7-16-92

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

JUL 16 1992

OFFICE OF
PESTICIDES AND TOXIC
SUBSTANCES

MEMORANDUM

SUBJECT: Additional Guidance for Conducting Plant and Livestock Metabolism Studies.

FROM: Ed Zager, Chief
Chemistry Branch II: Reregistration Support
Health Effects Division (H7509C)

and

Debra Edwards, Ph.D., Acting Chief
Chemistry Branch I: Tolerance Support
Health Effects Division (H7509C)

TO: D. Barolo, Director
Special Review and Reregistration Division (H7508W)

THRU: P. Fenner-Crisp, Ph.D., Director
Health Effects Division (H7509C) 7/22/92

Earlier this year a Rejection Rate Analysis for Residue Chemistry studies carried out by CBRS and CBTS and SRRD along with input from NACA representatives, indicated the need for the Agency to provide additional guidance on conducting plant and livestock metabolism studies. The attached paper addresses the points determined to need clarification. This paper was written by Dr. R. B. Perfetti, with thoughtful and welcome comments from a number of HED senior staff. This paper is not intended to replace existing documents but to expand upon them. It will be utilized by the Chemistry Branches in future reviews of metabolism studies.

We recommend that this paper be provided to the appropriate parties.

cc: P. Caulkins

Introduction

In the Rejection Rate Analysis conducted in the past year for List A chemicals, certain common reasons for rejection of residue chemistry studies were identified. The Agency then sought industry comment on the adequacy of the guidelines. With regard to metabolism studies industry provided numerous comments such as the need for EPA to provide more direction with respect to bound residues and to clearly distinguish between the terms "identification" and "characterization". As a result it has become evident that clearer guidance is needed on how to conduct metabolism studies and that is the purpose of this memorandum.

It should be emphasized that this memo is not intended to replace existing documents, but to expand upon them. In particular, it clarifies the guidance in the Residue Chemistry Guidelines (1982) and in the 7/25/89 Richard Schmitt memo entitled "Guidance on When and How to Conduct Livestock Metabolism Studies" (published in the 1989 FIFRA '88 Phase 3 Technical Guidance). Although portions of the present memo emphasize plant metabolism, the principles discussed also apply to livestock metabolism studies and should be considered thus.

Application of Radiolabeled Pesticide

The first consideration in designing a metabolism study is radiolabeling. The radiolabel should be positioned in the molecule so that potentially significant toxicological moieties can be tracked. This should involve ring labeling (preferred) or even double labels, i.e. molecules containing two rings are labeled in both or each ring is labeled in separate experiments. Carbon-14 is the preferred isotope when possible. The use of tritium as a label is strongly discouraged.

Other initial considerations include the method of application and the application rate of radiolabeled pesticide to be used. Since the primary purpose of a metabolism study is to identify the chemical components of the residue, the application rate must be high enough to result in sufficiently high radioactivity levels to allow for characterization/identification of the residue. A rate of at least 1X (the registered application rate) should generally be used for plant metabolism or dermal livestock metabolism studies. In the case of oral livestock metabolism studies, the dose should, at a minimum, approximate the maximum anticipated dietary burden, but in no instance should the level be less than 10 ppm in the diet (i.e. 10 mg per kg of feed) as stated in the 7/25/89, R. Schmitt memo. However, for certain pesticides/uses it is necessary to apply radioactive material at exaggerated rates. The decision as to what rate to utilize is contingent upon several factors. For example, in the case of herbicides, phytotoxicity which may stress or even kill the plant(s) may limit the exaggerated rate which can be used. For all pesticides, the minimum application rate required to allow

adequate characterization/identification of residues (up to a maximum of 10X as discussed further below) must be utilized in plant metabolism studies unless reasons such as phytotoxicity prevent this. Safety concerns when using large amounts of radioactivity must also be considered. In addition, the following should be considered when selecting the dosing material, a method of application and an application rate or dosage for plant or livestock metabolism studies:

- The plant should be treated with parent only.

- Livestock metabolism studies should reflect feeding of one compound, usually the parent. If the plant metabolites are also found to be animal metabolites, then additional livestock metabolism experiments which involve dosing with plant metabolites will not generally be required. However, if a plant metabolite comprises a major portion of the TRR on a feed item or is not found to be an animal metabolite, additional livestock metabolism studies involving dosing with the plant metabolite may be required.

- The specific activity of the labeled material should be as high as possible. In cases where there has been little or no characterization/identification of the residue, in crops or animal tissues because of low levels of activity, the Agency will make a determination as to the adequacy of efforts the Registrant has made to maximize specific activity such that application rates would yield characterizable/identifiable levels of radioactivity in edible plant parts.

- In cases where low levels of radioactivity are observed even at exagggerated rates, utilization of adjuvants or typical inerts may enhance absorption of the active ingredient into the plant or animal (dermal).

- Selection of specific crops and use patterns should reflect the situation where the highest amount of radioactivity would be expected in the edible portions of the plant at harvest. If a pesticide has two distinct use patterns that could lead to different metabolic situations (e.g., preplant soil application and a foliar treatment), then two metabolism studies may be required.

- If exaggerated application rates of a phytotoxic herbicide are necessary to achieve sufficient radioactivity for characterization/identification of residues, and the required rate causes phytotoxicity in the plant, metabolism information on the "sick" plant is preferable to having no information due to lack of sufficient

radioactive residue.

Sampling of Plant Parts

Samples of all raw agricultural commodities (racs) as defined in Table II of Subdivision O of the Pesticide Assessment Guidelines should be obtained for characterization/identification of residues. In some cases, collection of samples of immature plant parts not in Table II may be considered as an aid to facilitate the characterization/identification of residues when low residue levels are expected in the mature plants. Although collection of immature plant parts not in Table II (Note that materials such as corn forage are immature plant parts but are considered to be **racs**.) is not required, it may facilitate characterization/identification of residues in cases where the "trigger" values (discussed below) are exceeded, but residues present unusual difficulties in characterization/identification due to low residue levels or the nature of the metabolites. These data may provide adequate information to allow conclusions to be drawn about the identity of residue in mature parts of the plant. Registrants may also wish to use mature but inedible crop parts (e.g., apple leaves, potato foliage) to help identify residues on the mature rac. However, if this information is to be used in support of the study, evidence of similar chromatographic profiles for mature edible and inedible plant portions is preferred.

Analytical Phase

In the analytical phase of a plant/livestock metabolism study, the plant/animal parts to be analyzed are sampled, chopped or homogenized, total radioactivity is determined and the samples are extracted with a series of solvents and/or solvent systems (including aqueous) with various polarities and other characteristics depending on the nature of the expected residues. These initially obtained residues are defined as **extractable** residues. The required characterization/identification of extractable residues is summarized in Figure 1 (This is a diagram of "trigger" values described in the 7/25/89, R. Schmitt memo with some modifications.).

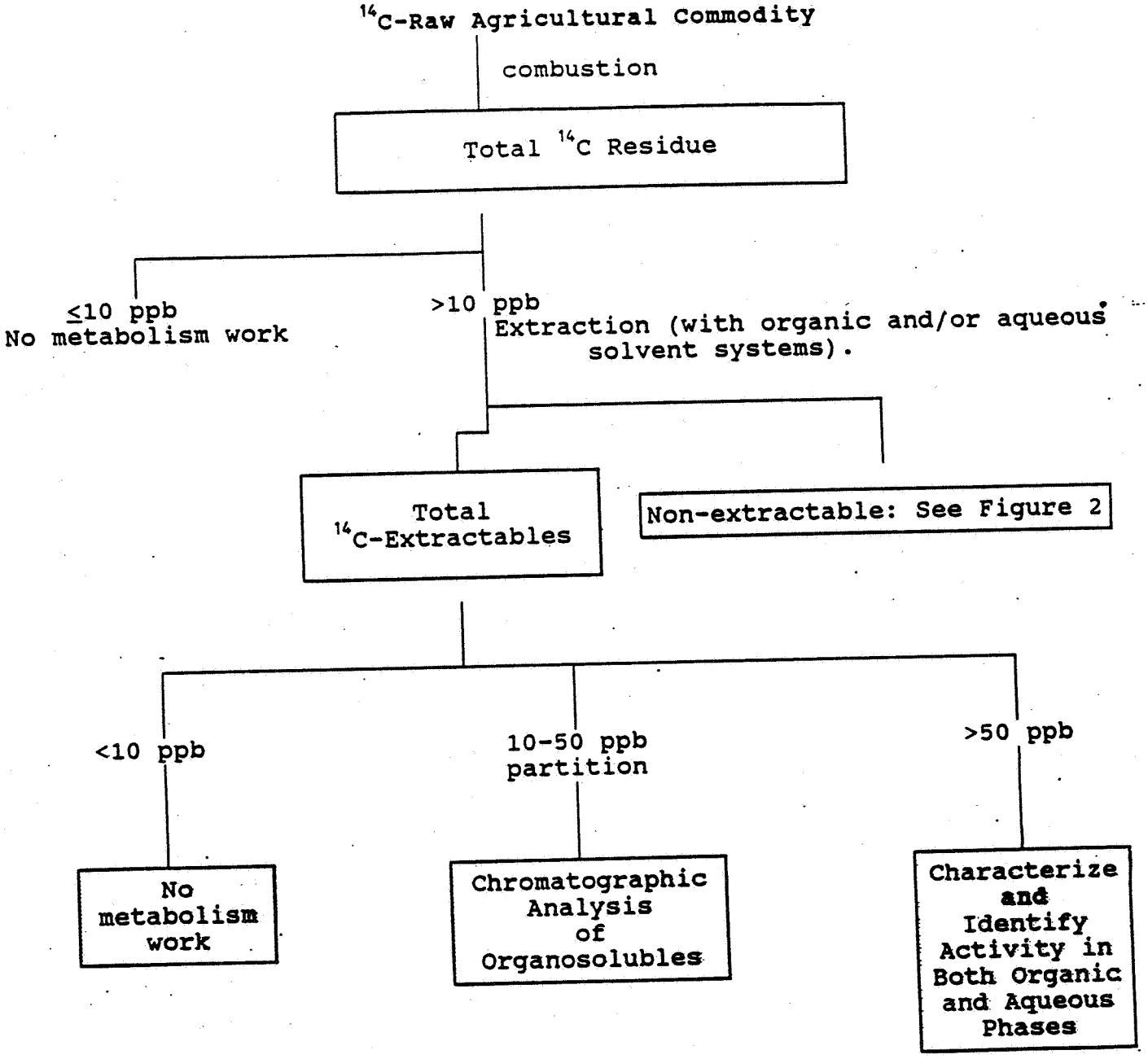
Before discussing Figure 1 in greater detail, the terms characterization and identification of residues will be defined as follows:

- **Identification** refers to the exact structural determination of components of the total radioactive residue. Typically, this is accomplished by comparing chromatographic behavior to that of known standards and/or actual spectroscopic analyses (MS, NMR, etc.).

- **Characterization** refers to the elucidation of the general nature/characteristics of the radioactive residue short of metabolite identification. Terms used to characterize residues include organosoluble, water or aqueous soluble, neutral, acidic or basic, polar, non-polar, non-extractable, etc. Characterization may also involve descriptions of chemical moieties known to be present in the molecule based on conversion to a common structure or due to reactivity with particular reagents. The degree of characterization refers to how close the assignment comes to structural identification. When identification of radioactive residues is not accomplished, the degree of characterization required for a portion of the total radioactivity will depend on several factors including the amount of residue present, the amount of the total radioactive residue already identified, the importance of the crop part as a food or feed, toxicological concern over a class of compounds, the suspected significance of the residue as determined by characterization already performed and the capability of analytical methods to detect characterized (i.e., by conversion to a common moiety) but unidentified residues. (This radio-validation of the method would be important both for future development of enforcement methodology and in a case where a significant amount of radioactivity is observed in a matrix but it consists of a large number of individual moieties at levels below "trigger" values but which can be converted to one or two distinct compounds by procedures such as oxidation or hydrolysis.). **Therefore, the terms characterization and identification clearly have different meanings and should not be used interchangeably.**

Identification of metabolites must be established using two different analytical techniques except when (a) unambiguous identification is made using a spectroscopic method such as GC/MS, or (b) the metabolite is determined to be of minimal importance due to its low absolute level (<0.05 ppm) or percentage of the total radioactive residue (<10% of TRR). In the case of (b), identification by one technique such as co-elution with standards will be acceptable. These trigger values are meant as rough guidance and may not apply to situations where a metabolite is suspected to be of particular toxicological concern, or where <10% of the TRR represents a high absolute residue level. In general, the Agency will not consider chromatographic techniques utilizing the same stationary phase with two different solvent systems to be adequate two-method verification of metabolite identity.

Figure 1: Strategy for Identification/Characterization of Extractable Residues from Plant Metabolism Studies.



Strategy For Determining When Identification Of Metabolites Is Needed

The strategy illustrated in Figure 1 for extractable **polar and non-polar** residues was developed by Ciba-Geigy and applied primarily to animal metabolism studies in the Schmitt memo of 7/25/89. The radioactivity trigger values shown in Figure 1 reflect the characterization/identification required for each rac. If total activity in a crop/animal part is ≈0.01 ppm (10 ppb) or less, no differentiation of the radioactivity would be required. For activity greater than ≈0.01 ppm, the sample should be extracted with solvents and/or solvent systems (including aqueous) of various polarities. The levels of extractable and non-extractable activity should then be quantitated to determine the degree of characterization that is needed. If the extractable activity represents ≈0.01 ppm or less, it need not be examined further. For extractable activity of ≈0.01-0.05 ppm, the partitioning behavior between aqueous and organic solvents should be determined followed by chromatographic (TLC, HPLC) analysis of the organosoluble activity. The chromatographic behavior of this activity can be compared to that of the parent pesticide and likely metabolites (characterization and/or identification). When the extractable activity exceeds ≈0.05 ppm, complete characterization and identification should be attempted for both organic and aqueous activity. It is important that the components of the aqueous soluble portions of the radioactivity be identified since they may contain toxic compounds. Given the present state of HPLC columns and detectors, this type of research is much simpler than previously. For the aqueous soluble portion of the activity however, the "trigger" values for characterization and identification would be levels down to 0.05 ppm or 10% of the TRR whichever is greater. The exception for this would, of course, be toxicology concerns over potential residues which might occur at lower levels. Identities of metabolites should be confirmed with a second technique, spectroscopic if possible, as discussed above.

The term "complete characterization and identification" for extractable residues above 0.05 ppm does not necessarily mean that individual components at this level need to be identified. Low level (in terms of both ppm and % of total residue) individual residues do not typically need to be identified if the major components of the residue have been identified. For example, if the total activity in a crop part is 3 ppm and 75% of that has been firmly identified, it is unlikely that identification of a series of individual residues in the 0.05-0.1 ppm range would be required. On the other hand, extensive efforts toward identification of 0.05-0.1 ppm residues would be expected when the total activity is only 0.3 ppm.

The radioactivity levels shown in Figure 1 apply regardless of the application rate used in plant metabolism studies. However,

this is not meant to discourage use of exaggerated application rates necessary to provide sufficient radioactivity for adequate delineation of the plant metabolism. If application rates are used which are insufficient to provide adequate radioactivity for characterization/identification of residues, additional studies may be required at increased application rates up to the point of unacceptable plant phytotoxicity. The maximum exaggerated rate which will be required for a plant metabolism study is 10X (The use of highly exaggerated doses in livestock metabolism studies is discussed in the 7/25/89 R. Schmitt memo for situations where low residues are present on feed items.). It is important to note that plant metabolism studies with little or no identification of residues will not normally be acceptable to support new uses which reflect different kinds of treatments, especially modes of applications that result in higher residues.

One recent technique which, depending on the circumstances, may be appropriate to utilize as an alternate extraction procedure prior to the techniques suggested in the next section is supercritical fluid extraction.

Release of Nonextractable/Bound Residues

The remainder of this discussion will pertain to non-extractable/bound radioactive residues and will provide guidance on what steps need to be taken to provide enough information to allow the Agency to draw conclusions as to the terminal residue of concern in plants/animals.

There are three situations in which radioactive residues are observed to be "non-extractable" in plants/animals.

(1) Incorporation into biomolecules (i.e., amino acids, sugars, etc.) which occurs when the test compound is degraded into small (usually 1 or 2) carbon units which enter the carbon pool, and which the plant uses to build new compounds.

(2) Chemical reaction with appropriate moieties in biomolecules to form bound residues which can be released via other chemical reactions (e.g., enzymatic or acid/base hydrolysis).

(3) Physical encapsulation or integration of radioactive residues into plant/animal matrices (such as cellulose and lignin for plants). Release of residues in this situation may require solubilization of the tissue, usually by drastic treatment with base, although use of surfactants may allow the radioactive residue to be released under less severe conditions.

The following general "road map" for dealing with non-extractable/bound residues is intended to provide clarification of Agency policy as well as more specific guidance regarding characterization/identification of these residues.

The extracted solid plant/animal material from Figure 1 should be assayed and, if radioactivity is present down to the "trigger" values of 0.05 ppm or 10% of the TRR whichever is greater, release of the activity should be attempted (See Figure 2). It is emphasized that, if toxicology expresses concerns over potential residues at lower levels, the "trigger" values will not necessarily apply. Treatments may be performed on either subsamples or sequentially. The types of treatments include dilute acid and base at ambient temperatures (Note that these procedures should be employed initially for both metabolism and method development considerations.), surfactants, enzymes and 6N acid and/or 10N base with reflux. It should be kept in mind that the milder procedures provide more accurate assignments of metabolite structures released, i.e., acid/base reflux would probably release moieties as their final hydrolysis products which could have only a minor relationship to the conjugated form of the radioactivity. An ambient temperature acid treatment followed by ambient temperature base treatment will provide a mild hydrolysis of conjugated moieties, and again possibly release any biomolecules containing incorporated radioactivity. The use of surfactants may release physically encapsulated or membrane bound residues. Because membrane and/or cell wall disruption may improve substrate accessibility to the enzyme, a sonication step should be employed followed by a carefully chosen enzymatic battery (Note: In each case the activity of each enzyme utilized should be confirmed using standard substrates and controls. These experiments should be documented.). These steps could release chemically-bound residues including any biomolecules containing incorporated radioactivity. The final release steps would involve reflux acid and base hydrolysis which will likely solubilize the plant part/ tissue. Radioactivity released at this time would probably reflect amino acids, sugars and encapsulated or conjugated compounds which may or may not have any relationship to the original bound/encapsulated structures. However, this step does provide evidence that residues of the pesticide can be released, and may provide data on incorporated radioactivity and limited information about the nature of the metabolites (See discussion above.). In all cases, samples, homogenates and extracts should be buffered and maintained at low temperatures except during hydrolytic steps in order to reduce degradation/artifact formation (See the discussion below regarding storage stability in metabolism studies.).

Figure 2 provides a visual description of the steps discussed above.

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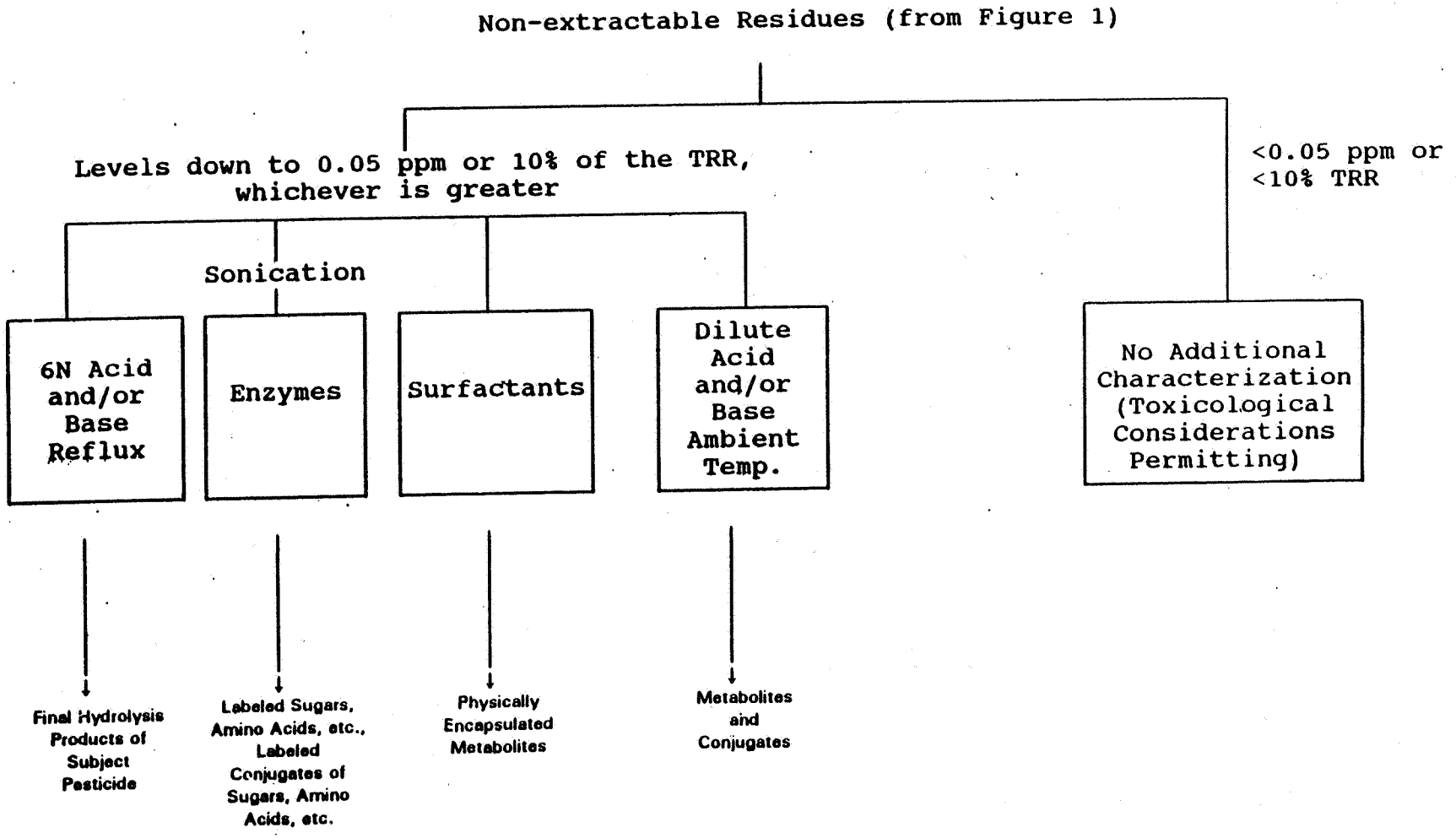
Figure 2: Characterization/Identification of Unextractable/Bound Residues



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Comments on Figures 1 and 2

1) At each step in Figure 2, the radioactivity of the released residues should be quantitated; and if the "trigger" values shown in Figure 1 for extractable residues are met, the activity should again be partitioned against various solvents/solvent systems and characterized and/or identified as required. With respect to characterization, it should be emphasized that the chromatographic behavior of the released activity (including water solubles) should be compared to that of the parent and likely metabolites which are close in structure to the parent. This will indicate whether the released activity is chemically different from the parent molecule. If the remaining unextracted activity after a given procedure is <0.05 ppm or <10% of the TRR further attempted release of activity is not necessary.

2) The trigger values shown in Figure 1 are meant to negate the need for characterization/identification of metabolites present at very low and insignificant levels. However, in many cases, a potentially important metabolite may partition into multiple fractions because of solubility characteristics, and/or because it is present in both free and conjugated forms. In order for the trigger values to apply, particularly in cases where the TRR is distributed among numerous fractions, it must be demonstrated (e.g. by HPLC analysis of each fraction) that no single metabolite is distributed among the various fractions in such amounts so that the combined level (sum) of this component significantly exceeds the trigger value.

3) Identification of specific radiolabeled amino acids, sugars, phenolic compounds, nucleotides, etc. may alleviate the need for further characterization of **bound** residues in many instances, since this usually means that the pesticide has been degraded into small carbon units which have entered the carbon pool. This conclusion does not, however, apply to tritium labeled compounds, or to pesticides in which the ^{14}C label is incorporated at a labile site in the pesticide molecule. This conclusion would also not apply in cases where a single released metabolite, which comprises a significant portion of the total radioactive residue (>10% of the TRR or >0.05 ppm), has not been identified.

4) When a fraction such as lignin, cellulose, or protein contains radioactivity, the radioactivity does not necessarily consist of radioactive amino acids or sugars. The radioactivity may consist of biological macromolecules having radioactive portions of the pesticide either chemically conjugated onto them, or physically encapsulated within them. This is an important distinction from having the macromolecules **constructed** from low molecular weight radiol-

abeled building blocks. The Registrant is responsible for providing such determinations in a scientifically supportable manner. The Agency will make an evaluation of the data and, if not already provided, require definitive information regarding which of the three conditions exist (i.e. incorporation, conjugation, or encapsulation).

Additional General Comments

The pathway described above should be viewed as a broad outline of the type of information needed to determine that a plant/animal metabolism study is acceptable. Different procedures and methodologies may be appropriate in a given circumstance. The basic concepts regarding "trigger" values for identification of radioactivity, methodologies required for characterization/identification of radioactivity, and steps which should be taken to assure adequate release of "non-extractable/bound" residues **must be** observed to assure that the submitted study is adequate.

The following additional comments should be considered in carrying out a plant/animal metabolism study.

(1) For a case where bound residues are present at levels down to 0.05 ppm or more than 10% of the TRR whichever is greater, the Agency will require workup and attempted identification.

(2) All unsuccessful attempts at releasing unextracted activity and characterization and/or identification of the TRR should be documented and submitted.

(3) The Agency will not accept situations where the exaggeration rate is used to calculate "trigger values". For example, if a crop is treated with radiolabeled material at an exaggerated rate (e.g., 5X), the resulting radioactivity levels should not be divided by the degree of exaggeration (e.g., 5) to arrive at "trigger values".

However, the following example should be considered. Assume the plant is treated at a 5X application rate resulting in 0.1 ppm radioactivity in an edible plant part. If the registrant identifies one component as 0.05 ppm of the TRR, and only characterizes 2 other components at 0.02 and 0.03 ppm, then consideration of the terminal residue to be regulated would take into account the 5X treatment with respect to the 0.02 ppm and 0.03 ppm materials.

(4) Consultation with the Agency prior to initiation and during the metabolism study is appropriate and encouraged.

(5) The discussion above is intended to provide guidance on how a plant/animal metabolism study is to be conducted. However, plant/animal metabolism studies are complex and defy a review which follows strict adherence to established criteria. The scientific techniques used to study xenobiotic metabolism and conjugate formation, isolation of plant/animal macromolecules and procedures for generating monomers/oligomers are constantly advancing. It is, therefore, the responsibility of the Registrant to utilize state-of-the-art techniques and provide citations of such techniques when they are used. Flexibility in review is necessary in determining whether a study is adequate for the intended purpose of identifying the nature of the terminal residue to be regulated. Plant/animal metabolism studies will always be examined on a case-by-case basis, and will frequently require scientific judgement to make sound conclusions and recommendations.

(6) The ideal result of a metabolism study is <u>identification</u> of 90% of the total radioactive residue in each raw agricultural commodity. However, the Agency recognizes in many cases this is not possible, especially when low total levels of residue are present and/or when the pesticide is extensively metabolized to numerous low level components. In the latter case it is important for the registrant to demonstrate clearly that numerous components are present and, as discussed above, attempt to characterize these residues by conversion to a common moiety where feasible.

<u>Storage Stability</u>

The issue of storage stability in metabolism studies has been discussed in earlier documents. For example, the Standard Evaluation Procedure (SEP) on "Metabolism in Food Animals: Qualitative Nature of the Residue" notes that "storage at freezer temperatures for a month or less is acceptable". The SEP on plant metabolism does not specify an acceptable storage period, but reminds reviewers to make a determination as to whether sample integrity was maintained during collection, preparation, and storage.

In light of the difficulty of spiking samples before the identity of the residue is known and the length of time needed for metabolism studies, the present Agency position is that storage stability data should not normally be required for samples analyzed within 4-6 months of collection, provided evidence is given that attempts were made to limit degradation of residues by appropriate storage of matrices and extracts during the analytical portion of the study. In other words, as stated in the SEP on animal metabolism, "The reviewer should be convinced that storage conditions have not invalidated the Registrant's results..."

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In those cases where a metabolism study can not be completed within 4-6 months of sample collection, evidence should be provided that the identity of residues did not change during the period between collection and final analysis. This can be done by analyses of representative substrates early in the study and at its completion. Such analyses should show that the basic profile of radiolabeled residues has not changed during that time. If changes are observed (e.g., disappearance of a particular HPLC peak or TLC spot), additional analyses or another metabolism study with a shorter collection to analysis interval may be required.

Further clarification of storage stability requirements in general will be provided in the near future in another paper.

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SODIUM ACIFLUORFEN (CASE 2605/CODE 114402)
UNOFFICIAL RESIDUE CHEMISTRY DATA SUMMARY THROUGH 12/9/92 [1]

REASSESSMENT OF U.S. TOLERANCES AND POTENTIAL FOR HARMONIZATION WITH CODEX[2]

Guideline Number and Topic[3]	Phase 5 data requirements satisfied?[4]	MRID(s)[5]
171-3 Directions for use		
171-4(a) Plant Metabolism	N[6]	42368301,42368302
171-4(b) Animal Metabolism	N	
171-4(c) Residue Analytical Methods - Plants	Reserved	
171-4(d) Residue Analytical Methods - Animals	Reserved	
171-4(e) Storage Stability	N	
171-4(k) Crop Field Trials		
171-4(k) Legume Vegetables (succulent/dried)		
Soybeans [see 171-4(l)]	N	
171-4(k) Foliage of Legume Vegetables		
Soybean forage and hay	Y[7]	
171-4(k) Cereal Grains Group		
Rice [see 171-4(l)]	N[8]	42330604
171-4(k) Forage, Fodder, and Straw of Cereal Grains		
Rice straw	N[8]	42330604
171-4(k) Miscellaneous Commodities		
Peanuts [see 171-4(l)]	N	
171-4(l) Processed Food/Feed		
Peanuts	N	
Rice	N[9]	42330605
Soybeans	N	
171-4(j) Meat/Milk/Poultry/Eggs	N	
171-4(f) Potable Water	N/A	
171-4(g) Fish	N/A	
171-4(h) Irrigated Crops	N/A	
171-4(i) Food Handling Establishments	N/A	
171-5 Reduction of Residues		

[1]Phase 4 Review issued 2/14/91 (S.R. Funk). This summary is unofficial and subject to correction.

[2]No Codex MRLs are established or proposed for sodium acifluorfen.

[3]N/A = Guideline requirement not applicable.

[4]Applies to List B only; List A chemicals were not subject to Phase IV of FIFRA '88.

[5]MRIDs that were reviewed in the current submission are designated in shaded type.

[6]CBRS 10199, 12/9/92, J. Abbotts: Further work is necessary before metabolism studies in peanuts and rice can be considered acceptable.

[7]Phase 4 Review: No data are required because of label restrictions on grazing/feeding.

[8]CBRS 9996, 12/4/92, S. Knizner: Magnitude of the residue data are acceptable, pending receipt of storage stability study results. Combined residues of acifluorfen and metabolites (acid, methyl ester, and amino analogues) did not exceed 0.1 ppm tolerance in or on rice grain and straw after plants were treated (mid tiller and early boot stage of growth) with either 0.125 lb ai/A per application for a total of 0.25 lb ai/A (1X) or 0.25 lb ai/A per application for a total of 0.5 lb ai/A (2X). Field trials took place in AR (6), LA (6), MS (4), and TX (6). Samples from 20 of the 22 sites were harvested with 50 day PHI, in other 2 sites PHI was 53 days. Samples were stored up to 268 days at <-5°C.
[Note: Metabolism in rice is not yet adequately understood.]

[9]CBRS 9996, 12/4/92, S. Knizner: Rice grain processing study is adequate, pending receipt of storage stability study results for rice grain (see footnote 7). Combined residues of acifluorfen and metabolites (acid, methyl ester, and amino analogues) were not detected (<0.01 ppm) in or on rice grain and all processed fractions (hull, brown rice, bran, and polished rice) after plants were treated (at both mid tiller and early boot stage of growth) with 0.5 lb ai/A per application for a total of 2.0 lb ai/A (4X). Field trials took place in AR (1), and LA (1). Samples were harvested with 48 or 50 day PHI. At 4X rate, plants sustained 30 to 40% phytotoxicity. Whole grain samples were stored for 216-232 days at <-5°C. Samples for processing were stored for 30-55 days at <-5°C; after processing, processed samples were stored for 177-186 days until extraction for analysis at <-5°C. No storage stability for rice grain processed fractions is needed because these are obtained by simple mechanical means.
[Note: Metabolism in rice is not yet adequately understood.]

cc: Abbotts; List B File for Sodium Acifluorfen; J. Ellenberger, SRRD.
2605.3

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