Agriculture Canada

July 8, 1987 T-1-249

FOOD PRODUCTION AND INSPECTION BRANCH	DIRECTION GÉNÉRALE, PRODUCTION ET INSPECTION DES ALIMENTS	SECTION PESTICIDES

TRADE MEMORANDUM

RE: PRODUCT-SPECIFIC REGISTRATION AND PROPRIETARY RIGHTS TO DATA

TABLE OF CONTENTS

A. INTRODUCTION

1. The purpose of this Memorandum is to outline new directions in Product-Specific Registration (PSR) and the related topic of proprietary rights to the data supporting registration of products under the Pest Control Products Act. In view of the concern that has been expressed regarding this subject, these amendments to PSR are presented as an interim measure. They will be implemented effective June 1, 1981 for all registered and unregistered pesticide products and active ingredients. Currently a study is proceeding within the Department to examine possible alternatives to PSR. The interim and alternative policies will be presented for consultation with industry, growers and their organizations and public interest groups, after which a final policy will be developed and implemented.

2. Under Section 9 of the Pest Control Products Regulations data are required to support the registration of control products. There are three options for companies to supply data. These are outlined below:

   2.1 Data sharing by business agreement. Where there is already one or more sources of an active ingredient registered, companies can come to agreements regarding the sharing of supporting data. The government would then be officially informed which companies can legitimately refer to existing data on file to support their products.

   2.2 Independent development of data required for registration. This applies to new active ingredients and is an option for a new source of an already registered active ingredient.

   2.3 Where there is already one (or more) source of active ingredient registered, and while companies cannot come to agreement amongst themselves on terms for data sharing, the terms of the interim policy will be used to set data requirements. (See Section I, Registration Procedures.)

3. Throughout this Memorandum, PSR will be referred to as follows:

   3.1 PSR Product-Specific Registration in the general sense;

   3.2 PSR80 The system as introduced on September 8, 1980, and observed up until June 1, 1987;

   3.3 PSR II The system that will be observed beginning June 1, 1987. It incorporates changes under discussion in 1985 (PSR 85) and results of consultations on PSR 80.

4. The objectives of PSR II are:

   4.1 To ensure that the safety, merit and value of products registered under the Pest Control Products (PCP) Act are supported to the maximum extent possible by modern data bases;

   4.2 To promote a climate favourable to the introduction of new products in Canada;

   4.3 To facilitate the registration of active ingredients from new sources and therefore assure competing products are available for use.

5. The first two objectives require a system which recognizes proprietary rights to data. The third objective requires that time limits be established on the protection of proprietary rights to data and that ways be found for companies to share both existing data bases and in the development of new data.

6. PSR II incorporates the following principles in an effort to achieve the objectives outlined in paragraph 4:

6.1 New data should add to total knowledge of the chemical, rather than duplicate studies in areas that are already documented. As a result of the "data call-in" program in the United States, many companies have produced substantial amounts of new toxicological data. Rather than encourage new applicants to duplicate these studies, Agriculture Canada would like to see new data in other categories, particularly environmental studies. With the increasing awareness of problems caused by pesticides in the environment, particularly in groundwater, more research in this area is clearly needed;

6.2 Repeats of studies involving the use of animals should be avoided if no new or useful information will result;

6.3 Industry should negotiate data-sharing agreements without government involvement. Agriculture Canada will not become involved in mandatory arbitration between companies over the use of data, but will instead require submission of new data from new sources if companies cannot reach an agreement.

B. BACKGROUND

7. PSR80 was introduced September 8, 1980 in relation to two issues:

7.1 Pressure from industry to recognize data ownership;

7.2 Concern about microcontaminants (e.g., dioxins, nitrosamines) in active ingredients.

8. PSR80 was based on two principles:

8.1 The source of the active ingredient in each formulation must be known;

8.2 Each source of active ingredient must have its own supporting data base to provide assurances of safety to human health and the environment.

9. PSR80 has netted some real and significant benefits. After September 8, 1980, applications for registration of new products were processed only on the basis of an updated chemistry package with specifications to a level of 0.1%

and an index to all data. This information has proven valuable in evaluating purity and acceptability of sources, establishing review priorities, explaining regulatory positions and in responding to enquiries.

10. In 1982 a proposal was put forward for registration of active ingredients to strengthen the regulatory process and streamline PSR operations. Industry was consulted by means of a memorandum and a consultation and responded favourably. This is described in Memorandum T-1-241, dated October 1, 1983.

11. In Memorandum R-1-219, dated February 1, 1984, the strengths and weaknesses of PSR80 were discussed and revisions to PSR were proposed. These proposals were discussed in a meeting with industry on May 1, 1984. Since then, written comments have been received from the Crop Protection Institute of Canada (CPIC, previously CACA), individual formulations and manufacturers.

12. Many comments have been received from growers' organizations, expressing concern about the effects of PSR80 on the availability of active ingredients from new sources and about the effect on the costs of pesticides.

13. Growers' organizations have stressed that any future directions should take into consideration their needs and comments.

C. PSR 80

14. The problems with PSR80 were described in detail in Memorandum R-1-219. They are summarized briefly below.

14.1 DIFFERENCES BETWEEN ACTIVE INGREDIENTS FROM DIFFERENT SOURCES: Differences between active ingredients from different sources are not always significant, either chemically or in terms of biological activity. Minor variations should not be a barrier to the development of data bases to be used in common by different manufacturers, either by industry task forces or by agreement to compensate.

14.2 NEW SOURCES: PSR80 has prevented or delayed registration in Canada of certain new sources of active ingredients.

14.3 DATA BASES: PSR80 has provided unlimited protection of data. This has provided little incentive to manufacturers to keep data current and in some cases, has even discouraged submission of new data. Data bases for older compounds are often inadequate, and even partial additions would be an improvement.

D. POINT VALUE SYSTEM

15. In describing PSR II, the term "point-value system" will be used frequently. This system (Appendix I) was developed by the Crop Protection Institute of Canada (CPIC), with input from the Canadian Manufacturers of Chemical Specialties (CMCS), to assign relative values to data bases. The points have been validated against a survey of contract laboratories conducted independently by the Pesticides Directorate.

E. PSR II

16. Agriculture Canada originally proposed a period of full data protection for 15 years from the date of first registration, after which all data would become generic. The inherent weakness in this proposal was a lack of incentive for either original owners or new applicants to maintain an up-to-date data package.

17. CPIC countered with a proposal that each individual study be protected for 15 years. This approach would encourage owners to maintain a current data package, but new applicants would always be obliged to produce full new data bases. Furthermore, it would favour unnecessary repetition of studies.

18. GIFAP has proposed that 15 years of protection be accorded from the date of first registration, after which compensation between companies for data less than 10 years old would become mandatory. This proposal does not provide incentives to keep data current.

19. The U.S.A. provides a 10 year period of exclusive use of data from the time of first registration followed by a 5 year period of mandatory arbitration on the same data. Each piece of data, therefore, has 15 years total of protection.

20. Table 1 describes the categories of active ingredients and the requirements for registration of new sources of active ingredients under PSR II. <u>All discussions assume that chemical equivalence among sources has been demonstrated</u>. If chemical equivalence cannot be demonstrated, these new sources of active ingredients will be treated as new active ingredients and will require a full data package.

21. PSR II grants the original owner of data a period of 10 years exclusive use of data required for registration, beginning at the time of first registration. After 10 years, the data are no longer protected. To encourage continued submission of data, each study submitted after registration will be given 15 years of data protection starting from the completion date of the study. This period may overlap the 10 year exclusive use period. (See Figure I).

Figure 1

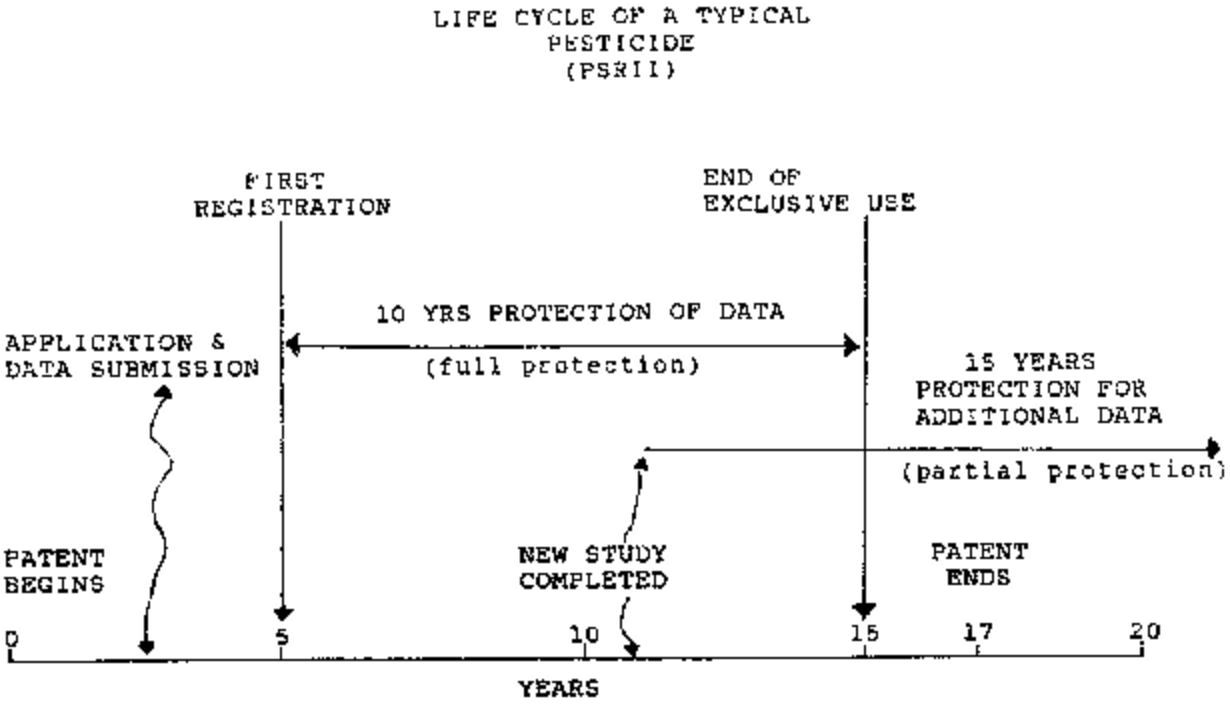

LIFE CYCLE OF A TYPICAL
PESTICIDE
(PSRII)
FIRST
REGISTRATION
END OF
EXCLUSIVE USE
10 YRS PROTECTION OF DATA
(full protection)
APPLICATION &
DATA SUBMISSION
15 YEARS
PROTECTION FOR
ADDITIONAL DATA
(partial protection)
PATENT
BEGINS
NEW STUDY
COMPLETED
PATENT
ENDS
0
5
10
15
17
20
YEARS

Table 1. Categories of Active Ingredients and Requirements for Data to Support Registration of Active Ingredients from New Sources

CATEGORY	CRITERIA FOR CATEGORY	REQUIREMENTS FOR REGISTRATION OF NEW SOURCE
NEW ACTIVE (Period of Full Data Protection)	- First Active ingredient end-use product(s) registered within the last 10 years	- Proof of authorization to use the existing data base OR - Full new data package
INTERME-DIATE* (Period of Partial Data Protection)	- First Active ingredient and end-use product(s) registered more than 10 years ago AND - Owner has kept the data base least partially up-to-date (some data <15 years old)**	- Proof of authorization to access existing data which is <15 years old OR - New data equivalent In at points to the new studies <15 years old in the existing data base (up to 75% of the total protected data package)
GENERIC (Period of No Data Protection)	- Active ingredient and end-use product(s) first registered more than 10 years ago AND - Owner has not kept the data base up-to-date All supporting studies > 15 years old or virtually no data.	- Minimal other data where necessary, i.e., acute studies.

* Where a company has committed to produce data, e.g., to support a new use, new sources of that active requesting similar uses will also be required to commit to providing an equivalent value (in points) of data.

** The 15 years is from the date of completion of the study.

F. NEW-ACTIVE-INGREDIENT CATEGORY

22. PSR II provides protection of the original data package required for registration for 10 years from the date of first registration. New sources applying for registration during the first 10 years are required to provide a complete, new data package, or proof of access to an existing data package on file with Agriculture Canada.

G. INTERMEDIATE CATEGORY

23. In the intermediate category, data submitted for first registration will no longer be protected. However, this category provides opportunities for registration of new sources of active ingredients as well as incentive to manufacturers to update data packages. New studies submitted after the date of registration will be protected for 15 years. Protection begins the date of completion of the study. The value of each study will be determined using the point-value system. Applicants of new sources of registered actives in this category will be required to submit new studies equivalent in points to the value of the protected studies. Agriculture Canada will determine which studies are required.

24. For registered products in the Intermediate Category with virtually complete data bases, companies applying to register new sources will be required to supply data to a maximum of 75% of the total protected data base for that active. This category therefore allows <u>partial protection</u> (for the modern studies) of a supporting data base.

H. GENERIC CATEGORY

25. In the generic category, data will no longer be protected. New sources will provide only minimal data related to product safety, e.g., acute studies. No significant comments were received on this category. It was agreed that products with seriously deficient or very old data bases should not be protected.

I. DATA DEVELOPMENT FOR REGISTRATION

26. <u>New Actives</u>
Applicants must provide a full data package.

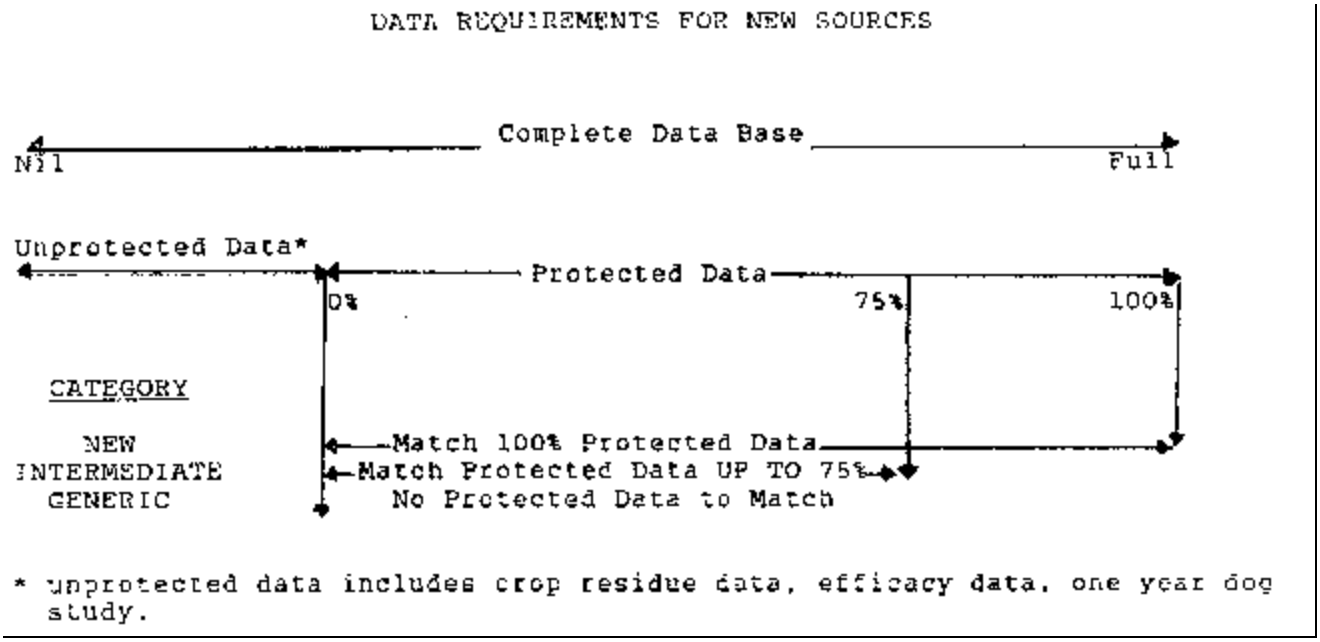
27. <u>New Sources of Registered Actives</u>

27.1 Applicants nay come to a business agreement to share existing data with the owner(s). In this case, written authorization to access the existing data package must be provided. Alternately, applicants may also develop an independent data package.

27.2 All new sources of active ingredient will be required to submit proof of chemical equivalency (T-l-23e) to the registered source(s) before registration (generics) is granted or point assessment (intermediates) is undertaken. This requires submission of label index or data and detailed chemistry specifications, as outlined in T-1-237 and T-1-238.

27.3 Where the applicant falls into the Intermediate Category, the Pesticide Directorate will request the registered data owner(s) to submit a point assessment of their protected data. The point value assessment must be provided within 60 days, otherwise Pesticides Directorate will assume there are no new data to be protected, and the active ingredient will be considered to be generic. The Directorate will confirm the point assessment and inform the new applicant of the assessment. 30 days will be allowed for existing data owners to challenge the assessment established. The new applicant will be required to provide new data equivalent to the final, combined point total to a maximum of75% of the full, protected data package, whichever is less. See figure 2.

FIGURE 2



* unprotected data includes crop residue data, efficacy data, one year dog study.

27.4 Multiple Sources. If the data base is shared equally by two or more companies, a new source will be required to provide data equivalent in point value to the total number of points carried by the registered data base divided by the number of registrants.

If the points are not shared equally by established sources, the new applicant will be required to provide data equivalent to the points held by the company with the highest point value (up to 75% of the protected data base).

28. REGISTRATION WILL BE CONSIDERED WHEN:

28.1 New Category
1) proof of chemical equivalency AND of access to an acceptable data base is confirmed.

OR 2) the independent data base meets registration requirements

28.2 Intermediate Category

proof of chemical equivalency is confirmed, AND
EITHER 1) authorization of access to an acceptable data base is confirmed.
OR 2) acute toxicology on technical material is complete, and registration will be negotiated with the registrant, based on, the type of studies to be undertaken.

28.3 Generic Category

proof of chemical equivalency is confirmed, AND acute toxicology on technical material is provided.

J. UPDATE OF INDEXES FOR REGISTERED PRODUCTS

29. In cases where only indexes were previously required, data originators may now be asked to submit data which are not in current PSR files within the Pesticides Directorate. Registrants should review their data indexes and ensure that an up-to-date version is filed with Agriculture Canada. A six month period after the date of issue of this memorandum will be allowed for companies to ensure their indexes are up to date. After January 15, 1988, the index on file with Agriculture Canada will be used, regardless of whether it is current.

K. VOLUNTARY SUBMISSION OF DATA

30. Voluntary submission.s of data should be made in the format specific in Memoranda T-1-237 and T-1-239. These Memoranda specify the number of copies needed.

31. If two or more registrations exist for an active ingredient from different sources, and only one registrant has data and wishes to submit it, Agriculture Canada will not require data from other sources. Voluntary submission of data will improve the registrant's position only in relation to other potential registrants who have not yet registered their actives.

32. If basic toxicological or environmental data have been submitted to support a new use on the label, other registrants of the active ingredient from other sources will be required to submit equivalent. data to register a product for the same use.

33. Voluntarily submitted data will not necessarily be reviewed immediately upon receipt. It will be reviewed at re-evaluation , or if a special need is identified.

L. EVALUATION

34. PSRII applies to data submitted in response to a formal re-evaluation in the following way:

35. If a <u>full</u> data package is generated for re-evaluation, either by a single or multiple sources, these data will be protected for 10 years. During the initial ten years following re-evaluation, a new applicant will be required to provide:

- proof of access to the existing data base as a result of successful negotiations with the owner(s); or

- data equivalent to that supplied by the established registrant(s).

36. If <u>any</u> gaps remain after re-evaluation, a 10 year exclusive use period will NOT be observed.

37. Start of 10 years: The beginning date of the 10 year period will be negotiable for each re-evaluation.

38. MULTIPLE SOURCES: If a group has collaborated to produce the data required for re-evaluation, new applicants will be required to produce data equivalent in point value to the total point value of the data base divided by the number of registrants who participated in data development.

39. If on review of a data base where there are multiple sources registered, it appears that one source has supplied the bulk of the data that is available and is useful, more onus will be placed on the other sources to supply data for re-evaluation.

M. DATA SUBMITTED FOR PURPOSES OF THE FOOD AND DRUGS ACT

40. Data developed and submitted to meet requirements of the Food and Drugs Act are not covered by the proposals in this Memorandum. This includes one-year feeding studies in the dog, and crop residue data, which are used exclusively by the Foods Directorate to establish Maximum Residue Limits (MRLs).

N. EFFICACY DATA

41. Efficacy data will not be protected under the interim policy.

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APPENDIX I

POINT VALUE SYSTEM
Crop Protection Institute of Canada

GUIDE LINE	STUDY	SPECIES	POINTS
	TOXICOLOGY		
	Acute Studies		
312	Acute oral (technical)	rat	3
		dog	3
313	Acute dermal (tech)	rabbit	5
314	Acute inhalation (tech)	rat	9
315	Eye irritation (tech)	rabbit	1
316	Dermal irritation (tech)	rabbit	1
317	Dermal sensitization (tech)	guinea pig	2
322	Acute oral (formulated)	rat	3
323	Acute dermal (form)	rabbit	5
324	Acute inhalation (form)	rat	9
325	Eye irritation (form)	rabbit	1
326	Dermal irritation (form)	rabbit	1
327	Dermal sensitization (form)	guinea pig	2
	Short Term		
332	Oral 90-day	rodent	50
	90-day	dog	50
333	Dermal 90-day	rat/rabbit	50
334	Inhalation 90-day	rat	200
343	Dermal 21-day	rat/rabbit	25
344	Inhalation 21-day	rat	50
	Long Term		
352R	1 year chronic feeding	rat	425
365	Lifetime oncogenicity	rat	600
		mouse	600
352R/ 365	Combined chronic and oncogenicity	rat/mouse	825

	Special Studies		
362R/R	Multi-generation repro	rat/rabbit	270
363	Teratogenicity	rabbit	140
		rat	140
364	In Vitro Mutagenicity:		
364	Point Mutation	microbial	15
		mammalian	15
364	Chromosome Abberation	--	15
364	DNA Repair	--	15
366	Delayed Neurotoxicity	chicken	45
368	Exposure Studies	---	150 (each study)

APPENDIX II

GUIDELINES TO DETERMINE POINT VALUE-ASSESSMENTS

1. Voluntarily submitted studies are eligible for points for 15 years from the date of completion of the study.

2. All studies older than 15 years on the date of point value assessment are no longer eligible for points.

3. Summaries, addendum and supplemental reports are not eligible for additional points. Points will be assigned once to each study.

4. All interim reports are eligible for points, but only until such time as the final report is listed in the index. The final report only will then be credited points.

5. Studies using metabolites or specific microcontaminants as a result of a regulatory requirement are eligible for points.

6. If there are two or more studies that satisfy the same category, only the most recent valid study will be given points. Points are not additive within a single category.

7. Invalid and published studies will not be assigned points (i.e., IBT).

8. In case of dispute, studies not on file with the Pesticides Directorate will be required before points are assigned.

9. Ensure all criteria indicated for the category are met before awarding points, e.g., species, tire frame, technical or formulated.

GUIDE LINE	STUDY	SPECIES	POINTS
	METABOL1SM		
420	Metabolism (labelled)	rat	225
		goat	270
		chicken	240
		cow	275
430	Metabolism (labelled)	plants	150
	Pharmacokinetic (unlabelled)	--	80
	ENVIRONMENTAL CHEMISTRY		
621	Hydrolysis		15
621	Vapour pressure		15
621	Photodegradation	soil	80
		aqueous	25
		air	15
621	Solubility in water		25
621	Octanol/water partition coefficient		5
622	Mobility: absorption/desorption		35
622	Leaching - lab study (cold)		42
	- field (labelled)		150
623	Soil metabolism	aerobic	42
		anaerobic	46
631	Soil dissipation study or crop rotation study		62
631	Soil accumulation		60
632	Pond study (run-off)		75
693/632	Aquatic degradation and persistence	aerobic	32
	ENVIRONMENTAL TOXICOLOGY		
712W	Acute oral	mallard	5
		bobwhite	5
713	Sub-acute oral	mallard	5
		bobwhite	5
714W	Avian reproduction study		15
722	Acute toxicity	rainbow trout	5
		bluegill	5
722/737	Acute toxicity	Daphnia	10
734	Toxicity	bee	5
737	Toxicity: non-target terrestrial invertebrate		20
742/743	Toxicity: non-target inhibition test	plant/algal	28

APPENDIX III

FORMAT FOR SUBMISSION OF INDEXES AND POINT ASSESSMENTS

INDEXES

Please include the following information for each study, where applicable.

1) corresponding guideline number, e.g., 312, 313
2) date of completion of study
3) type of test, e.s., acute, anaerobic, etc.
4) name of material tested, e.g., technical, metabolite, microcontaminant 5) duration of test, e.g., 14 day dermal, 90 day dermal
6) species tested, e.g., rat, dog
7) testing laboratory
8) type of report, e.g., preliminary, final, etc. - where commitment has been given but study is not complete, indicate target date for completion
9) number of pages in report
10) indicate, where appropriate, if study was submitted voluntarily, or as a result of a data call-in, (e.g., re-evaluation)

POINT ASSESSMENTS

The Pesticides Directorate will inform companies when an assessment is required. Please indicate the following information where relevant, when submitting point value assessments.

1) the active name, metabolite and microcontaminant names if tested (decode numbers for technical, etc.)
2) date of the index used
3) list studies in order of guideline numbers
4) list applicable index excerpt (see above) for each.study assigned points
5) indicate the number of points assigned to each study
6) total points