Random Sampling of HOCNFs and Underlying Test Reports

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Report number~C082/07

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Publication Date: August 31, 2007

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Summary

The random sampling of HOCNF registered chemicals, used in connection with offshore exploration & production, was performed by TNO IMARES. The underpinning test reports of the selected products were evaluated for their correctness and it was checked whether reported details were transferred correctly to the HOCNF.

For the random sampling, in total 12 products and 108 test reports were evaluated. The detailed results have been reported to SodM in separate confidential reports, while this report presents a general overview of the results of the random sampling.

In addition, a case study of interlaboratory differences was performed on a similar component that was used in two different products. This case study indicated both minor differences and as well as differences up to a factor 69 between the laboratory's results.

It appeared that all evaluated products contained anomalies in their HOCNF and/or underlying reports, such as test substances that could not be linked unambiguously to the components in the HOCNF, errors in the determination of end-points and GLP statements that are missing.

The observed errors occur both at the side of the laboratories and the side of suppliers. The anomalies occurring at the supplier's side can be reduced by minimising their role in providing or interpreting the ecotoxicological data (part 2 of the HOCNF). This can be achieved by, for example, constructing a standard form (with the details that are required in part 2 of the HOCNF) to be filled out and signed by the test laboratory. This document could replace part 2 of the HOCNF in order to minimise errors and omissions.

Contents

1 Method of Analysis

1.1 Approach

From 2003 up to 2006 TNO-Imares performed an advisory role in the registration of chemicals used in connection with offshore exploration & production in the Netherlands. This task was assigned to TNO-Imares by Staatstoezicht op de Mijnen (State Supervision of Mines or SodM). Part of the task is the random sampling, which means that a subset of the registered products is selected for the evaluation of the original test reports on which the Harmonised Offshore Chemical Notification Format (HOCNF) is based.
The selection of the products is arbitrary in basis, but remarks in the HOCNF can lead to a specific selection. An overview of the selected products is presented in paragraph 1.2 (product names are encoded). The suppliers of the selected products were asked to provide the original test reports, used in the HOCNFs of these products, to the registration desk. The reports that deal with bioaccumulation potential, biodegradation potential and/or toxicity of the components of the product, are evaluated to:

- check if the received test report and the test laboratory match with the information in the HOCNF (are all reports on which the HOCNF is based received?);
- check if the tests that are described in the reports are carried out according to Good Laboratory Practice (GLP);
- check if the identity of the substance, tested by the laboratory, demonstrably matches the product / component described in the HOCNF;
- check whether the tests are actually performed according to the accepted test protocols (e.g. right selection of test concentrations, right test conditions, etc);
- check if there are errors in the determination of end-points (e.g. Log POW, 28d degradation, NOEC, EC50, etc.), that are listed in the HOCNF;
- check whether all available data in the test report are transferred to the right location in the HOCNF;
- check whether the data are transferred correctly to the HOCNF.

The findings have been reported to SodM in detail per product in separate confidential reports. This report will only focus on general findings using codenames for the selected products. Chapter 2 describes the overall findings of the evaluation of the test reports by presenting them itemised by criterium in a paragraph each.
Since two products, contained the same component, a case study of the interlaboratory differences could be performed. This study has been executed and the results are presented in paragraph 2.6.

1.2 Selected Products

In total 22 products were selected for evaluation. The reports of 3 of these 22 products were not received from their supplier. The reports for one of these 3 products were not received because the firm no longer supplied it. For pragmatic reasons, only 12 of the 22 products were actually evaluated.
Table 1 provides an overview of the evaluated products. For these products, 109 test reports were received. One of the reports was not listed in the HOCNF (see product D) and is therefore excluded from evaluation. Hence, in total 108 reports were reviewed for the random sampling, the results of which are presented in chapter 2.

Table 1 Summary of evaluated products. As for the overview of results, the product names are not relevant, we have assigned codes to the products.

Product	Total number of components	Number of PLONOR components	Total number of reports in HOCNF	Total number of reports received
A	1	0	5	5
B	2	0	5	5
C	7	2	23	23
D	3	0	11	12[1]
E	2	0	6	6
F	3	1	5	5
G	7	2	21	21
H	4	1	10	10
I	2	0	5	5
J	1	0	6	6
K	3	2	6	6
L	5	0	22	5
Totals	40	8	125	109

[1] A report that was not listed in the HOCNF was received. This report is not included in the results.

2 Overall Synthesis of Results

2.1 Introduction

The criteria listed in paragraph 1.1 are transformed in such a way that they can be expressed as comparable percentages. These transformed criteria can be found in the first row of Table 2. The determination of end-points has been split into minor and serious anomalies. The splitting has been implemented to provide a better picture of our findings. This will be discussed in more detail in paragraph 2.4. The percentages in the table represent the number of reports in which the criterion is not met, relative to the total number of reports. Since all criteria are now expressed as such a percentage, they can be compared to each other directly.

Table 2 – Overview of anomalies in the HOCNF relative to the amount of reports

Product	Required reports that were not received (%)	Reports that could not unambiguously be linked to the report in the HOCNF (%)	Executing laboratories that do not match the HOCNF (%)	Test compounds that could not unambiguously be linked to the HOCNF (%)	No GLP statement present (%)	Protocols not as required (%)	Serious anomalies in determination of end-points (%)	Minor anomalies in determination of end-points (%)	Cases of data not included (%)	Cases of data transferred incorrectly (%)	Total number of reports
A	0.0	20.0	0.0	100.0	20.0	20.0	20.0	20.0	0.0	60.0	5
B	0.0	0.0	0.0	0.0	0.0	0.0	0.0	40.0	0.0	60.0	5
C	0.0	17.4	0.0	87.0	69.6	34.8	69.6	0.0	47.8	8.7	23
D	0.0	9.1	9.1	63.6	9.1	0.0	18.2	0.0	0.0	27.3	11
E	0.0	16.7	0.0	100.0	16.7	33.3	66.7	16.7	0.0	16.7	6
F	0.0	0.0	0.0	100.0	0.0	0.0	0.0	40.0	40.0	40.0	5
G	0.0	0.0	9.5	71.4	0.0	0.0	28.6	33.3	0.0	23.8	21
H	0.0	70.0	0.0	50.0	0.0	0.0	0.0	10.0	0.0	0.0	10
I	0.0	60.0	0.0	80.0	60.0	0.0	20.0	0.0	0.0	60.0	5
J	0.0	0.0	0.0	0.0	0.0	0.0	16.7	16.7	0.0	0.0	6
K	0.0	0.0	0.0	100.0	16.7	0.0	16.7	0.0	0.0	50.0	6
L	77.3[2]	20.0	0.0	100.0	0.0	20.0	20.0	40.0	20.0	60.0	22
Averages weighted by # of reports	13.1	16.7	2.8	72.2	21.3	11.1	31.5	14.8	14.8	25.0	

At the bottom of Table 2 averages of the results are shown. These averages are weighted to the number of reports. The values are also represented graphically in Figure 1. Figure 2 depicts the same numbers; in this illustration the anomalies are sorted by frequency of occurrence.

[2] Reports that were not received are not counted in the other anomalies.

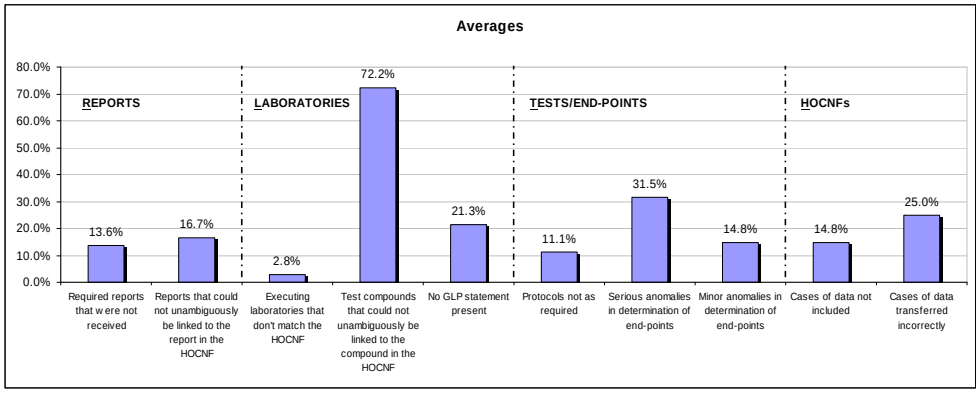

Figure 1 *Average percentage of anomalies in the HOCNF relative to the total amount of reports. The diagram is divided into four sections (Reports, Laboratories, Tests/End-points and HOCNFs) which correspond to the paragraphs 2.2 up to 2.5*

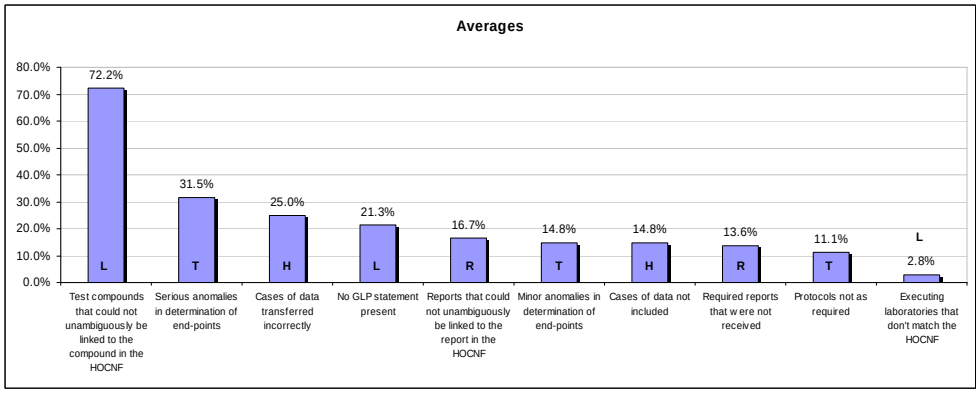

Figure 2 *Average percentage of anomalies in the HOCNF relative to the total amount of reports. The anomalies are sorted by frequency of occurrence. The letters 'R', 'L', 'T' and 'H' correspond to the paragraphs on Reports, Laboratories, Tests/End-points and HOCNFs respectively (paragraphs 2.2 up to 2.5)*

From the values listed in Table 2, it can be concluded that none of the products were free of anomalies in their HOCNF. The variation of anomalies found was great among the products. Some products had few anomalies (e.g. product J) in their HOCNF; others had lots (e.g. product L). Figure 2 shows that the most occurring anomaly is the missing of a proper link of the tested substance to the component in the HOCNF. This is followed by serious anomalies in the determination of end-points and subsequently the incorrect transfer of data. These and the other criteria will be discussed in more details in the following paragraphs.

2.2 Reports

2.2.1 No Unambiguous Link

16.7% of all evaluated reports could not be linked unambiguously to the HOCNF (see Figure 1). That is, the report number does not match the number listed in the HOCNF (e.g. the report number listed in the HOCNF is an internal reference of the supplier and is written by hand on the received report).

2.2.2 Not Received

17 out of the 125 required reports (13.6%) were not received. Although this is relatively much, it was only the case for 1 of the 12 evaluated products. In this case (product L), the supplier stated that it could not provide the reports without the permission of the producers of the components since the information is confidential. The supplier has a letter of access for these components.

2.3 Laboratories

2.3.1 Test Compound

The missing of a proper link of the test substance to the component described in the HOCNF is the most serious problem (see Figure 2). The problem manifests itself in several situations, of which the following are most frequently encountered:

- in many cases only the component's name or CAS number is provided in the test report, while further characterisation of the substance by physical properties was omitted. Mostly, this is because the supplier does not provide the physical properties of the component to the laboratory for comparison;
- a substance name is provided in the test report which does not match the HOCNF;
- the test report refers to a supplier's internal name of the component, while that internal name has changed over time. For instance: product F has provided reports for a single component referring to 4 different internal names.

In our opinion a substance can only be linked to the component described in the HOCNF, if it complies to the both following criteria: firstly, the test substance is characterised by it's physical properties in the test report (a GLP requirement) and matches the properties of the component in the HOCNF; secondly, either name or CAS number is provided in the test report, and matches the name/CAS number in the HOCNF. This was not the case for over 72% of the reports (see Figure 2); only 2 of the 12 products had a good link for all components on the HOCNF with the tested substances included in this report (Table 2).

2.3.2 GLP Statement

Of all evaluated reports, 21.3% had no GLP statement (see Figure 2). However, this does not necessarily mean that these tests were not conducted following GLP procedures. There are several possibilities that were encountered:

- the received report was incomplete, the GLP statement was either missing or was never there in the first place;
- a GLP statement is present, but is not signed;
- the test was not performed following GLP procedures.

If this problem is to be reduced in the future, our advice is to ask the suppliers to provide copies of the GLP statements together with the HOCNF.

2.3.3 Not as in HOCNF

The laboratory stated in the HOCNF did not match the laboratory in the report in only 3 out of 108 reports (2.8%) and 2 out of 12 products (see Figure 2). In one of these three cases, the report number did not

match the number listed in the HOCNF as well. Presumably, in this case, the wrong report was received. In the other 2 cases the report numbers did match with the HOCNF. In some cases the laboratory in the report and the one listed in the HOCNF differed in address. In those cases the P.O. Box was listed in the HOCNF while the street address was given in the report or vice versa. These situations were not counted as a mismatch here.

2.4 Tests/End-Points

2.4.1 Anomalies in End-Points

As indicated earlier the distinction between minor and serious anomalies has been made in Table 1. A serious anomaly is classified case by case as such when the anomaly could have affected the end-points. An anomaly is considered minor if it cannot affect the end-point. This distinction creates a more realistic view of the results. If the total amount of reports containing anomalies in the end-points needs to be known, the minor and serious anomalies can simply be added, because they were not counted doubly. Together they occur in over 46% of the evaluated reports (see Figure 2). All products had test reports that contain minor and/or serious anomalies in the end-points. This makes this anomaly the most serious problem after the missing link between the test compound en the HOCNF (see paragraph 2.3). Some of the anomalies that were encountered were:

- omission of raw data, only the end-points are presented;
- poor fitting of dose response curves to experimental data for EC50 determination;
- exclusion of measurements for end-point determination without (proper) explanation;
- incorrect determination of NOECs;
- simple compounds (that is, compounds that should contain no isomers, no homologues, no contamination) produced more than one peak using the HPLC method for determining the Log P_{OW}.

2.4.2 Wrong Protocols

The protocols were classified 'wrong' in 11.1% of all evaluated reports. For product A, the problem is probably a typo (the HOCNF states the procedure is according to OECD 310D, while the report uses protocol OECD 301D). Product L lists a different protocol in the HOCNF compared to the protocol described in the test report. However both protocols are accepted. In all other cases, the procedure is not (fully) described in the test report.
A point of attention in the toxicity tests is that the test concentration range is often poorly chosen. In most cases no range finding test was performed.

2.5 HOCNFs

2.5.1 Data Transferred Incorrect

Data not being transferred correctly from the test report to the HOCNF was observed for 25.0% of the reports and 10 out of 12 products. The observed mistakes were:

- values in the HOCNF differ from the test report;
- values in HOCNF incorrectly derived from the raw data (e.g. weighted average of Log P_{OW});
- biodegradation values listed at the wrong time indexes;
- errors in rounding the values;

– suggestive interpolation of the biodegradation curve between data points.

2.5.2 Data Not Included

Data that is provided in the test report, but not included in the HOCNF occurred for 14.8% of the evaluated reports (see Figure 2) and 3 of the 12 products. These situations occurred when data was omitted:
– only 1 out of triplicate measurements listed in the HOCNF for a biodegradation test;
– only 1 HPLC peak (in stead of all three observed peaks) listed in the HOCNF;
– toxicity parameters not listed for all exposure times;
– toxicity parameters not listed at all.

2.6 Interlaboratory Differences

When a single compound is tested by different laboratories, the produced results can deviate from each other. The protocols, allowed in the HOCNF, have been structured to minimise such differences. The random check gave the opportunity to investigate interlaboratory differences for a specific component, used in two products selected for the random check.

The two products (D and G) both contain the same component. Both suppliers had the component tested for bioaccumulation potential, biodegradation potential and toxicity. The laboratories that performed the tests, conducted them following GLP. The results of the laboratories were compared in detail in a separate confidential report. Here, general findings will be presented.

All tests (Log P_{OW}, biodegradation, algae, crustacean and fish test) showed different results for the two laboratories. The biodegradation tests were the most comparable. The end-points in the biodegradation tests were close. The toxicity test showed large differences amounting up to a factor of 69.

Considering that al the tests were performed following GLP and the protocols are equal and well established, it is remarkable that such large differences are observed. If the laboratories are assumed to meet the quality that should be expected from a GLP laboratory, then the logical conclusion would be that the test substance provided by the two suppliers are not similar.

For product D, the test substance in one of the reports could not unambiguously be linked to the component in the HOCNF. For product G, none of the reports in question linked the test substance unambiguously to the component in the HOCNF. This supports the conclusion that the substances tested might not be similar. It also emphasises the importance of a reliable link.

3 Recommendations

It is found that errors occur at all four previously described sections: reports, laboratories, tests/end-points and HOCNFs. Considering the high observed error rate (all evaluated products contained anomalies in its HOCNF), it is recommended to change the HOCNF. As most of the problems are related to either procedural errors on the side of the test laboratory or interpretation errors on the side of the supplier, we suggest to replace part 2 of the HOCNF by a series of forms. Each laboratory should in this case provide a 1-page form, together with the report, which will be attached to the HOCNF.

This form should request all information required in part 2 of the HOCNF and could also contain a checklist to make sure that the laboratory complies to all HOCNF requirements. The document should then consist of at least the following items:

- the laboratory's name and address, also the report number of the complete test report and a declaration of GLP-compliance;
- the test substance's (trivial) name and CAS number if available;
- a checkbox where the laboratory indicates that the supplied test substance is characterised (by a defined set of physical properties) and complies with the provided information of the substance;
- the applied test protocol. Here, the laboratory should only be able to select from a list of accepted protocols;
- all required end-points. For toxicity tests, inequalities (e.g. <100 mg/L) should not be allowed without comment, since this is usually a result of poor concentration range finding.
- the date and signature of an authorised laboratory employee.

If these forms become an integral part of the HOCNF, most flaws observed in this random sampling are minimised. Furthermore, the laboratories will have a clear guidance to produce the results that are expected and the supplier cannot make errors in transferring or interpreting the results.

4 Authentication

Rapport C082/07
Project Number: 199.75001.01

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This report has been professionally prepared by Wageningen IMARES. The scientific validity of this report has been internally tested and verified by another researcher and evaluated by the Scientific Team at Wageningen IMARES.

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Number of copies: 3
Number of pages 13
Number of tables: 2
Number of graphs: 2
Number of appendix attachments: -