the coherence to the Community effort.

The first of these objectives could be nullified if the internal operations of the Member States of Euratom simply resulted in funds handled by the Commission being offset by corresponding losses from national funds which would otherwise be applied to much the same ends. But in biology these Governments have shown full awareness of this danger to their collective offspring. As the high percentage of association and contributory contracts shows, so far from reducing their domestic activity in areas entered by the Division, they have usually responded by a parallel increase. They are doubtless guided by the assurance, which it is imperative that Euratom continue to give them, that they thereby make their contribution more effective by setting it in a wider coherent framework.

The need for the Division to have a distinctive scientific policy of its own derives from the fact that more agreement between several parties is very often just the lowest common denominator of their ideas, a fact better known to diplomats than to working scientists. Avoidance of this pitfall is indeed one very good reason for the existence of the Commissions of the three European Communities. But this policy does not have to be — indeed must not be — independent in any extreme "go it alone" sense. It must at least agree with a consensus of informed opinion in the Member States which are ultimately responsible and be continuously evolved with and explained to the Governments of these States and to their experts and representatives so as to be assured of their continued support [2]); and it must be a policy which in conception applies to the effort of the whole Community but in execution takes full account of what others are doing, leaving alone, for example, what is already well done by the nuclear authorities of the separate States.

In recent years, biological research has become technologically so complicated and its different areas so interdependent, that a key to many individual problems, and perhaps to the general speed of advance, is coherence of effort throughout the Community. By this is certainly not meant authoritative coordination which is not possible for the Euratom as now constituted amid the diversity and number of independent bodies engaged in nuclear biology. It means rather a very free exchange of information and ideas at the planning stages between the Division and the many other organizers of biological research.

Even this is not enough. Real coherence needs to start from the roots. In a Europe in which, because of linguistic, national, institutional or other boundaries far too few people talk to each other, this means a continuous series of free discussions, at the level of the individual research worker, between those who, whatever their affiliations, face the same technical problems. This we expect to be a major and continuing part of the Division's programme, in the form of the small "contact groups", limited to ten or twelve invited participants, with which we have begun to experiment this year.

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[1]) Unofficial estimates based upon private communications and deductions from official reports.

[2]) In Community practice, discussion and acceptance of programmes by the Advisory Committees of Euratom described in section 1.3 of the present report provide the machinery for this.

2.2 Scientific Considerations : General Analysis and Particular Priorities

2.2.1 *General Analysis*

Of the three main fields of biological research laid down in Annex I of the constitutive Treaty of Euratom, namely, applications of nuclear technology to agriculture and to medicine, and research related to the hazards of radiation, the last is clearly central for a nuclear authority, even though it may be argued that until recently more real benefit had come to mankind from the first two than from all other nuclear affairs put together. It therefore constitutes the bulk of the Euratom programme.

We have chosen, among many possible and arbitrary ways, none of them wholly satisfactory, to analyze this hazard problem as follows : the effects of a given dose may be upon the individual irradiated (*somatic effects*) or upon his descendants (*hereditary effects*). The somatic effects may be *early*, and mainly of significance for diagnosis or treatment of injury, or *late*, and at present mainly of significance in connection with hazard evaluation, population risk, and the fear of radiations.

However, the causal pathways leading to somatic or hereditary effects do not diverge at once from the initial ionization. A wide area of *research into radiobiological mechanisms*, including important questions of cell genetics and of chemical protection against radiation are common to both and we have chosen to treat this as a separate sector of the programme following the practice already adopted by the United Nations Scientific Committee on the Effects of Atomic Radiation.

Falling logically within this sector, although for practical purposes often within the areas of genetic or developmental problems, lies the whole explosive advance of modern biology at the molecular and cellular level, one of the most exciting chapters of intellectual advance of our life-time and one which is bringing to bear on all radiobiological problems a host of new conceptions and technical possibilities. This field has posed a serious problem of policy to Euratom. It is not the function of a nuclear authority simply to support a field of biological research because placing the phenomena of life on a sound physical and chemical footing is exciting and will later be rewarding in the general humanitarian sense. Euratom is neither a vague philanthropy nor is it yet a fully fledged European Scientific Community. What is significant is that the work in this field already sheds a bright light not only upon the basic mechanics and substrates of the actions of ionizations, but upon the nature of its genetic consequences, upon the nature of its carcinogenic consequences, indeed upon almost every underlying facet of what may be called the amplifying systems (see paragraph below). Moreover, it is from this area alone that will come the newer cellular and molecular techniques able to improve examination or control of events in man and to contribute that understanding which will always be necessary to piece together the growing but ever inadequate and dispersed body of factual observations concerning our own species. It therefore behoves a nuclear authority on the one hand to strengthen corresponding efforts in its area and on the other hand to see that they remain in close contact with some of the uglier realities of the world at large.

Unravelling the effects of a given dose, be they somatic or genetic, is a long term problem, which will be with us for tens of years. Nuclear authorities tend to set it on one side by adopting, usually on the recommendation of the International Commission on Radiological Protection or some other group acting upon collective judgements of very high calibre individuals, basic standards for maximum tissue exposures (The I.C.R.P. which, on the contrary, must look the problems in the face, has not the massive resources of the nuclear authorities to pursue them by itself). The problem which then faces nuclear authorities is a shorter-term and more technological one : what may be the tissue dose under various real or imagined circumstances ? We have felt it right, during the launching period of the Euratom programme, to resist the naturel temptation for a nuclear Community to attack primarily these shorter-term and more obvious gaps. Rather, we have placed primary emphasis upon the need to tackle the greater uncertainties, in our ignorance of the effects of even a known tissue exposure, recognizing as we do so that this is a longer and less spectacular, if finally more fruitful road.

But we have not, for all that, neglected the phenomena determinative of radiation exposure or of its calculation. Nuclear operations, if they are well designed and do not undergo what are euphemistically called "super-critical excursions" give rise to possible radiation exposures mainly through the use or production of radioactive materials. In this respect their problems differ essentially from those of others, for example, of most hospital radiological departments. They must look to problems of *movement, uptake, retention and loss of radioactive isotopes*, first and foremost in man (or experimental animals as a substitute), second, in the environment and especially in the food chains leading to man, starting with soils or waters and with plants.

To be sure, there exists, as in other fields, the problem of *improvement of devices which measure radiation exposure or tissue dose of all kinds*. This is only partly a task for technological research and development based upon existing or exciting new physico-chemical systems of measurement. It is also a field in which somewhat more than physico-chemical methods are needed. The connection between the dose to the gonads, or the relevant dose to the bone marrow and a small instrument worn on the shoulder lapel or in the pocket can never be better than very imperfect, especially under conditions of accident. We need therefore to pursue research which will enable us to estimate the real relevant tissue or total body dose *in situ* under a variety of circumstances : and the pursuit of this objective ranks high among the preoccupations of the Division in this sector.

In the long run, the strength of research in "nuclear biology" in Western Europe will depend on our ability to provide trained brains to do the work. Throughout most of this field — since irradiation modifies biological systems by a physico-chemical agent — the running is now largely being made by individuals who to thorough grounding in one branch of science have added further training in a second, usually by combining a physico-chemical with a biological discipline. Such double training is not easy or short. Moreover it is extremely difficult to combine with the somewhat rigid excellence that has long been the hall mark of the European scientist. Yet the forward surge of research guarantees for the future a considerably expanded demand for the individual whose knowledge and experience spreads beyond a single discipline : the existing plans and programmes of Euratom and its associates described in these pages, may alone absorb an increased output of them amounting to fifteen or twenty per year. In the long run, it is as certain as anything can be that Euratom can do more for the nuclear biology of the Community by promoting a corresponding increase in the supply of such people than by any other line of action. All the programming, all the finance and all the planning, contracting and rearranging of groups in the world adds not one man-year to the research effort under way if it does not add appropriately trained men.

The analysis of the Division's activity into different programme sectors in radiation hazards, applications of nuclear technology to agriculture and medicine and support activities including the headquarters of the Division with its various study, working and contact groups is summarized in graphical form in Figure 2, which shows also the approximate percentages in financial terms of the effort that goes to each sector. It will be observed that these percentages show one considerable imbalance : that between research on the applications of nuclear technology to medicine and to agriculture, a disparity whose correction by expansion on the medical side must be a major objective of the Division in future planning.

2.2.2 *Particular Priorities*

Within the framework of our general analysis a number of quite simple factors, discussed at greater length either in the preceding paragraphs or under particular programme points below, have combined to dictate the particular priorities of the Division's scientific policy especially in the radiation hazards field. In summary, they include the need, intensified rather than diminished by much experimental work on animals, for quantitative information directly derived from man; the remarkable degree by which the uncertainties in the consequences of a given dose exceed the uncertainties in our estimates of it; the increasingly dominant role of the hemopoietic system; the key part played by study of the few amplifying processes, such as carcinogenesis and mutation, by which ionisations or other events involving one or a few molecules can eventually overwhelm large organisms of many millions of cells; the relative sensitivity to irradiation of early developmental stages of living organisms; the extent to which the advance of this whole field is held up less by a shortage of direct experiments with ionizing radiations than by a lack of understanding of the phenomena and systems which irradiation modifies; and the extraordinary new light being shed on many of the most crucial aspects of radiobiology by the new advances in cellular and molecular biology. To these must be added more practical points, such as the need to measure received dose *in situ* rather than on a film badge in dubious geometrical relation to the tissue. Together with them we recall the elementary truth that only by an increased provision of correctly trained research workers can the European effort be increased, as distinct from merely rearranged.

These considerations have led the Division :

— to devote, among its long-term objectives, highest priority to an advanced interdisciplinary training programme for young research workers,

— among its middle-term aims to give very high priority to clinical research on the hemopoietic system and to human cytogenetics; and to expend almost twice as much upon examination of the effects of given doses as upon examination of the possible magnitude of received doses,

— in the short-term to look for and explore systems which may constitute biological measures of exposure *in situ,*

— to relate the whole Euratom biology programme correctly to its necessary sources in molecular and cellular biology through a series of selected projects in that area.

While these points constitute particular priorities in the Division's thinking, they by no means dominate the whole of its programme which remains a general and balanced effort based on the general analysis of paragraph 2.2.1.

3 — PRACTICAL DEVELOPMENT OF PROGRAMMES

3.1 Chronological Development

Systematic development of the Euratom biology programme was not begun until February 1961. However, two essential preparatory tasks were undertaken. First, a survey was made of what was actually being done within the Community. A questionnaire was sent to many laboratories and institutes of the six member countries. The replies received made up a picture of the existing Community effort and in particular of that part of it receptive to cooperation with Euratom. The survey by questionnaire was followed up by personal contact with some two hundred laboratories. At the same time, during the period 1956-1961, the United Nations had undertaken a general survey of the field on a world-wide scale, as part of the activities of its Scientific Committee on the Effects of Atomic Radiation. Many of the results, ideas and conclusions of this survey were immediately transferable to the conduct of the Euratom programme in 1961 [1]).

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[1]) The present writer served as Secretary to the United Nations Scientific Committee on the Effects of Atomic Radiation from 1956-1961 and was in charge of the scientific staff assigned to the work of the Committee by the United Nations Secretary-General.

During 1961 not only were some of the first contracts of the biology programme negotiated and signed (the earliest actually dates from 1959) but a first general plan of work was outlined and accepted by the Commission and the Scientific and Technical Committee. It was both necessary and possible at that time to act with considerable speed : in 1961 three years of the first 5-year programme of Euratom had been nearly completely lost in getting biological research under way and it was essential to have some structure in being before the second 5-year plan came to be formulated, just as it is now necessary that the formed Biology Division have results as well as intentions to show when the third 5-year programme comes to be discussed.

In fact, the winter of 1961-1962 and the summer of 1962 were spent in examination of these plans by the Governments of the Member States as part of the preparation of Euratom's second 5-year programme. This phase of dialogue between Commission and Governments fixed the order of magnitude of the programme in terms of both money and men for the period 1963-1967 and so determined the eventual outcome of the build-up which was already under way. Following these discussions, in late 1962 a final plan was established and is being closely followed. The programme it outlines will achieve financial maturity near the end of 1964. Its chronological development is illustrated in Figure 3 A, B and C.

3.2 Development of Individual Sectors [1])

3.2.1 *Genetic Effects*

In the field of human genetics two advances of recent years have pointed the way to obtaining relevant information directly about man.

One is the intense technical development of human cytogenetics coupled with studies of the connection between specific chromosomal abnormalities and diseases in man. It is clearly necessary to measure not only the numbers and types of chromosomal anomalies induced by ionizing radiation, but their normal frequencies in human populations. These questions are tackled both by the Euratom cytogenetics unit of the University of Pavia (20) set up by contract between the University and the Euratom Commission in mid 1963 and in cooperation with the Istituto di Radiologia of Rome (22). In accordance with its usual policy the Division has not confined itself to this but has given active support to other pioneering work in human cytogenetics within the Community.

The other advance which has made possible the acquisition of an entirely new kind and scale of information about the structure and risks of the population genetics of man is the application of modern data processing techniques to various types of national or other vital and health records. This field was systematically examined by the Seminar convened under the auspices of the United Nations Scientific Committee on the Effects of Atomic Radiation in 1960 [2]). It has been pioneered partly in Canada by Dr. H.B. Newcombe and his colleagues, partly in Italy by Dr. L.L. Cavalli-Sforza's group. The Biology Division has given support and encouragement to the work of this group since mid 1962 through its association with the International Institute of Genetics and Biophysics of Naples (27), of which the group, although still located at Pavia, now forms an integral part. Through this association, one of the Division's major enterprises, Euratom and its staff also participate fully in a broadly based experimental genetics centre of the Community whose work includes biochemical studies of Drosophila, biophysical and

[1]) Throughout section 3.2 reference numbers in brackets refer to contracts and authorized programmes listed in Appendix 3.

[2]) The proceedings of this Seminar were published by the United Nations in 1962 under the title "The Use of Vital Statistics for Genetic and Radiation Studies".

genetic studies of bacteriophage and mutational studies of cultured mammalian cells, biophysical studies of the nucleic acids and of abnormal proteins — all studies which contribute to the Division's programme of cellular and molecular biology.

Our ideas concerning gene mutagenesis by radiation and how to investigate it have changed greatly in recent years. It is now clear that the primary substance concerned is nucleic acid and that two avenues of approach to the problem are likely to be extremely fruitful, especially when coupled together. These are the study of the chemical products of the action of radiation upon DNA and its components (28); and the action of various chemical mutagens and comparison of their effects with those of irradiation (18, 19, 25). Both are under study by the Division.

Since the dramatic demonstration by the Russells of a dose-rate effect in mice shattered the older simplest views of the genetic hazards of radiation, it has become increasingly clear that gene mutation by radiation, in the cells which matter from the hazard point of view, is a complex, even lengthy process which can certainly be influenced after as well as *during* the exposure. The Division participates in the study of these matters (32) and plans to pursue them in increasing biochemical depth, where they should eventually join up with the group of studies mentioned in the previous paragraph.

The Division also gives attention to the special problems posed by biometrical characters (such as intelligence in man) which are under highly multiple genetic control (21, 24), to the possibilities of micro-irradiation of chromosomes (17) to microbial systems capable of acting as rapid mutagenic screening agents and able rapidly to distinguish breaks, somatic recombinations and true intragenic mutations (23). In association with the Gesellschaft für Strahlenforschung, it is also exploring the interaction of dose-distribution with mutational effect in mice and the suitability of fish for particular radiation genetic problems (10).

3.2.2 *Somatic Effects of Radiation*

3.2.2.1 *Early Effects*

It is convenient to consider first questions of early post-irradiation damage, diagnosis and treatment. Among the systems of the body which determine its reaction to irradiation, at dose levels where this reaction may be important, the hemopoietic system is dominant. It determines : resistance to post-irradiation infection; death by failure of the bloodforming system and the possibility, however remote, of tissue transfer therapy; incidence of leukemia as a delayed effect; hemorrhagic complications (3); some current "biological" attempts to estimate exposure. All hinge upon it. To study it and its relevant behaviour in man seems a central task for nuclear biology and medicine; yet few clinical research centres of adequate scale in the world — and none in Europe — have hitherto devoted themselves to it as primary objective.

The Division has associated itself with the Gesellschaft für Strahlenforschung, acting for the German Ministry of Scientific Research, to set up a programme of clinical research of this kind (4). The project is dual : one part, located at the University of Freiburg will concentrate primarily upon kinetic studies and upon very fully integrated "total" studies of patients whose hematological conditions either are of radiological origin or resemble these in significant respects. The other will primarily be constituted by a fusion of clinical and non-clinical research groups at the University of Munich and will take as its starting point morphological and biophysical studies of the bone-marrow and certain aspects of the biochemistry of leukemia and of its genesis.

One of the most challenging questions currently raised by the action of radiation on the hemopoietic system is that of its immunological consequences, with the associated long-range possibilities and speculations concerning tissue-transfer therapy. In close relationship with the clinical radiation-hematology units described above and with each other therefore lie the pioneering work of Mathé in direct bone-marrow therapy (5), and work upon post-irradiation immunological changes in primates and rodents (1, 2, 6), their genetic and developmental control and their consequences for tissue transfer.

Western Europe is fortunate in having very capable research groups and workers in all these areas : in all, the Division has intervened in order to expand the physical possibilities and to improve the links necessary for satisfactory progress in this rapidly developing area, significant far beyond the bounds of nuclear affair.

Other projects stand a little aside from this group. One is an outgrowth of clinical observations made by Dr. Massart, direktor of Euratom's Medical Service, on the curative effect of the pancreatic preparation "Padutin" when applied to superficial radiation burns. The Division is pursuing the development of a reproducible experimental system by which these observations may be extended more rapidly and in some respects more surely than is possible by purely clinical trials (16).

Finally, among the possibilities of dose estimation immediately after accidental or other heavy exposure, certainly lie those biochemical criteria based upon early metabolic disturbances. In view of the importance attached to biological estimations of exposure, the Division has felt it necessary to include such biochemical investigations in its programme and has particularly concentrated upon the catabolism of DNA (43).

3.2.2.2 Late Effects

The principal known late effects of radiation are carcinogenesis and non-specific shortening of the life span : we are far from a sound basis for early diagnosis or treatment of them, and good ideas in this field are urgently needed. There is, however, a more practical and pressing, if shorter-term need. It is to increase the statistical studies being made of suitable irradiated groups of persons, and, by studies on animals, to underpin the few human statistics which are available, interpret them and draw prudent conclusions from them. In this respect, a considerable body of expert opinion feels that systematic studies of the R.B.E. of radiation of different kinds and particularly of its changes in the lower dose region could now make a key contribution. Particularly in the light of other extensive work in delayed effects going on outside the Community, the Division has limited its intervention in animal experiments to this and related problems (8, 10, 35), including specific photodynamic effects (34). At the clinical level it has helped clinics of one country of the Community to participate in a broad survey of leukemia among special classes of medical patients initiated by the World Health Organization (9) : and it supports biochemical research into the behaviour and nature of the human leukemic cell (7). Finally, the Division has remained acutely conscious of the impossibility of completely separating cause, nature and cure of those malignant diseases which can be induced by radiations. It has therefore participated actively in the formation of a European grouping of programmes and institutes in the field of cancer chemotherapy (12), believing that such a costly and complex field can only progress satisfactorily by some such spontaneous rationalization of tasks within it.

It is generally accepted today that the embryo or foetus, and perhaps the differentiating cell *per se*, is particularly susceptible to damage by ionizing radiations.

Certainly, immediate small errors made by such cells and systems may have grave after-effects for the adult individual. Perhaps even very common but tiny radiation-induced changes may frequently produce relatively small changes in important and complex organs such as the brain which, individually small, may yet amount to a significant population hazard in case of widespread exposure. In the coming years, there is good reason to anticipate a good deal of light on these problems, for few will dispute that the next decade is likely to see a massive advance in all our knowledge of morphogenesis and developmental biology. The Division has therefore undertaken a group of projects which together form a single programme on the effects of irradiation on the embryo. They include an empirical examination of the learning capacity in rodents (10), experiments upon selected organizer-inducer-receptor systems in which biochemical identification is particularly advanced (11), studies of the rapid and sensitive stages which immediately follow fertilization (15) and kinetic and other studies based upon the use of *in vitro* cultures of developing organs (13, 14). The whole is complemented by a general programme of research on the control mechanisms at the cellular level involved in differentiation and allied phenomena, and the effects of radiation upon them (13, 26).

3.2.3 *Studies common to both Somatic and Genetic Effects*

These studies embrace two different but overlapping and closely interlocking fields : on one side, the immediate mechanics by which ionizing radiation acts, which form a large part of classical radiobiology; on the other, the newer ideas and techniques thrown off by recent advances in molecular and cellular biology. As already mentioned in paragraph 2.2.1 this last constitutes an essential source of advance for all radiation biology which cannot afford to be separated from it either in concept or execution.

"Molecular biology" has progressed from pioneering experiment to advanced technology in ten or fifteen years. It is of the utmost importance to the future of all biological research. Yet much needs to be done for it in Europe : there is a dearth of well-equipped institutes : there is a lack of mobility or even communication between both individuals and laboratories : there is a shortage of men trained in the right combinations of disciplines. The Division has therefore directed its effort in part toward making up these deficiencies and in part toward the development of programmes by which the flow of new possibilities and conceptions from cellular and molecular studies into the stream of radiological progress may be increased and speeded up. Three major associations are involved which together constitute a unified programme.

They are

— in the field of molecular genetics, the association with the International Institute of Genetics and Biophysics at Naples (27);

— in the field of macromolecular biochemistry, and especially in the study *in vitro* or *in vivo* of complex synthetic systems, the association with the biochemical and genetic departments of the University of Leiden (32);

— in the field of morphogenesis and developmental biology, the association with the Université Libre de Bruxelles (26).

Because of the singular importance of this field as a source programme, from which new advances will originate, the Division hopes in the future to complete it by extension not only to other regions of the Community but to other topics currently in a phase of intense development.

Classical radiobiology, in its mechanistic sense, has been the subject of a great deal of work in a great many countries for a long time. Consequently, the Division has adopted a more restricted approach, largely centred around the problems of DNA. Within the Division's programme the direct and indirect actions of ionizing radiation upon this compound and its chemical components are under study (28); the radio-restorative action recently attributed to it by some workers is under exploration (33); so is the disturbance both of its synthesis and of its breakdown under irradiation (29, 43). The study of radiobiological mechanisms also leads to more immediately practical outgrowths, among them, the study of chemical protective agents. Here the Division's programme is based upon a wide variety of biological materials (30). Particular attention is given to systems which display very rapid changes after irradiation, and to comparison of radiations of different qualities. The effects of radiation upon permeability of cells to macromolecules (29) and upon complex cellular organelles (31) are also under study.

3.2.4 *Movement of Isotopes in Man and in Experimental Substitutes*

All problems of maximum permissible levels of radioactivity or of assessment of tissue doses from given quantities of ingested isotopes end up with the same question : how much of the isotope is taken up by the human body, where does it go, how long does it stay there, how is it released? And can the behaviour be modified?

Direct experiment upon man is almost excluded although, unhappily, accidents and incidents continue to give a steadily growing if haphazard body of quantitative information. The primary task has therefore been one of research aimed at plugging the holes and arriving at a correct interpretation of the existing limited data. Where no quantitative information exists at all in man, responsible authorities such as the International Commission on Radiological Protection have rightly recognized that it is better to base a responsible judgement upon an experiment with rats than upon nothing at all : and where experiments upon a range of species yields a consistent picture, the basis of judgement is already considerably strengthened. But the corresponding experimental work is a heavy burden. Costly instrumentation such as whole body counters equipped with multichannel analysers must be backed by computer facilities for analysis of data. Expensive facilities for handling highly radioactive animals must be built and maintained. The range of species which must be examined is neither small nor cheap as may be seen by considering those which resemble man most closely in various respects : the pig for the skin, or the cat for the respiratory system. In the case of long-lived and long-retained isotopes, the animals must be kept and studied for corresponding periods of time. Considerable credit must go to the United States authorities for pioneering this field with a number of massive programmes.

The Euratom Biology Division has felt that one major experimental effort on the continent of Europe was essential : that it should be of sufficient scale and scope to be able to tackle *ad hoc* problems from time to time in its stride; that it should be closely linked to the gathering of data on man wherever this is feasible : that it should pursue semi-practical aims and yet a definite intellectual philosophy of its own, without which there is no guide among the vast number of experimental combinations of species, isotopes, modes of ingestion and tissues studied. An association (39) has therefore been formed with the C.E.A. to conduct such a programme, of which the principal objectives will be : distinction between the effects of the physical form in which an isotope is presented and the effects of its chemical nature; concentration upon isotopes of elements important in peaceful nuclear industry (for example Pu, Am); concentration upon forms of ingestion likely in nuclear industry, in particular surface wounds and inhalation; basic studies of location and transport at the cellular level; and attention to localized lesions, in particular those capable of setting up a vicious circle by affecting the processes of retention or release of the activity itself.

Outside this principal project, only small programmes are pursued by the Division, both concerned with the problem of strontium incorporation and removal. One attempts to shed new light on the whole problem of biological distinction between Sr and Ca by studies of the mechanisms by which certain Acantaria living in sea-water build up skeletons of pure Sr sulphate (36). Another explores the use of bifunctional decontaminating agents having simultaneously a chelating and a diuretic action (37). Yet a third is devoted to improvement of measurements of radioactivity in individual teeth and its correlation with body burden (38).

3.2.5 *Movement of Isotopes in the Environment*

Most radioactive contamination of the surroundings reaches man by various food chains. Because animal food is derived from vegetable, the primary steps in terrestrial food chains are the absorption, location and retention of the isotopes concerned in plants. While direct foliar or stembase absorption has been shown to be of great importance in the case of the radioactive fall-out due to nuclear explosions, the fate of isotopes either in the soil or through the soil-plant relationship may still be decisive in the case of possible contamination by peaceful nuclear industry. Therefore, the programme of the Division assigns high priority to the research necessary to evaluate the contamination channels, particularly in the surroundings of the Euratom's main reactor center at Ispra. This area, in the case of terrestrial and aquatic food chains (I 1), presents unique features which must be specially examined as part of the necessary safeguarding of the Commission's own operations.

Movements of isotopes in soils and plants are also studied within the programme of the Euratom-ITAL association, the principal vehicle of the Division's agricultural research (40a). This programme takes as its departure point the existing body of information gathered with great skill on semi-empirical lines, mainly outside the Community, and will attempt in the first instance to extend and deepen our understanding of this, by laboratory work under closely defined experimental conditions, concentrating in the first instance upon the behaviour of strontium and to some extent of caesium.

Contamination of waters presents a different problem. Cultivation is a relatively uniform process about which valid generalisations may be established. But each body of water and its living content is an individual wild ecosystem and must — at least at our present stage of knowledge — be studied in rather the same way, as an integral and individual case.

The programme of the Biology Division includes two such studies : one in fresh water, one in salt. The first, not unnaturally, is that of the Lago Maggiore upon the shores of which is located the Commission's principal research establishment at Ispra (41). The Lake is not only a binational tourist area. It is one of the three great lakes of Europe; it has a particularly low mineral content; it supports commercial fisheries. The salt-water research is carried out off the Mediterranian coast, since the Mediterranean coast-line of the Community is perhaps its longest and most valuable and since some relevant studies are already undertaken off its other coasts by national authorities. The programme is carried out in association with the Comitato Nazionale per l'Energia Nucleare at Fiascherino, by its marine station in Italy (42) : it is hoped that it will later be extended to the French Mediterranean coast.

3.2.6 *General Scope of Euratom Research on Movement of Isotopes*

It will be seen that the principal programmes of the Biology Division, described above, cover the movement of radioactive isotopes in ecological systems as a whole and in salt and fresh waters, soils, crops and man or experimental substitutes. They are completed and complemented by a programme of determination of levels of contamination in the food chain throughout the Community conducted through an association by the Commission's Health and Safety Directorate. Reciprocal representation on the management Committees of these programmes ensures that the Commission is provided with a single coherent effort covering most of the major aspects of radioactive contaminations, with the possible exception of animal and animal products, in respect of which a major programme has not yet been formulated. Initiation of such a programme, if it proves necessary, will be a task for the third Euratom five-year programme.

3.2.7 *Dosimetry*

To some extent questions of dosimetry are inevitably tackled within other programmes of the Division : to some extent they involve rather expensive physico-chemical developmental and instrumental programmes beyond the scope or resources of the Division. Nevertheless we consider it essential that the Division's group at Ispra be equipped, through its measurement section (I 4), to control or improve any or all of the dosimetric procedures in use throughout the Division's other programmes; and that the section be built up to a corresponding level of size and competence.

The Division is also preoccupied with possible *in situ* biological indicators of exposure or dose among which the approach via chromosomal analysis of somatic cells is often considered the most hopeful, but the biochemical approach, especially in relation to the metabolism of DNA, is not without promise. Both, as already mentioned earlier, receive attention within the Division's programme (I 3, 20, 22, 43).

For the rest, there have been exciting recent developments in dosimetric science and technology, such as the use of glasses and other solid-state indicators, the use of low pressure tissue and cell-like chambers, the techniques of neutron dosimetry and new light on whether the classical "dose" is really the most meaningful measure we can establish. Nevertheless, the resources of the Division have not yet permitted the formulation of a systematic programme. This none the less remains an essential priority as soon as circumstances allow.

3.2.8 *Applications of Nuclear Technology to Agriculture*

Two broad applications of radiation in agriculture currently engage the attention of the Division, as that of many other organizations.

The first of these is the improvement of cultivated plant species by artificial mutagenesis, a possibility now known to have practical value, for example, through the production of *erectoid* barley by Gustaffson in Sweden. The second is the preservation of foodstuffs by irradiation, already passing into commercial practice in substantial areas of the world.

The primary Euratom effort in both areas is carried out by the same large association (40*b*) responsible for the Division's main effort in experimental studies of movement of isotopes in soils and plants : the three subjects, together with the development of new analytic techniques constitute the entire programme of the association. In forming this association the Division took advantage of the presence at Wageningen of the Agricultural University, the largest collection of agricultural research institutes in Europe; and it provided this complex of research institutes both with a centre and focus for radiobiological activity and with a range of radiation facilities which includes the only reactor in Europe specifically constructed and primarily available for radiobiological research. This instrument, in particular, is available for use throughout all the Division's programmes.

Certain special aspects of plant mutagenesis are dealt with outside the association, notably the particular problem of chimera uncovering and other aspects of chimerism and inter-cell selection (44). The programme of the association itself is partly carried out by subcontracts with a number of Institutes throughout the Community, between which it affords a useful link making possible for example, a unified programme of research on many phases of radiogenetics of the tomato which will be carried out by a group of laboratories of diverse specializations.

In the food irradiation field, by contrast, the programme is so far limited to the ITAL Institute and others at Wageningen and to so-called "pasteurization" levels of radiation exposure. Particular attention is paid to surface pasteurization of soft fruits and to biochemical studies of the ripening processes of fruits. It will certainly be necessary to extend the biochemical studies to cover problems of induced biochemical changes, in view of the many empirical questions to which answers are already needed.

A more difficult problem has been how far the association should pursue research relevant to the problems of toxicology of irradiated foodstuffs. It is an area in which excellent research is under way outside the Community. On the other hand, very large-scale animal experiments indeed could conceivably be required if complete resolution were to be aimed at. Yet it is almost certain that, as in other fields, the health authorities will eventually be led to specify definite and practicable criteria based upon limited numbers, and primary responsibility for the necessary underlying research must rest with these authorities. In the meantime, it is possible that useful information may be obtained by any of various techniques which allow large numbers of cells to be screened without undue labour : so far, we have limited our effort through the association to preliminary scrutiny of a few methods of this kind.

3.2.9 *Application of Nuclear Technology to Medicine*

The development and use of the many tools placed by nuclear science in the hands of medicine is an enormous challenge. To the extent that every medical use of radioisotopes is embraced by it, every medical school in the Community is almost certainly engaged in it, and every major nuclear centre furnishes material and know-how for it. The very limited resources of which Euratom biology disposes are therefore totally inadequate for anything like a general support effort. On the contrary, the Division has had to limit itself very strictly to the initial development of new techniques.

To avoid the draining away of the Euratom effort in a mass of miscellaneous projects, only a single major programme has been undertaken. Through it, the work of two groups in different universities having largely complementary view-points and programmes is combined in a single association (45). The programme of the association covers a number of current medical problems : the dynamics of iodine metabolism in thyroid function; a variety of coronary, renal and other circulatory questions; the treatment of experimental tumours with tritiated thymidine, studies of hormonal control of metabolism of certain tumour cells, precocious tests for and localization of malignancy by external counting methods; modification of hemopoiesis during radiological treatment of malignant and blood diseases; general metabolic problems including turnover of serum albumin under "non-steady" conditions, phospholipid pools and turnover absorption of fats. In particular, great attention is being paid to definition of the conditions under which radioisotope techniques may be expected to give a rigorously correct picture of metabolic behaviour. These studies are supported by a separate investigation of the extent to which the labelling of proteins modifies their behaviour (46).

3.2.10 *Interdisciplinary Research Training*

As explained earlier, the Euratom Biology Division has considered it an inescapable obligation not only to execute research in nuclear biology but to train men for it, at least on a scale commensurate with the needs of its own programmes. For this purpose it is associating itself (47*) with a group of leading Institutes, each differently specialized and from a different region of the Community. These Institutes will give in rotation a short course each year, jointly staffed, so as to introduce interested young scientists to the ideas and techniques of other disciplines. Each Institute will moreover hold open for the joint scheme two or three places for young research workers who may come there for a year or two to be retrained and restarted in research in another field. The advantage of such a cooperative scheme is, first, that it is built upon what exists and constitutes a logical extension of existing efforts; second, by passing beyond the limited frame of the existing European—sized nation — state, it assures to each specialized laboratory a wider range of candidates for its places and to each candidate a wider choice of institutes, since by selection from a single joint list the possibilities of good "fits" may be much improved.

APPENDIX 1

Staff of Biology Division [1]

Headquarters Staff

R.K. APPLEYARD, Doctor of philosophy (Director)

A. BERTINCHAMPS, Docteur en médecine

F. BONN, Docteur en droit (Administration)

L. JACOBY, Ingénieur agronome

F. VAN HOECK, Ingénieur agronome

Secretarial Staff

G. GERSTER

L. MORREN

S. NAEYE

C. ROEGIERS

H. SCHWAPPACH

M. SOLLNER (Ispra Group)

E. KEMPEN (I.T.A.L. - Wageningen)

Research Staff

K. ALTMAN, Medical Doctor

H. BALNER, Doktor in de medicijnen

A. BERG, Ingénieur agronome

D. BOOTSMA, Doktorandus biologie

P. BOURDEAU, Doctor of philosophy

F. CAMPAGNARI, Laurea in medicina

R. CAVALLORO, Laurea in scienze agrarie

M. DALEBROUX, Ingénieur agronome

M. DEVREUX, Ingénieur agronome

E. DI FERRANTE, Laurea in chimica

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[1]) At 1st June 1964.

G DORIA, Laurea in medicina

J. DUMONT, Docteur en médecine

R. ECOCHARD, Ingénieur agronome

L. FEINENDEGEN, Doktor der Medizin

T. FLIEDNER, Doktor der Medizin

M. FRACCARO, Laurea in medicina

K. GERBAULET, Doktor der Medizin

G. GERBER, Doktor der Medizin

J. GILLOT, Ingénieur agronome

A. GOFFEAU, Docteur ès-sciences

M.L. ILARDI, Laurea in scienze biologiche

E. LEVI, Master of science

F. MARCHETTI, Laurea in farmacia

M. MERLINI, Doctor of philosophy

C. MYTTENAERE, Ingénieur agronome

G. MOLINARO, Laurea in medicina

W. MULLER, Doktor der Chemie

H. NEUNES, Staatsexamen in Zoologie

O. RAVERA, Laurea in scienze

R. RECHENMANN, Docteur ès-sciences

A. RINGOET, Docteur ès-sciences

J. RODESCH, Docteur ès-sciences

G. VERFAILLIE, Licencié ès-sciences

J. WHITFIELD, Doctor of philosophy

E. WHITEHEAD, Doctor of philosophy

Assistant Staff

A. BRAZZELLI

H. BROHEE

G. COGLIATI

G. DELFANTE

L. GIANONI

S. GRASSI

M. MASSET

D. PIRRWITZ

L. POZZI

T. YOUDALE

APPENDIX 2

Membership of Advisory Committee for Biology

Dr. M. BERNARD

Prof. E.J. BIGWOOD

Prof. L. BUGNARD

Prof. J.A. COHEN (chairman 1961-1964)

Prof. J. COURSAGET

Prof. L. GEDDA

Prof. A. GILLES

Dr. H. JAMMET

Prof. J. KUPRIANOFF

Prof. H. LANGENDORFF

Prof. H. LETTRE

Prof. A. MONROY (chairman)

Prof. A.C. SCHUFFELEN

APPENDIX 3

List of Contracts and Authorized Programmes * +)

Ref. No. in Text	Institute	Director of Research	Subject Matter
	I Direct Research		
	Ispra Group : Sections	Dr. BOURDEAU	
I 1	Ecology	Dr. BOURDEAU	Movement of radioisotopes in environs of Ispra
I 2	Toxic products	Dr. GERBAULET	Assay, localization and detoxication of irradiated and non-irradiated polyphenyls
I 3	Cellular technology	Dr. WHITFIELD	Assays of human chromosomal abnormalities and properties of irradiated thymocytes
I 4	Measures		Supporting services as required
	II Contractual Programme		
			1. *Early somatic effects*
1	Medisch-Biologisch Laboratorium RVO-T.N.O. Rijswick	Dr. VAN BEKKUM	Post-irradiation therapy of monkey, including bone marrow transfer; use of specific pathogen free rat in radiobiological studies
2	Comitato Nazionale per l'Energia Nucleare, La Casaccia	Dr. DORIA	Post-irradiation immunological studies in mouse : graft-host relations and role of thymus
3	Association Claude-Bernard, Paris	Dr. BERNARD	Radiobiological damage to platelets

+) Programmes executed by temporarily detached research workers are denoted by +.
*) Programmes which have been authorized by the Euratom Commission but are not yet the object of a signed contract are distinguished by an asterisk in this list (as of June 1st, 1964).

Ref. No. in Text	Institute	Director of Research	Subject Matter
4 *	Gesellschaft f. Strahlenforschung, Karlsruhe	Dr. FLIEDNER Prof. STICH	Studies of hemopoietic system in man and animals : morphological, biochemical and kinetic studies of normal and abnormal conditions
5 *	Hôpital St. Louis, Paris	Prof. MATHE	Immunologically competent cells and bone marrow transfer therapy
6 *	Istituto di Genetica Medica, Torino	Prof. CEPPELLINI	Studies of the leucocyte and histoincompatibility antigens of man
			2. *Late somatic effects*
7	Università di Torino	Prof. GAVOSTO	Biochemistry of human leukemic cells
8	Université Libre de Bruxelles	Prof. MEWISSEN	R.B.E. for induction of low dose range
9	Institut Gustave Roussy, Paris; Centre Léon Bérard, Lyon	Prof. DENOIX Prof. DARGENT	Leukemia survey of patients treated for uterine cancer
10 *	Gesellschaft f. Strahlenforschung, München	Prof. HUG	The late effects of ingested radioisotopes in the mouse : R.B.E. studies. The effect of irradiation in utero upon leaning ability in the mouse. Radiation genetic studies in animals
11 *	Heiligenberg Institut	Prof. LANGENDORFF	Effects of radiation upon organizers in the amphibian egg. Embryological effects of low doses
12 *	Istituto Farmacologico Mario Negri Milano	Prof. GARRATINI	Chemotherapy of leukemia and chemical protection against ionizing radiations, in connection with the European Cancer Chemotherapy Group
13 *	Laboratoire d'embryologie, Paris	Prof. WOLFF	Radiobiology of differentiating cells and systems, with special reference to dose fractionation and to separate irradiation of inducer and competent tissue
14 *	Università di Napoli	Prof. BORGHESE	Variation of radiosensitivity during embryological development, studied especially by methods of organ culture
15 *	Università di Palermo	Prof. MONROY	Free radical studies in the newly activated amphibian egg

Ref. No. in Text	Institute	Director of Research	Subject Matter
16	Université de Strasbourg	Prof. MANDEL	Action of preparation "Padutin" on radiation-induced lesions of skin
			3. Genetic effects
17	Université de Louvain	Prof. GILLES	Microirradiation of plant chromosomes
18	Institut Nat. Agronomique, Paris	Prof. HESLOT	Comparative studies of action of chemical and physical mutagens on yeasts and plant materials
19	Université de Liège	Prof. VERLY	Mutagenic effect of an alkylating agent (myleran) and its binding to DNA
20	Università di Pavia	Prof. FRACCARO	Radiation aspects of human cytogenetics
21 +	University of North Carolin	Mr. DALEBROUX	Theoretical and experimental studies of bristle number in Hebrobracon
22 *	Istituto di Radiologia, Roma	Prof. TURANO	Chromosomal abnormalities resulting from clinical irradiations
23 *	Istituto Superiore di Sanità, Roma	Prof. SERMONTI	Mutagenesis in Aspergillus
24 *	Università di Pavia	Prof. SCOSSIROLI	The radiation genetics of quantitative characters under "statistical" genetic control in plants
25 *	Università di Roma	Prof. MONTALENTI	Comparison and interaction between X-ray and U.V. treatments of mammalian chromosomes, using chinese hamster cells in culture
			4. Studies common to both somatic and genetic effects
26	Université Libre de Bruxelles	Profs. BRACHET, JEENER, CHANTRENNE, ERRERA, THOMAS	Studies of morphogenesis, genetic control systems and radiobiological mechanisms
27	Laboratorio Internazionale di Genetica e Biofisica, Napoli	Prof. BUZZATI-TRAVERSO Prof. CAVALLI-SFORZA	Studies of human population genetics and of experimental genetic systems with special reference to radiological problems and to genetic control systems

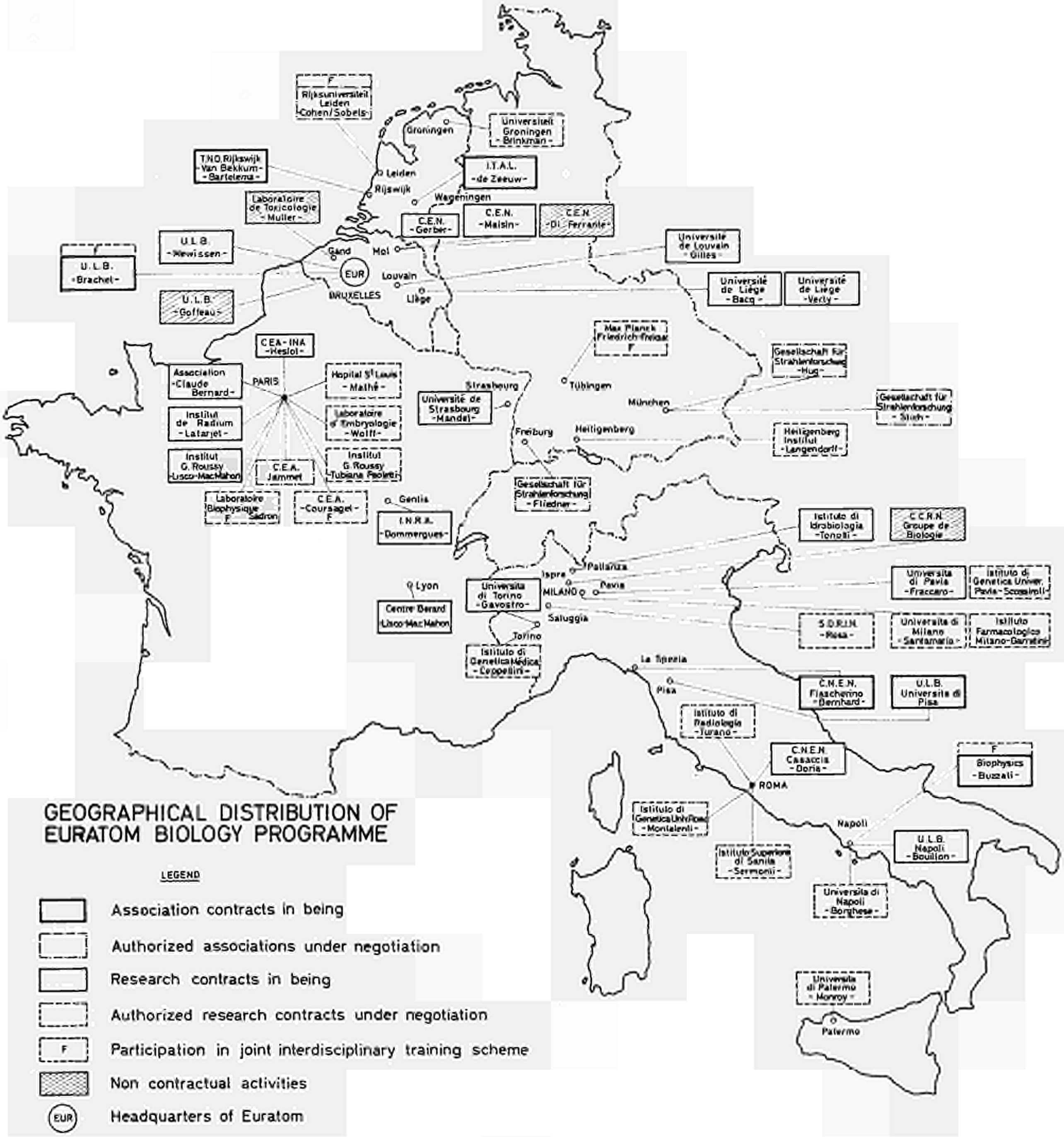
Ref. No. in Text	Institute	Director of Research	Subject Matter
28	Institut du Radium, Paris	Prof. LATARJET	Effects of radiation upon DNA and its chemical components
29	Centre d'Etude de l'Energie Nucléaire, Mol	Dr. MAISIN	Effects of irradiation upon protein and nucleic acid synthesis and upon cell permeability to macromolecules
30	Université de Liège	Prof. BACQ	Chemical protection
31 +	Université Libre de Bruxelles	Dr. GOFFEAU	Protein synthesis by isolated chloroplasts
32 *	Rijksuniversiteit Leiden	Profs. COHEN SOBELS	Studies of post-irradiation modification of mutagenesis and of complex biochemical systems and the effects of irradiation upon them
33 *	Institut Gustave Roussy, Paris	Profs. TUBIANA PAOLETTI	Possible radiorestorative action of DNA and associated questions of stability of DNA
34 *	Università di Milano	Prof. SANTAMARIA	Construction of an absolute spectrofluormeter
35 *	Universiteit Groningen	Prof. BRINKMAN	Studies of RBE under conditions of abnormal oxygen effect

5. *The movement of isotopes in man and experimental substitutes*

Ref. No. in Text	Institute	Director of Research	Subject Matter
36	Université Libre de Bruxelles - Naples	Prof. BOUILLON	Mechanism of utilisation by certain Acantaria of strontium in preference to calcium of sea water
37 +	Université de Gand	Dr. MÜLLER	Studies of decontamination by chemical agents having both a chelating and a hormonal action
38 +	Centre d'Etude de l'Energie Nucléaire, Mol	Mlle DI FERRANTE	Estimates of body-burden of certain natural radioactive isotopes from measurements on individual teeth
39 *	Commissariat à l'Energie Atomique, Paris	Dr. JAMMET	Uptake, retention and movement of isotopes in man and in experimental animals

Ref. No. in Text	Institute	Director of Research	Subject Matter
			6. The movement of isotopes in the environment
40 *a*	Instituut voor Toepassing van Atoomenergie in de Landbouw, Wageningen	Dr. DE ZEEUW	Movement of radioactive isotopes in soils and plants under precisely controlled conditions
41	Istituto di Idrobiologia, Pallanza	Dr. TONOLLI	Ecology of elements of food chain in the Lago Maggiore
42	Comitato Nazionale per l'Energia Nucleare, Fiascherino	Dr. BERNHARD	Movement of radioisotopes in marine ecosystems of the Mediterranean
			7. Dosimetry, techniques and instrumentation
43	Centre d'Etude de l'Energie Nucléaire, Mol	Dr. GERBER	Biochemical indicators of exposure : catabolism of DNA, perfused liver studies
			8. Applications of nuclear techniques to agriculture
40 *b*	Instituut voor Toepassing van Atoomenergie in de Landbouw, Wageningen	Dr. DE ZEEUW	Radiation mutagenesis in crop plants; surface pasteurization of food by irradiation; analytical methods using nuclear techniques
44	Institut National de la Recherche Agronomique, Genlis (Dijon)	Prof. DOMMERGUES	Mutagenesis and the uncovering of plant chimaera by irradiation
			9. Applications of nuclear techniques to medicine
45	Université Libre de Bruxelles and Università di Pisa	Drs. ERMANS, DONATO, DUMONT	Development of new nuclear techniques in connection with selected problems of thyroid and general metabolism, circulatory conditions, malignancy and disturbances of hemopoiesis

Ref. No. in Text	Institute	Director of Research	Subject Matter
46 *	Società Ricerche Impianti Nucleari, Saluggia	Dr. ROSA	Development of new physical and chemical techniques aiming at an improved and controlled distribution of radiation compounds in tissues and organs
			10. Interdisciplinary research training
47	Laboratoire de Biophysique, Muséum d'Histoire Naturelle, Paris	Prof. SADRON	Provision of advanced interdisciplinary training for young research workers
	Commissariat à l'Energie Atomique, Paris	Prof. COURSAGET	
	Max Planck Institut, Tübingen	Prof. FRIEDRICH-FREKSA	
	Université Libre de Bruxelles	Prof. BRACHET and colleagues	
	Rijksuniversiteit, Leiden	Prof. COHEN	
	Laboratorio Internazionale di Genetica e Biofisica, Napoli	Prof. BUZZATI-TRAVERSO Prof. MONROY	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Universiteit Groningen - Brinkman -
Groningen
T.N.O. Rijkswijk - Van Bekkum - - Barteleme -
Leiden
Rijswijk
I.T.A.L. - de Zeeuw -
Wageningen
Laboratoire de Toxicologie - Muller -
C.E.N. - Gerber -
C.E.N. - Maisin -
C.E.N. - Di Ferrante -
U.L.B. - Hewissen -
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Université de Liège - Verly -
U.L.B. - Goffeau -
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Association - Claude Bernard -
PARIS
Hopital St Louis - Mathé -
Strasbourg
Université de Strasbourg - Mandel -
Tübingen
Gesellschaft für Strahlenforschung - Hug -
München
Gesellschaft für Strahlenforschung - Stich -
Institut de Radium - Latarjet -
Laboratoire d'Embryologie - Wolff -
Freiburg
Heiligenberg
Heiligenberg Institut - Langendorff -
Institut G. Roussy - Lisco-MacMahon
C.E.A. Jammet
Institut G. Roussy - Tubiana Paoletti
Gesellschaft für Strahlenforschung - Fliedner -
Laboratoire Biophysique F Sadron
C.E.A. - Coursaget - F
Genlis
I.N.R.A. - Dommergues -
Istituto di Idrobiologia - Tonolli -
C.C.R.N. Groupe de Biologie
Pallanza
Ispra
Pavia
MILANO
Lyon
Universita di Torino - Gavosto -
Universita di Pavia - Fraccaro -
Istituto di Genetica Univer. Pavia - Scossiroli -
Centre Berard Lisco-MacMahon
Saluggia
Torino
S.O.R.I.N. - Rosa -
Universita di Milano - Santamaria -
Istituto Farmacologico Milano - Garattini
Istituto di Genetica Médica - Ceppellini -
La Spezia
Pisa
C.N.E.N. Fiascherino - Bernhard -
U.L.B. Universita di Pisa
Istituto di Radiologia - Turano -
C.N.E.N. Casaccia - Doria -
F
Biophysics - Buzzati -
ROMA
Istituto di Genetica Univ. Roma - Montalenti -
Napoli
U.L.B. Napoli - Bouillon -
Istituto Superiore di Sanita - Sermonti -
Universita di Napoli - Borghese -
Universita di Palermo - Monroy -
Palermo
GEOGRAPHICAL DISTRIBUTION OF EURATOM BIOLOGY PROGRAMME
LEGEND
Association contracts in being
Authorized associations under negotiation
Research contracts in being
Authorized research contracts under negotiation
F Participation in joint interdisciplinary training scheme
Non contractual activities
EUR Headquarters of Euratom

APPENDIX 6

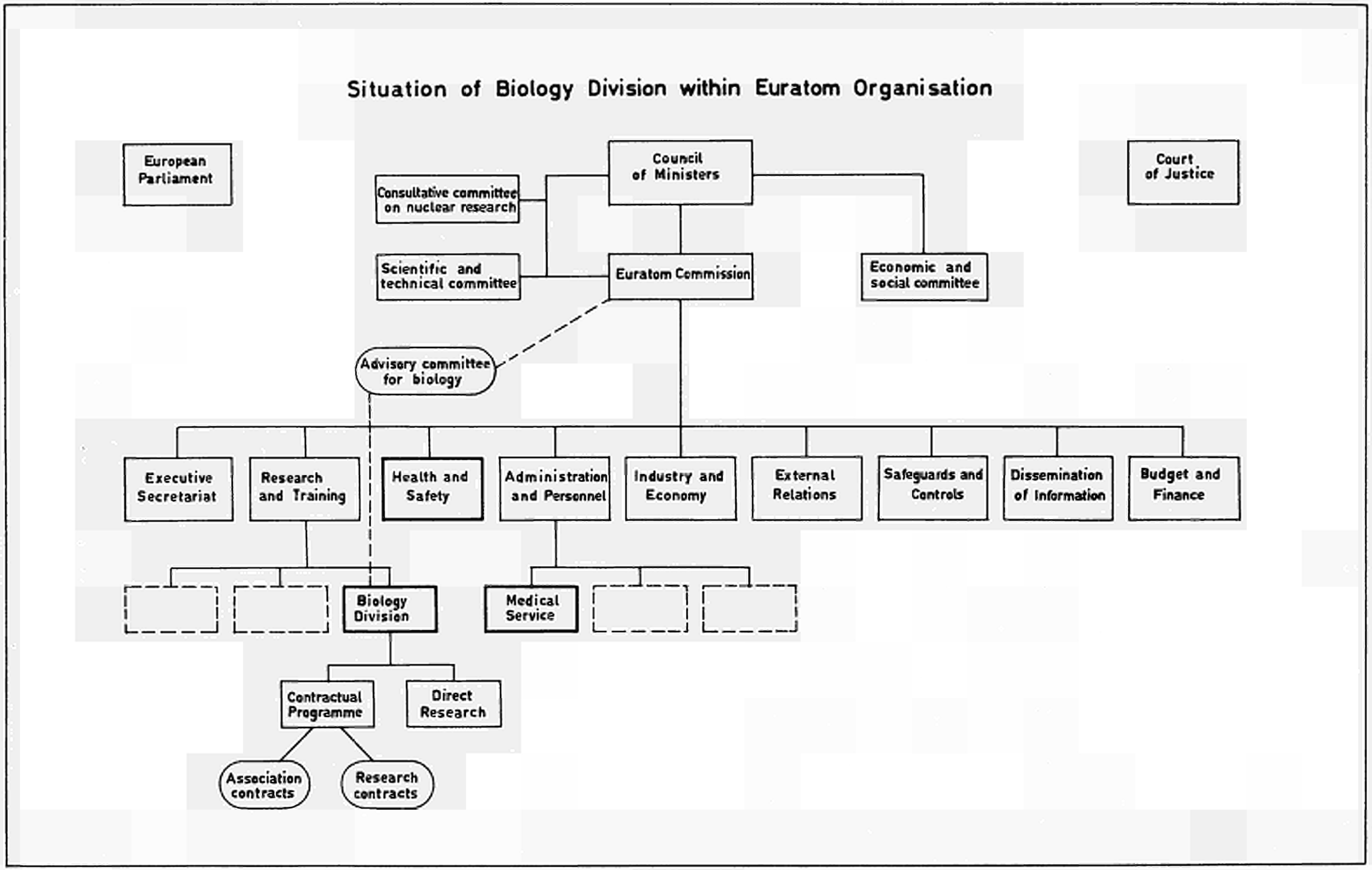

Situation of Biology Division within Euratom Organisation
European Parliament
Consultative committee on nuclear research
Council of Ministers
Court of Justice
Scientific and technical committee
Euratom Commission
Economic and social committee
Advisory committee for biology
Executive Secretariat
Research and Training
Health and Safety
Administration and Personnel
Industry and Economy
External Relations
Safeguards and Controls
Dissemination of Information
Budget and Finance
Biology Division
Medical Service
Contractual Programme
Direct Research
Association contracts
Research contracts

Fig. 1

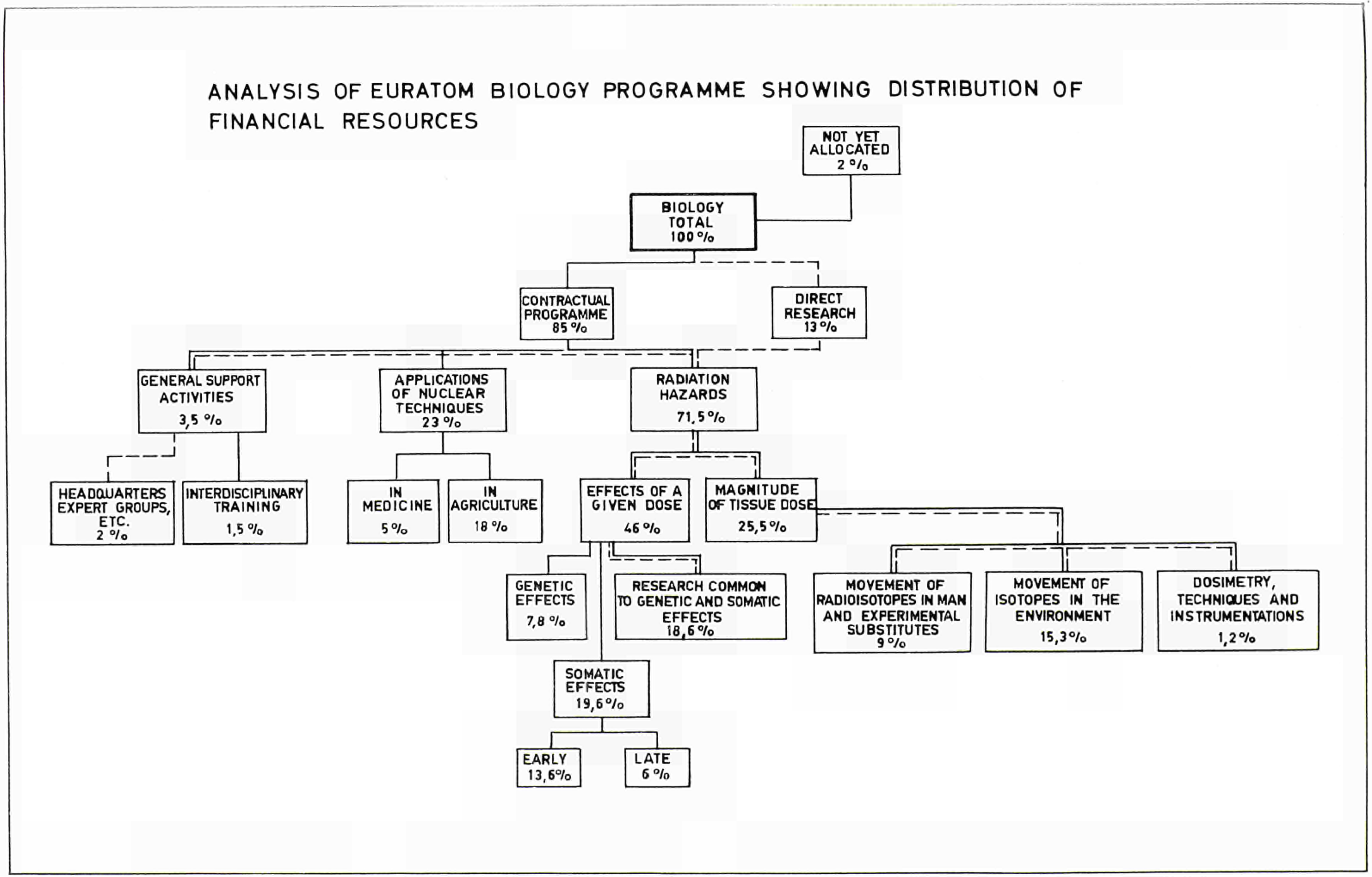
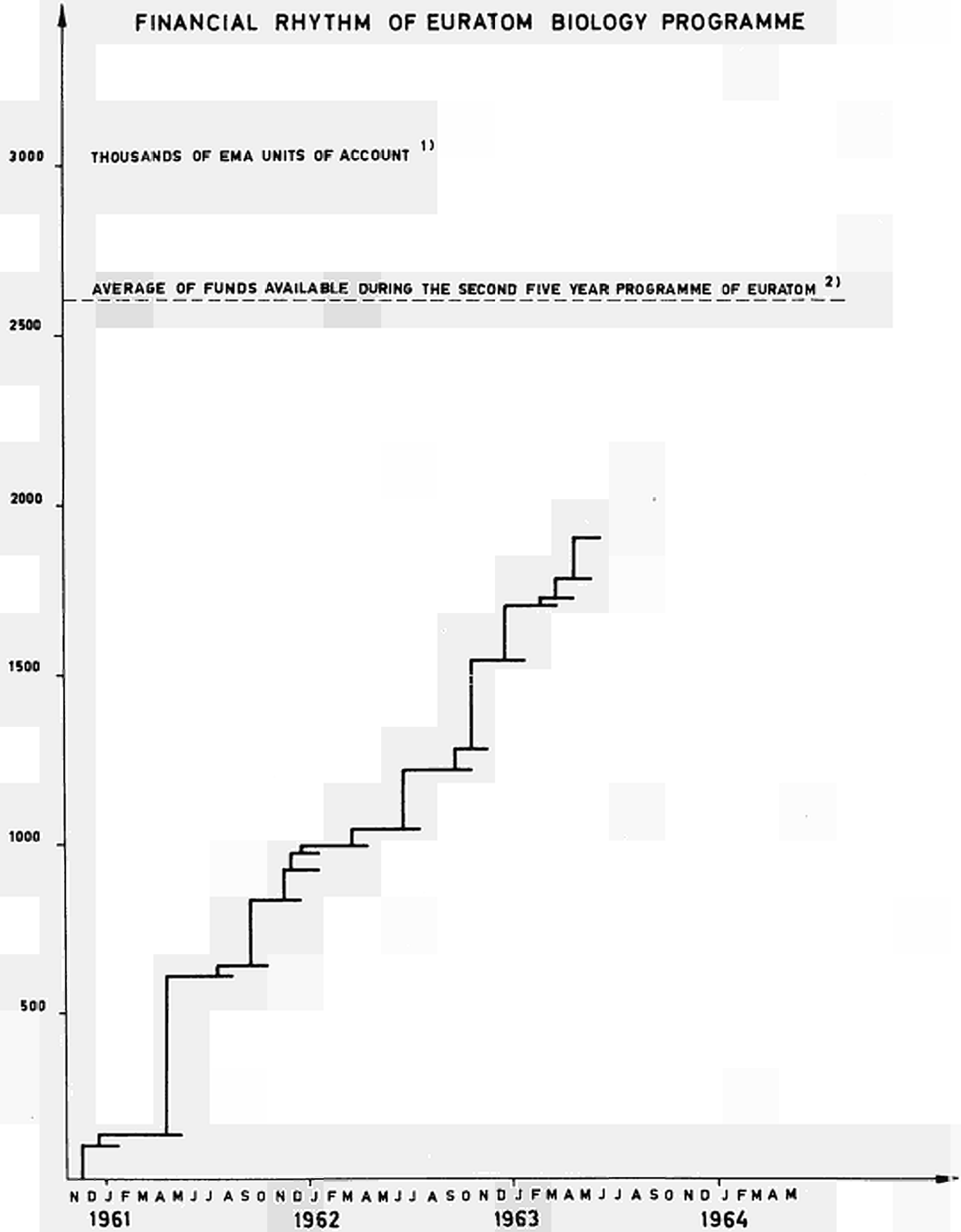

ANALYSIS OF EURATOM BIOLOGY PROGRAMME SHOWING DISTRIBUTION OF FINANCIAL RESOURCES
NOT YET ALLOCATED 2 %
BIOLOGY TOTAL 100 %
CONTRACTUAL PROGRAMME 85 %
DIRECT RESEARCH 13 %
GENERAL SUPPORT ACTIVITIES 3,5 %
APPLICATIONS OF NUCLEAR TECHNIQUES 23 %
RADIATION HAZARDS 71,5 %
HEADQUARTERS EXPERT GROUPS, ETC. 2 %
INTERDISCIPLINARY TRAINING 1,5 %
IN MEDICINE 5 %
IN AGRICULTURE 18 %
EFFECTS OF A GIVEN DOSE 46 %
MAGNITUDE OF TISSUE DOSE 25,5 %
GENETIC EFFECTS 7,8 %
RESEARCH COMMON TO GENETIC AND SOMATIC EFFECTS 18,6 %
MOVEMENT OF RADIOISOTOPES IN MAN AND EXPERIMENTAL SUBSTITUTES 9 %
MOVEMENT OF ISOTOPES IN THE ENVIRONMENT 15,3 %
DOSIMETRY, TECHNIQUES AND INSTRUMENTATIONS 1,2 %
SOMATIC EFFECTS 19,6 %
EARLY 13,6 %
LATE 6 %

Fig. 2

FINANCIAL RHYTHM OF EURATOM BIOLOGY PROGRAMME



1) 1 EMA unit of account = 1 U.S. dollar.

2) This figure corresponds to the total of 16.000.000 for biology programme during the 5 year period under review corrected for certain fixed expenditures not directly connected with specific research projects

FIG. 3A

BUILD-UP OF STAFF OF EURATOM BIOLOGY DIVISION

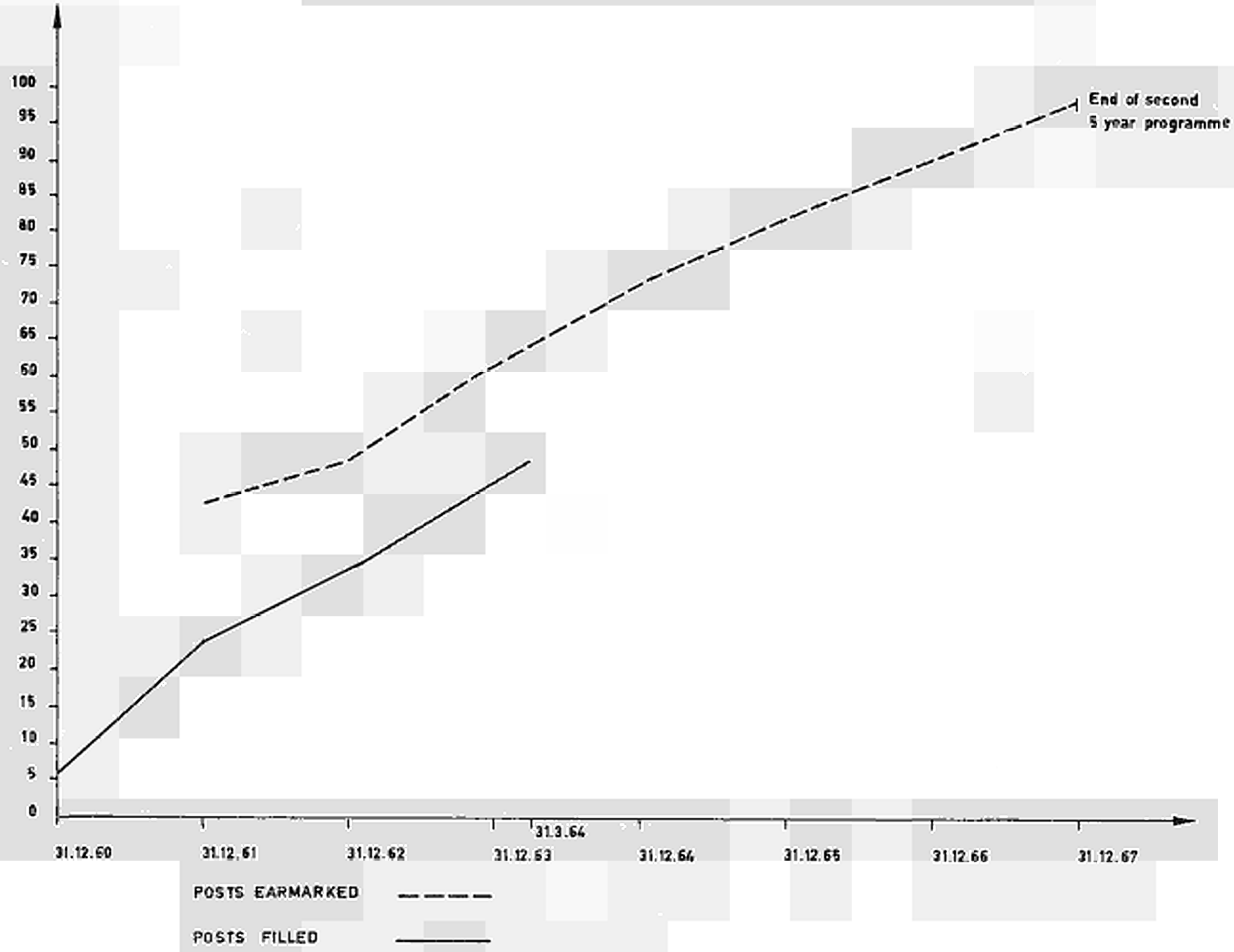


FIG. 3 B

PUBLICATIONS AND COMMUNICATIONS FROM THE EURATOM BIOLOGY PROGRAMME

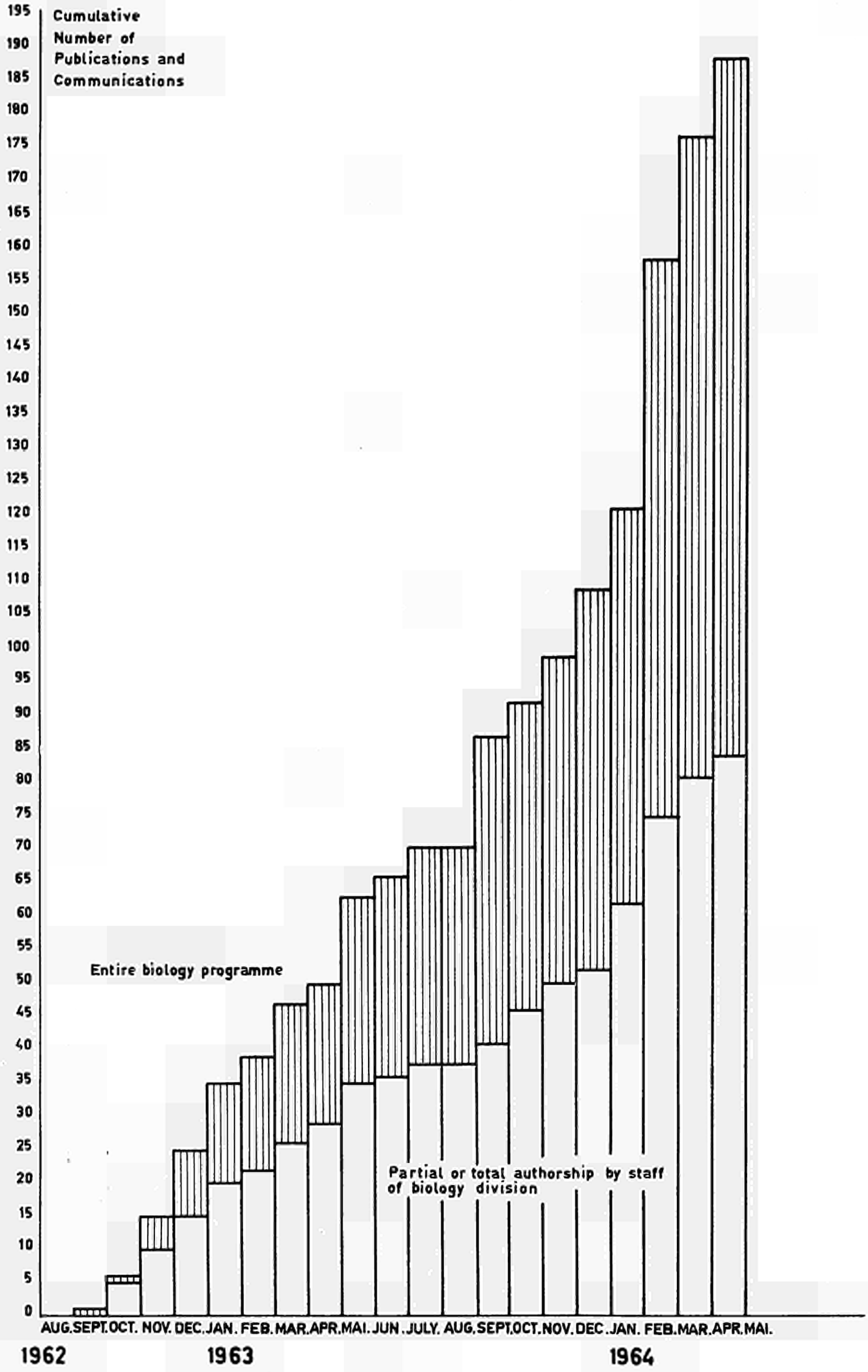


FIG. 3C

To disseminate knowledge is to disseminate prosperity — I mean general prosperity and not individual riches — and with prosperity disappears the greater part of the evil which is our heritage from darker times.

Alfred Nobel

CDNA01884ENC

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Bruxelles (Belgique)