

LABELLED COMPOUNDS FOR AGROCHEMICAL RESIDUE STUDIES IN DEVELOPING COUNTRIES

**REPORT AND RECOMMENDATIONS OF AN ADVISORY GROUP
JOINTLY CONVENED BY THE
INTERNATIONAL ATOMIC ENERGY AGENCY
AND THE
FOOD AND AGRICULTURE ORGANIZATION
OF THE UNITED NATIONS,
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1. REPORT

1.1. Introduction and objectives

Stable or radioactive isotopic tracers are important, widely used and often unique tools for studying trace contaminant problems. Suitable isotopic labelling of compounds enables their chemical and physical fate to be followed in environment, food and in plant or animal organisms. Moreover, the labelled compound can be traced in the presence of an existing and chemically identical contaminant, with great sensitivity and specificity and, sometimes, by the use of non-destructive analytical or remote detection techniques. Less conventionally, by labelling chemical reagents or metabolic intermediates, the effects of the non-labelled contaminant or pollutant on the living system, or on a test enzyme preparation can also be studied quantitatively (1.8.6, 1.8.9, 1.8.12).

These techniques are extensively and routinely used in laboratories of advanced countries and a wide range of labelled compounds is available commercially and from national centres. Many of the laboratories undertake independent isotopic syntheses for their own use or purposes.

A major handicap in developing countries faced with significant residue problems, and which otherwise possess the necessary facilities and expertise, is the lack of availability, or high costs, of suitably labelled compounds. Thus, in developing countries dependent on an agricultural economy an ever growing range of pesticides (insecticides, fungicides, herbicides, etc.) are needed for animal and plant protection. Similarly, plant production in terms of both quality and quantity, is becoming heavily dependent upon fertilizer inputs, especially nitrogen. The conservation of the soil nitrogen residue (i.e., that part of the added nitrogen not usefully recovered in the crop) and the attenuation of its loss through leaching and of its potential to pollute ground water are of growing importance. There is consequently a need to study the behaviour and persistence of these substances under the local conditions and for which purpose suitable radioactive and stable isotopically labelled

materials are often indispensable. These problems of availability have been emphasized by experts participating in the Joint FAO/IAEA Chemical Residue and Pollution Programme. It has led to recommendations to improve the collection and dissemination of relevant information on, and to facilitate the preparation and supply of, isotopically labelled compounds for use in developing countries.

While some efforts have been made to provide information (e.g., see 1.8.10 and 4.1) the essential problem remains unsolved. The Advisory Group whose report follows was convened with the following objectives: -

- 1.1.1. To discuss ways and means of improving the collection and dissemination of information on the preparation, supply, costs and availability of labelled compounds with a view to helping scientists of developing countries concerned with problems of trace contaminants which affect agriculture, fisheries and food.
- 1.1.2. To discuss possible international cooperation to facilitate more centralized and economic preparation and to facilitate the distribution of labelled intermediates and compounds for the use of scientists as above.
- 1.1.3. To formulate recommendations for action in relation to 1.1.1 and 1.1.2 above.

The Group was not concerned with the preparation and supply of radioactive and stable isotopes per se but only with the problems of isotopic synthesis with stable or radioactive isotopes already available and the problems of making prepared labelled derivatives more easily available to scientists of developing countries.

1.2. Trace contaminants of agriculture, fisheries and food in developing countries

Objectives of the Joint FAO/IAEA chemical residue and pollution programme (1.8.1, 1.8.2, 1.8.3, 1.8.5 and 1.8.8) are to assist and advise

member states of IAEA and FAO to make safe and effective use of isotope and radiation techniques for studying and, thereby, controlling chemical or radioactive residues which appear as undesirable trace contaminants of agriculture, fisheries and food. One important aspect of the programme is the support and encouragement of scientists in developing countries who are studying their own problems under their own conditions. This is usually done on the basis of contracts involving modest financial support and within the framework of a "coordinated research programme" designed to attack related residue problems or to develop and apply specific techniques. These research programmes also involve the participation of scientists in advanced countries on the basis of "cost-free" research agreements. While the "agreements" do not provide for direct financial support they do enable, at Agency expense, participation of the scientists concerned in the research coordination meetings convened periodically within the coordinated programme.

A second important aspect of this programme relevant to the Group's discussions, has been the provision of FAO/IAEA/SIDA or FAO/IAEA/UNDP training courses in "nuclear techniques for studying chemical residue and pollution problems". Three 4-week courses have been held (Vienna, 1972, Sao Paulo, 1974, Cairo, 1975), the first two financed by SIDA*), the third by UNDP and a fourth (financed by SIDA) will be held in Sri Lanka in 1977. They have been successful and attracted far more applicants than places available. Each course provided for lectures for some 15 students by international experts, laboratory practical work and demonstration at well-equipped isotope centres. The syllabus covers the preparation of stable and radioactive isotopes, their properties, assay; and the preparation and use of labelled compounds for studying persistence, fate and biological significance of trace contaminants in environment, food and living organisms. Isotopic synthesis per se of labelled compounds has been the subject of lecture material only, the emphasis throughout being on application of labelled compounds to problems of agriculture, fisheries and food, especially pesticide and agrochemical residues (see 1.3) and of drugs, etc. used for veterinary purposes.

*) Swedish International Development Authority

The coordinated research programmes have led to several publications (1.8.3, 1.8.4, 1.8.7, 1.8.8). The associated meetings have enabled scientists of both developed and developing countries to meet and exchange views on problems of mutual interest. On the one hand scientists from developing countries are able to meet colleagues from advanced institutes and so obtain first-hand advice on advanced methodology. On the other hand those from advanced institutes become familiar and often interested in the problems of the developing countries. In some cases the exchanges have led to fruitful collaboration at laboratory level. These programmes have demonstrated clearly the existence of significant and often serious trace contaminant and chemical residue problems in developing countries. Moreover, many are of a continuing nature - e.g., as a result of the constant need to evaluate alternative chemicals for pest control. A common and persistent handicap to the study and solution of these problems has been that of obtaining suitable isotopically-labelled compounds for use in developing countries.

1.3. Isotopes and labelled compounds used or needed for investigations in developing countries

Acquisition of radioisotopes of elements significant as trace contaminants or in the simple chemical forms dispensed by commercial or national radiochemical centres have presented no serious problems except possibly minor ones of timing (short half-lives, etc.) and logistics. When not available radioactive elements have sometimes been prepared by radioactivation in the local research reactors available in some developing countries.

Quite a number of compounds, mainly pesticides and labelled substrates or biochemical intermediates, have also been obtained without difficulty and used in the programme. These have been mainly supplied on a commercial basis by well-known radiochemical centres.

The major problem has been due to the lack of availability of the labelled compounds; costs involved; lack of information on existing sources; lack of expertise and facilities to conduct even simple isotopic

syntheses or chemical manipulations locally; or time and costs involved in conducting the required preparations locally. Some of the problems and the measures taken are illustrated in Table I.

Table I suggests that the problem is not always one of complexity of the labelled compound or of its isotopic synthesis. It is often more a problem of limited demand which, understandably, is a condition of commercial interest and contingent supplies at costs within reach of scientists of the "Third World" or associated UN subsidies. Relatively new compounds are sometimes important to the agriculture of developing countries. E.g., leptophos for controlling cotton pests in the Near East, substitutes for organomercurial seed dressings, alternative insecticides for controlling resistant strains of the rice stem borer in rice growing areas, or resistant capsids in West African cocoa. These same compounds are of course not yet in demand and often not yet subjected to independent research and study in the developed countries where both crops and pests differ markedly.

Experience in the Joint FAO/IAEA chemical residue and pollution programme has indicated that the principal requirement is for longer-lived radioisotopically labelled pesticides (insecticides, acaricides, fungicides, herbicides, fumigants, etc.) for studying their behaviour. Such pesticides are usually well-established and tried in developed countries. The studies must, however, be made under the local and often novel conditions of environment, climate, crop, pest control, harvest, storage, processing and transport. The problem of the shorter-lived radioisotopes (^{35}S , ^{32}P , ^{82}Br , etc.) is the loss of valuable radioactivity due to the inevitable delays of transport, official clearance, etc.

Important requirements for the near future appear likely to include stable isotopically labelled materials such as ^{15}N , ^{13}C or ^2H -labelled fertilizers and fertilizer additives such as nitrification inhibitors. Their importance is suggested by the growing need to study the behaviour of fertilizer nitrogen residues in soil and their regulation and conservation under developing country conditions. Requirements will clearly

continue for a range of radioisotopically-labelled pesticides - especially those under trial in developing countries for the protection of tropical products such as rice, cotton, cocoa, coffee and groundnuts. The use of ring-labelled materials will be important for studies of the long-term and ultimate fate of soil and water residues (e.g. ultimate breakdown or persistence of stable ring systems of insecticides, fungicides and herbicides).

Nitrogenous fertilizers labelled by ^{15}N depletion or enrichment are available in large quantities and already find application in developing countries. Although the analytical techniques tend to remain sophisticated and costly, compounds multiply labelled with stable isotopes like carbon-13 can be detected with great sensitivity under field conditions and are potentially useful for tracer and toxicological studies with agricultural chemicals.

The Group felt that the use of stable isotopically-labelled compounds was of particular value for studying residue problems in developing countries on the field scale. Firstly, there was no loss of detectability through radioactive decay. Secondly, there were none of the problems of handling, use, storage or of waste disposal associated with the use of radioactive materials. Training was, however, of particular importance in this context and the Group noted with interest an FAO/IAEA course in cooperation with the Government of the German Democratic Republic held in Leipzig, October 1976, on the "Use of nitrogen-15 in soils research". This provided training for some 15 graduates from developing countries (cf. 1.2).

Attention was drawn to the extensive programmes in the USA for the preparation and use of stable isotopes and their derivatives. The ICONS (stable isotopes of C, O and N) programme at the Los Alamos Scientific Laboratory (New Mexico) has been operated as a national stable isotopes resource since 1970 and is currently supported by the Energy Research and Development Administration and the National Institutes of Health. The programme encompasses: -

- (a) The production of large quantities of separated ^{13}C (90 atoms % excess at 5 kg/yr), ^{14}N (<100 ppm ^{15}N at 3000 kg/yr), ^{15}N (+ 40 atoms % excess at 5,0 kg/yr), ^{15}N (at + 99 atoms % excess, 5,0 kg/yr), ^{17}O (at + 20 atoms % excess at 0,4 kg/yr) and ^{18}O (at + 95 atoms % excess) by the low temperature distillation of carbon monoxide and nitric oxide.
- (b) The preparation by inorganic-, organic, and bio-synthetic methods of appropriate isotopically-labelled compounds for use in biological research and in agricultural, medical and environmental studies. Examples include ^{13}C -labelled sugars, amino acids, proteins, lipids, and aromatic hydrocarbons; and ^{15}N - and ^{14}N -labelled fertilizers and amino acids.
- (c) The development of an active programme of research collaboration with extramural investigators providing, as necessary, labelled compounds, isotopic analysis, and data interpretation, especially in mass spectrometry, emission spectrometry, and nuclear magnetic resonance spectroscopy.
- (d) The provision of advice and assistance to extramural investigators regarding experimental plans and operations, and the hosting of visiting scientists for training in the use of stable isotopes.
- (e) The performance of core research to keep the resource at the "state of art" level.

The Tennessee Valley Authority Centre concentrates on processing nitrogen-15 and nitrogen-14 (<100 ppm ^{15}N) into a variety of labelled fertilizers prominent among which is ammonium sulphate. Process development of others like urea is in progress. The centre has an extensive programme of collaborating with universities, state agricultural experiment stations, and other institutions in nation wide studies of the fate of nitrogen-14 tagged fertilizers under field conditions. In these programmes the centre provides labelled materials, mass spectrometric analysis, and training where required.

TABLE I

Examples of labelled compounds requiring special synthesis or otherwise presenting problems in FAO/IAEA programmes

Labelled compound required	Location and purpose	Action taken, difficulties encountered
$[^{32}\text{P}]$ - leptophos* (phosvel)	Arab Republic of Egypt, Pakistan. Studies of residues in cotton seed and oil products	Prepared locally from $[^{32}\text{P}]$ PCl_3 or $[1-^{14}\text{C}]$ -benzene and made available to other collaborators
$[^{14}\text{C}]$ -ring - leptophos		
$[1-^{14}\text{C-naphthyl}]$ -carbaryl**	Arab Republic of Egypt, Pakistan, Philippines. Studies of residues in maize	Prepared locally from $1-^{14}\text{C}$ -naphthol obtained commercially and labelled insecticide made available to other contractors
$[^{32}\text{P}]$ - phosphine	Canada, UK Studies of residues in fumigated cereals	Synthesized from $[^{32}\text{P}]$ - ALP purchased commercially
$[^{14}\text{C}]$ Various complex metabolites of aldrin, dieldrin, heptachlor and PCBs	Federal Republic of Germany. For studying fate and persistence of residues in soil-crop systems	Local syntheses using advanced and well-equipped facilities
$[^{14}\text{C}]$ P - nitrophenol	India. Study its persistence and fate in rice paddy as a metabolite of parathion	Local facilities not available at the Institute concerned for synthesis of nitrophenol. This undertaken by collaborators in Switzerland - commercial synthesis too expensive
$[^{14}\text{C}]$ - Triarimol***	Israel. Absorption and translocation studies in plants	Small quantity supplied by manufacturer
$[^3\text{H}]$ - Triarimol	"	Prepared locally by catalytic exchange at specific activity of ca. 92 Ci, Mole^{-1} . Difficulties on account of radiochemical clean-up required

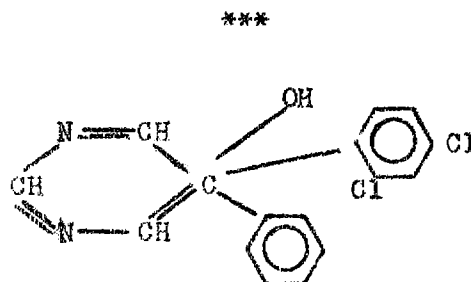
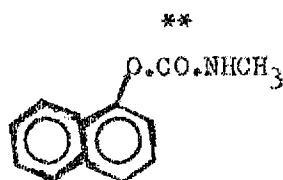
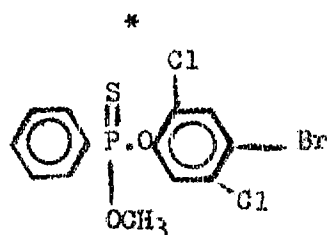


Table I- - Continued

$[^{35}\text{S}]$ - Padan ^(R) (cartap)*	Japan. Studies of novel rice stem borer insecticides	Synthesis locally from $[^{35}\text{S}]$ KONS
$[^{35}\text{S}]$ - Hokupanon**	"	Synthesized locally using $[^{35}\text{S}]\text{CH}_3\text{SH}$
$[^{32}\text{P}]$ - Kitazin - P ^(R) ***	Japan. Residue studies in rice of novel fungi- cides for rice blast control. Possible sub- stitute for organo- mercurials	Synthesized locally
$[^{35}\text{S}]$ - "		
$[^{32}\text{P}]$ Hinosan ^(R) ****		
$[^{35}\text{S}]$ - "		

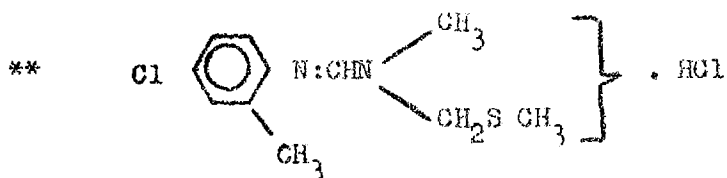
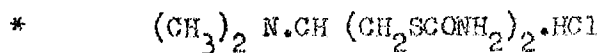
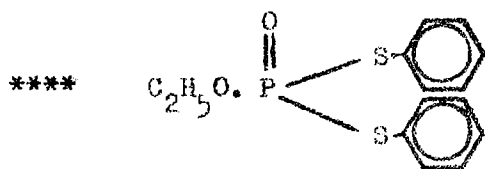
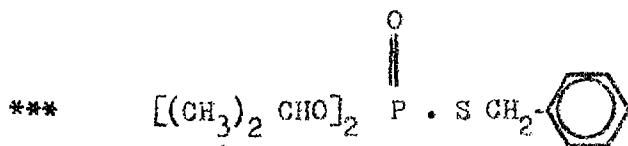
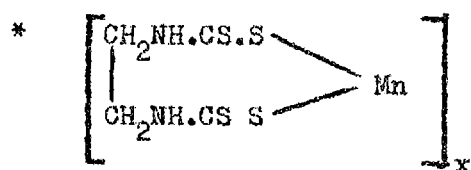
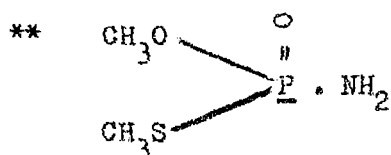


Table I - - Continued

$[^{14}\text{C}]$ - maneb*	Netherlands. Residue studies of vegetable crops	Prepared locally and methods published
$[^{14}\text{C}]$ - nabam*		
$[^{14}\text{C}]$ - zineb*		
$[^3\text{H}\text{-ring}]$ - parathion of high specific activity (ca. 300 mCi, mMole ⁻¹)	USA. Development of radioimmunoassay procedures	Prepared locally by condensation of $[^3\text{H}]$ p-nitrophenol in butanon with appropriate dialkyl thiophosphorylchloride
^{13}N (as NO_3)	USA. Short-lived radioisotope of nitrogen for research on denitrification from aquatic systems	Produced in local cyclotron ($^{16}\text{O}\text{-p, a-}^{13}\text{N}$ reaction) Example of isotope use limited to most advanced countries only
$[^{14}\text{C}\text{-methyl}]$ - metamidophos	** Venezuela. For studying residues of the insecticide in tomatoes	Prepared locally and methods published
$[^{32}\text{P}]$ - metamidophos		
$[^{32}\text{P}]$ - labelled organophosphorus insecticide	-	Unlabelled compound mixed with carrier-free $[^{32}\text{P}]\text{PO}_4$ on assumption that insecticide would become suitably labelled (1)



, nabam and zineb are sodium and zinc analogues



1.4. Problems of availability and supply of labelled compounds

The Group discussed these problems against the background of prepared working papers (4.1 - 4.14) and IAEA publications (see 1.8). It was clear that in developing countries there were important residue or trace contaminant problems. Labelled compounds would be useful and, often, essential for the study and solution of these problems. The laboratory and field facilities, expertise in the application and use of labelled materials were often adequate. However, the chronic problem was that of availability of the labelled compound due to one or a combination of more than one of the following restraints: -

- 1.4.1. Not available from local national sources
- 1.4.2. Unavailable internationally
- 1.4.3. Prohibitive costs of importation
- 1.4.4. Available but availability not known to potential users
- 1.4.5. Lack of expertise or suitable facilities for local synthesis or synthesis uneconomic on scale required.

1.5. Sources of labelled compounds

The major existing and potential sources of isotopically-labelled agricultural chemicals were identified as follows: -

- 1.5.1. Government, university and independent research laboratories where labelled compounds were prepared mainly for local use
- 1.5.2. Regional and national isotope research and teaching centres where specific compounds were occasionally prepared for local, regional and international use (e.g. at MERC, Cairo, Arab Republic of Egypt, and CENA, Piracicaba, Brazil, and BARC, TROMBAY, India - see appendix 6.3)
- 1.5.3. National or independent commercially-operated centres which produce and make available labelled compounds (see appendix 6.1)

1.5.4. Agrochemical manufacturers and associated industrial research divisions labelling their own products for research, development and evaluation. These included the major agrochemical manufacturers of Western Europe, North America and Japan.

The sources collectively designated as 1.5.1 undoubtedly represented an immense range of labelled agricultural chemicals, metabolites, intermediates, and precursors. Small quantities were often available on the basis of a gift or of an agreed exchange for use by a qualified worker elsewhere. The principal problem was to establish communications between need and source. Personnel concerned at the source were often unaware of the need of some distant but qualified scientist in a foreign laboratory. Similarly research workers faced with the problem were likely to be unaware of the existence of the sources unless a suitable reference had appeared in the published scientific literature and this had been seen by the research workers in need.

Recognized regional and national isotope centres also represented a source of labelled materials but, usually, of a very limited range representing their local or regional programmes. Research workers in the country or region would probably be aware of such centres and likely to address enquiries on the basis of their needs. Brief descriptions of the Middle Eastern Regional Radioisotope Centre for the Arab Countries (MEREC) and the National Centres for India and Brazil which the Group felt had particular potential for developing facilities on a regional basis will be found in appendix 6.3.

With regard to centres for the commercial production (1.5.3) these could usually be identified on the basis of their catalogues and through advertizing media. With regard to industrial sources (1.5.4) it was known that many of the major manufacturers of agricultural chemicals almost invariably prepared these in labelled form for their own research, development and evaluation. The existence of these labelled materials and associated technical data might understandably not appear in the published scientific literature. Manufacturers would also and understandably feel cautious about the gift of their labelled materials. They would expect to be

satisfied that it would not lead to the publication of data which posed a threat or potential threat to the products' reputation for safety and/or effectiveness on the basis of inexperienced or unsound experimentation.

The meeting was advised that, as part of an OECD development, cooperative pre-market screening of all new chemicals provision will be made for the accumulation of data on biodegradability, bioaccumulation, etc. It was likely that within the OECD, manufacturers would be obliged to prepare any new products in isotopically-labelled form and make them available to researchers on the basis of an agreed research programme.

1.6. Sources of information

An obvious desideratum for successful and economic isotopic synthesis was access to existing information and experience. The Group identified the following major sources: -

- 1.6.1. The scientific literature (see appendix 6.2 for relevant examples)
- 1.6.2. Individual scientists experienced in the preparation of the required compounds or in the appropriate methodology
- 1.6.3. Laboratories or institutes with ongoing programmes of relevant isotopic synthesis.

In considering 1.6.1. the Group recognized that relevant information on such diverse classes of chemicals involved are found in hundreds of different journals or other literature sources, only a few of which are exemplified in appendix 6.2.

The Group also considered the value of computerized information programming, storage, and retrieval services. In particular the possible use of INIS (the IAEA administered international nuclear information system). Expertise on this subject was made available by the IAEA Secretariat. Discussions suggested that the INIS system was unlikely to provide information on labelled syntheses of the kind usually sought in connexion with chemical residue and pollution problems.

In relation to scientists, laboratories and institutes (1.6.3 above) specializing in a given class of agrochemicals information could best be obtained through the media of abstracts and review publications (see 6.2). Appropriate contacts or communications with these sources often provides up-to-date information on recent isotopic syntheses or those in progress or planned. Such an awareness is essential in avoiding duplication and making the best utilization of the newly prepared radiochemicals or agrochemicals and their intermediates.

Another important source of information is represented by the research and development laboratories of primary manufacturers of agrochemicals. These products can be identified in pesticide lists (e.g. Martin, H., Pesticide Manual, British Crop Protection Council, London, UK, 1972 and Thomson, W.T., Agricultural Chemicals, Thomson Publications, Indianapolis, Indiana, 46250, USA, 1973); or compilations published either at a national level (e.g. Departments or Ministries of Agriculture) or involving an international compilation (e.g. CIDA Handbook, Weed Science Society of America, Bulletin of the Entomological Society of America, etc.). The primary manufacturers generally maintain complete files of published studies on their own compounds including radiosyntheses and utilization of the tagged materials.

A final information source is through the relevant section of international organizations, e.g. IAEA, FAO, INRIS of EURATOM, and ESNA.

1.7. Possible action at international or regional level

The Group considered the following possibilities for international action: -

- 1.7.1. More frequent updating, extension, and much wider distribution of the kind of information illustrated as working paper 4.1 based on updated and as complete a collection of catalogues, addenda, etc. as possible from the commercial sources illustrated in appendix 6.1.

- 1.7.2. To finance the visit of the scientist of a developing country to a possible non-commercial source of the kinds identified as 1.5.1, 1.5.2 or 1.5.4 (above) with a view to arranging an actual gift of materials or temporary facilities for work during the visit and to present the research programme to the supplier.
- 1.7.3. To make special provision for information on relevant isotopic syntheses and labelled compounds in the Joint FAO/IAEA Summaries (see 1.8.11).
- 1.7.4. To establish an international "bank" or "centre" for the conservation, storage, dispensing and distribution of selected labelled compounds, intermediates, metabolites, synthetic precursors, etc.
- 1.7.5. To provide for better coverage of the problems of isotopic syntheses in the FAO/IAEA training courses (see 1.2).
- 1.7.6. To encourage individual scientists to attempt their own isotopic syntheses by means of specific training, fellowships, or by the preparation of a laboratory manual on isotopic syntheses of selected agrochemicals.
- 1.7.7. To compile a list of information sources defined as 1.6.2 and/or 1.6.3 above and make such an updated list periodically available to scientists of developing countries.
- 1.7.8. To provide improved coordination of activities and information exchange between users and sources.

The Group considered the following possibilities for regional action: -

- 1.7.9. To encourage the use of existing regional centres (e.g. MERC, Cairo) for the preparation of labelled compounds for local, overseas or multinational use on the basis of local expertise but imported precursors or intermediates where problems of economics or availability so indicated.

1.7.10. To encourage the creation of new centres on the basis of existing and appropriately equipped national centres with a potential and possible interest in this (e.g. Trombay, India; Piracicaba, Brazil).

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2. CONCLUSIONS

The effective lack of availability of suitably labelled compounds for the use of otherwise qualified and adequately equipped investigators in developing countries is often a serious handicap to the study and solution of a local or regional problem. Typical problems were the need to study the magnitude and nature of a pesticide residue or the need to conserve and regulate the behaviour of a fertilizer residue under the local conditions.

The labelled compound needed must either be obtained by isotopic synthesis "on site", or obtained as a gift, or by purchase. Adequate specification for the purpose of purchase or other method of acquisition, safe, effective and economic preparation, storage and use of the material required a good understanding of the nature and properties of labelled

compounds, and understanding of the principles of their preparation and use. This in turn implied access to information and the importance of adequate training (see 1.2).

Isotopic syntheses, like most other applied scientific activities, required a continually increasing range of equipment and materials and exacting laboratory standards. Therefore, efficiency tended to increase with centralization and pooling of resources and expertise.

The expertise and facilities for the effective use of labelled compounds for studying residue problems of agriculture, fisheries and food often involved quite different training and facilities than those required for their preparation, appropriate storage, purity testing, etc.

Except in special cases where no other solution was apparently available more difficult isotopic syntheses or ones likely to involve inexperienced personnel should not be encouraged (cf. 1.7.6 above). When an individual isotopic synthesis is required this should, where possible, be undertaken at a suitably equipped regional centre with the necessary expertise and facilities and which works in cooperation with national centres, or at suitably equipped national centres.

Action involving international travel of users for the purpose of visiting possible donors (1.7.2) was felt not to be economic. Within the resources available or likely to be available to the Joint FAO/IAEA Secretariat it would, however, be practicable to initiate new or improved collection, dissemination and exchange of relevant information (cf. 1.7.1, 1.7.3, 1.7.7 and 1.7.8 above).

With regard to training (cf. 1.7.5) the Group felt that the FAO/IAEA training courses should increase the emphasis on the principles of isotopic syntheses with a view to helping the user to identify and adequately specify a requirement which could be reasonably met economically, logistically, safely and effectively from the point of view of solving this problem.

With regard to improving or developing the services of appropriate regional or national centres (1.7.9 and 1.7.10 above) there appeared considerable potential and justification (see third paragraph of section 2 above) but the initiative would have to be taken by the regional and other centres. The Joint FAO/IAEA Secretariat is available to advise in formulating suitable requests to UN.

An international "bank" or "central collection" of selected labelled substances (cf. 1.7.4 above) was not considered practicable within the present resources available to the Joint FAO/IAEA Secretariat. Technical difficulties of storage, dispensing and distribution to users under acceptable specifications could also be envisaged. However, the Group considered the idea in principle to be important and the possibility of creating such a bank on the basis of a comparative agreement between IAEA, interested governments and existing regional and national centres should be explored.

3. RECOMMENDATIONS

Against this background above and noting: -

- (a) The growing need of developing countries to make safe, effective and efficient use of agrochemicals (insecticides, herbicides, fungicides, fertilizers, veterinary drugs, etc.)
- (b) The corresponding need to have access to modern and effective research tools for local use to help meet this need
- (c) The handicap to otherwise suitably-qualified scientists of developing countries of lacking appropriate isotopically labelled chemicals or access to relevant information
- (d) The growing costs and complexity of safe and economic preparation of isotopically-labelled compounds and the advantages of pooling relevant resources and expertise.

The Advisory Group addressed the following recommendations to the Directors General of FAO and IAEA: -

- 3.1. To identify better and more systematically sources of relevant isotopically-labelled chemicals, sources of information on relevant isotopic syntheses and techniques, and specific needs for labelled chemicals.
- 3.2. To make information on these sources and needs available by publication and/or "information circulars" to scientists of developing and developed countries.
- 3.3. To explore the possibility of establishing an international bank or collection of labelled compounds on the basis of cooperation between IAEA, interested governments and existing national and regional centres.
- 3.4. To seek ways and means of supporting existing regional isotope centres of developing countries.
- 3.5. To seek ways and means of supporting existing national centres and to extend their services to meet regional needs.
- 3.6. To explore the possibility of establishing an ongoing cooperation between the regional or appropriate national centres and UN agencies concerned.
- 3.7. To encourage appropriate contacts between scientists of advanced countries and of developing countries in order to facilitate better coordination at international level in the area of isotopic syntheses.

4. WORKING PAPERS

- 4.1. FAO/IAEA Secretariat, List of commercially available radio-isotopically labelled pesticides, Vienna, 1972 (prepared for use of collaborators and correspondents in the Joint FAO/IAEA Chemical Residues and Pollution Programme - copies available on request).
- 4.2. Benakis, A., Isotopic syntheses with particular reference to ^{14}C . IAEA Panel Proceedings Series, Vienna, 1974, STI/PUB/363, pp. 11-19.
- 4.3. Winteringham, F.P.W., FAO/IAEA Advisory Group on the preparation and supply of isotopically-labelled compounds for chemical residues and pollution studies - Introductory notes.
- 4.4. Viswanathan, K.V., D'Souza, A.B. and Dhane, D.L., Labelled compounds production programme in India.
- 4.5. Viswanathan, K.V., D'Souza, A.B. and Dhane, D.L., Addendum to 4.4.
- 4.6. Hashish, S.E., FAO/IAEA Advisory Group on the preparation and supply of isotopically labelled compounds for chemical residue and pollution studies - Notes and comments.
- 4.7. Matwiyoff, N.A., Considerations in the development of the utility of stable isotopes in science, medicine and agriculture and environmental studies.
- 4.8. Benakis, A., Labelled compounds and intermediates relevant to trace contaminant studies.
- 4.9. Plessy, L., The contribution of the department of R & A in the fields of study of traces of pollutants.
- 4.10. Plessy, L., Costs of materials, (Addendum to 4.9).

- 4.11. Buchtela, K., Coordinated preparation and supply of labelled compounds for international distribution and use.
- 4.12. Benes, J., Storage and supply of commercially unavailable labelled compounds for international distribution and use in developing countries: Possible problems connected with the stability of labelled compounds.
- 4.13. Klein, W., Sources of information on the preparation and supply of labelled compounds: suppliers' catalogues, scientific literature, reports from research institutes, reports from industry.
- 4.14. IAEA, INIS - International nuclear information system, Vienna, 1975.

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6.1. Commercial and other sources of labelled compounds including those relevant to trace contaminant problems of agriculture, fisheries and food.

(Note: Ct = Catalogues issued
R = Radioactive isotopically-labelled compounds available
S = Stable isotopically-labelled compounds available
P = Labelled materials supplied on a commercial basis
at agreed or published prices.)

Absence of letters indicates relevant information not available to the Group.

In all cases, up-to-date information should be sought by direct enquiry to the address indicated)

ARGENTINA: Comision Nacional de Energia Atomica Argentina
Avenida del Libertador Gral, San Martin 8250
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Buenos Aires - Suc 29
(R, Ct, P) (no recent information received)

BELGIUM: Institut National des Radioelements
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IRE
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6220 Fleurus
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Tracerlab
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Antwerpse Steenweg 277
2800 Mechelen
(Ct,P) (no recent information received)

BULGARIA: Chimimport
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(no recent information received)

BRAZIL: Centro de Energia Nuclear na Agricultura
(CENA) Caixa Postal 96
Piracicaba, Sao Paulo
(S, P)

CANADA: Merck, Sharp and Dohme of Canada, Ltd.
Isotopic Products Department
P.O. Box 99, Montreal 3
(Ct, R, S, P)
(no recent information received)

Stohler Isotope Chemicals
P.O. Box 1134
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(no recent information received)

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APC-Azote et produits chimiques
Departement des ventes 75646
62, Rue Jeanne d'Arc
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Gebrüder Schoeller
1110 Wien
Simmeringer Hauptstrasse 28
Austria

DEMOCRATIC
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GERMANY

Isocommerz GmbH
705 Leipzig
Permoserstr. 15
(R, S, Ct, P)

FEDERAL
REPUBLIC OF
GERMANY

CIS
Isotopen Dienst West GmbH
An der Trift 9-11, Postfach 2025
6079 Sprendlingen
(R, Ct, P)
(no recent information received)

NEN Chemicals GmbH
Research Products
Postfach 1240
D-6072 Dreieichenhain bei Frankfurt/Main
Daimlerstrasse 23
(R, Ct, P)

Radiopharmaka "Hoechst" A.G.
vorm. Meister, Lucius & Brunning
D6-6320 Frankfurt (Main) 80
(Ct, R, P)
(no recent information received)

Becton, Dickinson GmbH
Waldhaferstr. 3
6900 Heidelberg-Wieblinger
(represents Schwarz/Mann for European market)
(R, Ct, P)

Rohstoff-Einfuhr GmbH, Abteilung Isotope
Faunastrasse 61
4000 Dusseldorf
(R, S, Ct, P)

Amersham-Buchter GmbH & Co. K.G.
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Sharp and Dohme GmbH
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POLAND: Metronex
c/o Osrodek Produkcji i Dystrybucji Izotopow
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K/OTWOCKA
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(R, S)

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CH-9053 Teufen
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Stohler Isotope Chemicals
Im Baugarten
CH3044 Innerberg
(S, Ct, P)

Technosa SA
1009 Pully Lausanne
Avenue General-Guisan 58
(R, S, Ct, P)

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Dinting vale training estate
Dinting Lane, Glossop
Derbyshire, SK 13 9 NU
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Huntingdon Research Center
Huntingdon PE18 6ES Cambs.
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PROCHEM (British Oxygen Co., Ltd.)
Deer Park Road
London SW 19 3 UF
(S, Ct, P)

The Radiochemical Centre Amersham
White Lion Road
Buckinghamshire
(R, Ct, P)

UNITED STATES
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Arthur D. Little, Inc.
Acorn Park
Cambridge, Mass. 02140
(no recent information received)

Bio-Rad Laboratories, Stable Isotope Sales
2400 Wright Avenue
Richmond, California 94804
(S, Ct, P)

UNITED STATES
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Calatomic, Inc.
P.O. Box 54984
Los Angeles, California 90054
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Amersham-Searle Corporation
2636 S. Clearbrook Drive
Arlington Heights, Illinois 60005
(R, Ct, P)
(marketing area: North, Central, South America and the
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DHOM Products, Ltd.
1120 Cumpston Street
North Hollywood, California 91601
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Monsanto Research Corporation, Stable Isotopes Sales
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Research Products International
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U.S.S.R.:

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Yugoslavia
(no recent information received)

6.2. Some journals and monographs on labelled compounds and their synthesis

6.2.1. Journals

- 6.2.1.1. International journal of applied radiation and isotopes.
Deals with the preparation, use and measurement of stable and radioactive isotopes. Relatively little emphasis on isotopic synthesis per se.
Published by Pergamon Press, Oxford, UK

- 6.2.1.2. Isotopenpraxis
Deals with use, control and analysis of radioactive and stable isotopes.
Published by Akademie Verlag GesmbH, Berlin, German Democratic Republic
- 6.2.1.3. Journal of labelled compounds and radiopharmaceuticals
Deals with preparation, purification, storage and analysis of isotopically-labelled compounds
Published by John Wiley and Sons, Brussels, Belgium
- 6.2.1.4. Radiochemical and radioanalytical letters.
Deals with application of nuclear techniques including few radio-isotopic syntheses.
Published by Elsevier Sequoia S.A., Lausanne, Switzerland and Akademia Kiado, Budapest, Hungary.
- 6.2.2. Monographs
- 6.2.2.1. Murray, A. and Williams, D.L., Organic synthesis with isotopes. Interscience publishers, New York, 1958.
- 6.2.2.2. Catch, J.R., Labelling patterns: Their determination and significance
UKAEA, Radiochemical Centre, Amersham, UK, Review No. 11, 1971.
- 6.2.2.3. Catch, J.R., Purity and analysis of labelled compounds.
UKAEA, Radiochemical Centre, Amersham, UK
Review No. 8, 1968.
- 6.2.2.4. Bayly, R.J. and Evans, E.A., Storage and stability of compounds labelled with radioisotopes.
UKAEA, Radiochemical Centre, Amersham, UK
Review No. 7, 1968.
- 6.2.2.5. Bayly, R.J. and Catch, J.R. The stability of labelled organic compounds
UKAEA, Radiochemical Centre, Amersham, UK
Review No. 3, 1968.
- 6.2.2.6. Evans, A.E., Self-decomposition of radiochemicals: principles, control, observations and effects. Radiochemical Centre, Amersham, UK
Review No. 16, 1976.

- 6.2.2.7. Sheppard, G., The self-decomposition of radioactively labelled compounds. Atomic Energy Review. Vol. 10, No. 1, IAEA 1972.
- 6.2.2.8. Anonymous, Guide for users of labelled compounds. Radiochemical Centre, Amersham, UK, 1972.
- 6.2.2.9. Anonymous, Special syntheses. Radiochemical Centre Amersham, UK, Technical Bulletin, 75/1, 1975.
- 6.2.2.10. Anonymous, Tritium labelling services. Radiochemical Centre, Amersham, UK, Technical Bulletin 74/1, 1974.
- 6.2.2.11. Evans, E.V., Tritium and its compounds, 2nd Edition, Butterworth, London, 1974.
- 6.2.2.12. Moghissi, A.A., Carter, M.W., Tritium. Medsenger Graphics, USA, 1973.
- 6.2.3. Journals and incidental information sources on labelled compounds and their preparation

Journals of most chemical, biochemical and agricultural chemical societies contain, incidentally, descriptions of the preparation and synthesis of labelled compounds. These can only be located from titles, abstracts or indices including, of course, contents lists and indices of the journals themselves. Relevant abstracts and indices include:

- 6.2.3.1. Chemical abstracts
- 6.2.3.2. Isotope titles, Akademie der Wissenschaften der DDR
- 6.2.3.3. INIS (see 4.14)
- 6.2.3.4. Chemischer Informationsdienst, FRG
- 6.2.3.5. Chemical and biochemical titles
- 6.2.3.6. Trace contaminant abstracts
Oak Ridge National Laboratory, Oak Ridge, Tennessee 37830, USA.
- 6.2.3.7. Current contents

Some journals published in English dealing in part with agrochemical residue and pollution problems of agriculture, fisheries and food and the incidental preparation of the labelled compounds used would include particularly:

- 6.2.3.8. Archives of environmental health, American Medical Association, Chicago, Illinois, USA.

- 6.2.3.9. Chemosphere, Pergamon Press, Oxford, UK.
- 6.2.3.10. Drug metabolism review, Marcel Dekker, Inc., New York, USA.
- 6.2.3.11. Environmental pollution, Applied Science Publishers, Ltd., Essex, UK.
- 6.2.3.12. Environmental science and technology, American Chemical Society, USA.
- 6.2.3.13. European journal of drug metabolism and pharmacokinetics, Edifor, 49 rue Saint-André-des Arts, 75006, Paris.
- 6.2.3.14. Journal of agricultural and food chemistry, American Chemical Society, Washington, D.C.
- 6.2.3.15. Journal of economic entomology, Entomological Society of America, College Park, Maryland, USA.
- 6.2.3.16. Journal of environmental quality, American Society of Agronomy, Madison, Wis., USA.
- 6.2.3.17. Marine pollution bulletin, Mcmillan Journals, Ltd., Essex, UK.
- 6.2.3.18. Pesticide abstracts, Environmental Protection Agency, Washington, D.C.
- 6.2.3.19. Pesticide science, Society of Chemical Industry, London, UK.
- 6.2.3.20. Plant physiology, American Society of Plant Physiologists, Waltham, Mass., USA.
- 6.2.3.21. Residue reviews, Springer-Verlag, New York and Berlin
- 6.2.3.22. Societe chimique de France bulletin, Mason et Cie, Paris.
- 6.2.3.23. Toxicology and applied pharmacology, Academic Press, Inc., New York.
- 6.2.3.24. Water, air and soil pollution, D. Reidel Publishing Co., Dordrecht, The Netherlands.
- 6.2.3.25. Water pollution research, Atlantic House, Stevenage, England.
- 6.2.3.26. Water research, Pergamon Press, Inc., Oxford, England.
- 6.2.3.27. Weed science, Weed Science Society of America, Illinois, USA.
- 6.2.3.28. Xeno biotica, Taylor and Francis, Ltd., London, UK.

6.3. Regional and national centres of developing countries with facilities for the preparation of labelled materials, training and research.

- 6.3.1. Middle Eastern Regional Radioisotope Centre for the Arab countries (MEREC), Cairo, Egypt.

This Centre was initiated in 1963 in Cairo in cooperation with the IAEA (until 1968) and with continuing membership of thirteen Arab States since

then. MEERC works in close cooperation with other national nuclear centres of the Arab States, the national research centres, universities and other scientific institutes. The main functions of MEERC are: -

6.3.1.1. Training courses on radioisotopes application in different field. Two courses (general and special) are held every year (20 trainees per course) from different Arab States. African trainees attend the courses. International courses are also held in the Regional Centre with the participation of IAEA, FAO and other UN agencies. A 4-week course on nuclear techniques for chemical residue and pollution problems was held in November 1975 and was attended by 15 trainees from Arab and European countries. The course was very successful. Six of these trainees were chosen for IAEA/UNDP fellowships to enable them to follow-up the course by suitable visits to European institutes.

6.3.1.2. Research involving the use of radioactive and stable isotopic techniques in medicine, agriculture, industry, biology, entomology, hydrology and basic sciences is carried out in the laboratories of the centre and allied research centres.

6.3.1.3. Research projects and contracts are granted by the centre to scientists in the region.

6.3.1.4. A journal is published bi-annually by the centre covering papers, reviews and relevant activities of the region.

6.3.1.5. Seminars, symposia and scientific meetings for Arab nuclear scientists to attract UN Agency representatives and invite foreign institutes are held yearly.

The Centre is well-equipped with training and research facilities. In addition to the standard radioisotopic equipment there are additional facilities, e.g., mass spectrometer, liquid scintillation spectrometer, multi- and single channel analysers, etc.

Storage facilities for radioisotopes are present.

Radioisotopes are obtained from its two radiochemical centres in Cairo and Baghdad, and also from international radiochemical centres.

Qualified chemists capable of labelled pesticide synthesis from radioactive precursors are permanent and part-time workers in the Centre.

Current projects include those undertaken in cooperation with UN Agencies, Federal Republic of Germany and Poland, and research projects on pesticide residue and pollution problems with support from the FAO/IAEA, and EPA of USA.

In addition to the library of the Centre, the documentation centres of NCR -Cairo, ARE; Atomic Energy INIS services and universities' libraries are rendering assistance to scientists and trainees of MERC.

The nuclear facilities and other research laboratories are under its disposal according to its status.

6.3.2. Labelled Compounds Section, Isotope Division, Bhabha Atomic Research Centre (BARC), Trombay, Bombay-85, India.

This Section functions as a National Centre for the production and supply of isotopically-labelled compounds. It has developed methods for the routine production of nearly 200 different labelled compounds such as amino acids, carbohydrates, fatty acids, purimides, nucleosides, nucleotides, carcinogens, insecticides, herbicides, etc. The Section's laboratories are equipped with a number of well-ventillated hoods, an inert atmosphere box and a facility for storage at temperatures down to that of liquid nitrogen. Instrumentation provides for amino acid analysis, gas chromatography, U.V. and I.R. spectrometry, liquid scintillation counting, radiochromatogram scanning, automatic fraction collection, etc.

In addition to the routine production and supply of tritiated compounds, a tritium labelling service is also available.

The Labelled Compounds Section has built up the necessary facilities and expertise for training on the safe handling of radioisotopes, tracer methodology and isotopic synthesis.

The Chemical Engineering Division has developed a number of deuterium labelled organic solvents and other compounds with an isotopic abundance better than 95% and a few ¹⁵N-labelled compounds such as urea, nitric acid, ammonium sulphate, etc. Facilities for mass spectrometric analysis of these products are also available.

Facilities also exist for packaging and dispatching the labelled compounds by air, sea and rail either by freight or post conforming to international regulations for transport of radioisotopes.

6.3.3. Centre de Energia Nuclear na Agricultura(CENA), Piracicaba, Brazil.

This Centre is a joint enterprise between the Brazilian National Nuclear Energy Commission (CNEN) and the University of Sao Paulo. It has facilities for training, for the preparation and handling of isotopically-labelled compounds, and a stable isotope (especially ^{15}N) production programme. It has an on-going environmental science programme and a range of well-equipped laboratories.