FIFTH JOINT CIPAC/FAO/WHO OPEN MEETING
(52nd CIPAC Meeting and 7th JMPS Meeting)

FEDERAL OFFICE OF CONSUMER PROTECTION AND FOOD SAFETY (BVL) BRAUNSCHWEIG, GERMANY

9 June 2008

Summary record of the meeting

Agenda

1. Opening and welcome

Dr Ralf Hänel, Chairman of the Collaborative International Pesticides Analytical Council (CIPAC) and organizer of the meeting, welcomed participants, in particular Mr Dr Helmut Tschiersky-Schöneburg, Head of the Federal Office of Consumer Protection and Food Safety (BVL), Mrs Dr Karola Schorn, Head of Unit 517 Plant Protection at the Federal Ministry of Food, Agriculture and Consumer Protection, and Mr Dr Hans-Gerd Nolting, Head of the Department of Plant Protection Products at BVL, for their support of CIPAC and the meeting and their attendance at the Open Meeting. He outlined some administrative matters related to the operation of the meeting.

Madam Yong Zhen Yang, FAO Joint Secretary of the Joint Meeting on Pesticide Specifications (JMPS), welcomed all participants to the 5th Joint CIPAC/FAO/WHO Open Meeting, notably Dr Helmut Tschiersky-Schöneburg (Head of BVL), Dr Hans-Gerd Nolting (Head of BVL Department of Plant Protection products) and Dr Karola Schorn (Federal Ministry of Food, Agriculture and Consumer Protection) for their support to the work of JMPS and the meeting. Thanks were extended to Dr Ralf Hänel (CIPAC Chairman) and his team for all their efforts in organizing the meeting, to Dr Morteza Zaim, Manager of the WHO Pesticide Evaluation Scheme (WHOPES) and to Mr Denis Hamilton (JMPS Chairman) for their contribution to the preparations for the meeting. She hoped that good collaboration could be continued among partner organizations in relation to pesticide specifications and pesticide quality.

Madam Yang further indicated that the new challenges in the development and implementation of FAO/WHO pesticide specifications have been faced in terms of the increased importance of the work of JMPS, the increased need for the FAO/WHO specifications and the increased difficulty in developing FAO/WHO specifications, notably the challenges associated with the new procedure for equivalence determination, which has created a need for greater transparency.

The meeting noted the absence of Dr Gero Vaagt (FAO), who had accepted a new position in Nicaragua, and acknowledged his contribution to JMPS. Dr Vaagt, the previous FAO Joint Secretary of JMPS, sent a message to the meeting thanking JMPS, CIPAC, CropLife International and the other members for their collaboration, support and friendship during the years. He commended the unique spirit of collaboration, cooperation and comradeship at these meetings, which should be well preserved and which contributed to the success of these meetings. He wished all the participants another productive meeting.

Dr Zaim welcomed Dr Schorn, Dr Tschiersky-Schöneburg, Dr Nolting, Dr Hänel and all the participants to the 5th Joint CIPAC/FAO/WHO Meeting and to the 7th FAO/WHO Joint Meeting on Pesticide Specifications. He thanked the Federal Office of Consumer Protection and Food Safety (BVL) and also Dr Hänel for their agreement to host the meeting at BVL, and for their excellent preparations and warm hospitality.

Dr Zaim also welcomed his new counterpart in FAO, Ms Yang, as the joint secretary of JMPS, and wished the outgoing secretary Dr Vaagt success in his new position as FAO representative in Nicaragua.

Since the previous open meeting held in Umhlanga Rocks, South Africa, WHO has made significant progress in assisting Member States in sound management of public health pesticides (reported under another agenda item). He thanked the individuals and organizations represented at the meeting for their valuable support to the work of the three organizations as it related to quality control of pesticides in particular and to pesticide management in general. Dr Zaim wished participants a productive and interactive meeting as well as a pleasant stay in Braunschweig.

Dr Hänel (CIPAC) welcomed the Mr Tschiersky-Schöneburg(Head of BVL), Mrs Karola Schorn, the representative from the Ministry, and other guests as well as all the other participants and acknowledged the hard work of CIPAC colleagues in organizing the meeting. He n wished everyone a successful meeting.

Madame Yang invited Dr Tschiersky-Schöneburg to address the meeting. He thanked Dr Hänel for his kind introduction, and welcomed everyone to the Federal Office of Consumer Protection and Food Safety (BVL). In 2002, Germany set up the BVL, which reports to the Ministry. This German authority for food safety and consumer protection enjoys good cooperation with the European Commission in the area of risk communication. BVL carries out the following tasks:

- food, feed and commodities (coordination of food control, crisis management, authorization);
- plant protection products (authorization);
- veterinary medicinal products (authorization);
- genetic engineering (approval procedure and monitoring);
- analysis (national and European Community Reference Laboratories);
- economic consumer protection (European Union (EU) contact point).

BVL is located on two sites (Braunschweig and Berlin), with approximately 460 employees. Its role as an interface with Federal states and the Federal Government involves:

- general administrative procedures (AVVs) as an instrument to standardize enforcement procedures in the food safety system within Germany and to use resources efficiently;
- coordination of national food control programmes;
- preparation of recommendations for food control;
- multi-annual national control plan (MANCP) and annual report according to Regulation (EG) No 882/2004.

The following specific focal points and objectives were mentioned:

Development of minimization concepts

- introduction of dynamic adjustment processes using indicators as a new instrument for crisis management;

Emerging risks identification and prediction of collective behaviour

- development of information technology (IT) programmes for automatic analysis of documents and for predicting collective behaviour, systematic IT based evaluation;

Information systems and knowledge management

- compilation and documentation of all information in electronic data files;
- organization of workflows on the basis of file processing systems;
- establishment and operation of a web-based information system;
- identification of similar contents of documents through enhanced (web-based) search engines.

Madam Yang invited Dr Schorn to address meeting. She welcomed to the meeting the more than 100 participants from governmental and other bodies worldwide and mentioned that it is the 5th time the CIPAC-meeting has been held in Braunschweig. The last time was in 1991. She was sure that BVL would continue its activities and contribution to the work of the JMPS and CIPAC. The harmonization of methods and the setting of specifications are very important for consumer and food protection. Furthermore, a guarantee of high-quality plant protection products is vital. The importance of this work is confirmed by the EU directives, where FAO specifications and CIPAC methods are references for the assessment of pesticides. This year BVL will have completed its contribution to the peer review programme of pesticides under EU Directive 91/414, considered to be a significant process and which took 15 years to complete.

The process will continue, but with some new aspects and under a new regulation (follow-up of 91/414).
Some points on the programme are:

- Maintain current high level of quality and good active ingredients
- Scope of work will include food safeners and synergists
- possible zonal authorization and mutual recognition
- Parallel import of plant protection products

A Joint Meeting with good discussion and interchange is encouraged. She wished everyone every success at this meeting. Madam Yang thanked the guests for their attendance and the participants for their support for the meeting and the development of the specifications.

2. Arrangements for chairmanship and appointment of rapporteurs

Chairmanship of the Open Meeting rotates between the three organizations (FAO, WHO and CIPAC). This year, it was the turn of FAO to facilitate the meeting, with Madam Yang as Chair.

Three rapporteurs were proposed: Mr Steve Funk (FAO), Mr Tony Tyler (WHO) and Dr Eric Sandmann (CIPAC), and they were duly appointed.

3. Adoption of the agenda

The agenda of the Open Meeting was amended with the addition of several new agenda points originating from the JMPS Closed Meeting.

Two further points were added under Item 8:

8.4 Proposal for basic specification with greater than 1 x AI in the mixture
8.5 Temporary Reference Profiles

Two further issues were added under Item 11:

11.6 Review and publication of FAO/WHO specifications, delay of specifications
11.7 Letter of access

The agenda was adopted and approved. The floor was informed that the new agenda items would be provided in writing.

4. Summary record of the previous meeting

4.1 Fourth Joint CIPAC/FAO/WHO Open Meeting; 51st CIPAC Meeting; and 6th JMPS Open Meeting, Umhlanga Rocks, South Africa

The summary record of the previous open meeting, held at the Protea Hotel, Umhlanga Rocks, South Africa, on 11 June 2007, has been published and is available on the FAO/WHO web site. There being no objections, the Minutes of the last CIPAC/FAO/WHO Open Meeting (2007) were accepted.

5. Summary of actions taken after the 51st CIPAC and 6th JMPS meetings

5.1 CIPAC

Dr Hänel presented an outline of CIPAC. The daily business is run by a chairman, a secretary, an assistant secretary and a treasurer, all of whom are volunteers.

Handbook M is to be published in the second half of 2008. Ongoing work includes:

- a systematic review of CIPAC methods;
- a pre-publication scheme;
- the development of a guideline for independent laboratory validation for relevant impurities.

Since the last 2007 meeting, CIPAC had:

- finalized documents on its web site, and the
- pre-publication method scheme, which should now be functional.
- strengthened its cooperation with ASTM;

- continued with the review process for analytical methods;

Dr Hänel thanked Dr Walter Dobrat and Dr Albertus Martijn, the editors of the CIPAC manuals for their work. The CIPAC Handbook M will be published later this year (2008).

Further work is needed on the long-lasting insecticidal nets (LNs) and newly concepts to produce good outcomes. Further activities are ongoing concerning the peer review of MT methods and the finalization of the guidance document on relevant impurities.

5.2 FAO

Madam Yang gave a presentation of FAO activities after the last meeting, including:

Meetings and workshops

(i) October 2007 – 3rd International Symposium on Pesticide and Environmental Safety and 7th International workshop on Crop Protection and Regulatory Harmonization, Beijing, China, attended by Dr Vaagt;
(ii) November 2007 – Training courses on equivalence determination held in Lima, Peru for Andean countries, and in San José, Costa Rica, for Central American countries;
(iii) November 2007 – Regional conference for North Africa and Middle East and Regulatory meetings took place in Amman, Jordan: JMPS and equivalence determination on the agenda.

Documents and publications

(i) Regular reference made in JMPR reports and evaluations to FAO/WHO specifications;
(ii) FAO/WHO have published the Manual on Development and Use of FAO and WHO Specifications for Pesticides (March 2006 revision of the 1st edition) in Arabic;
(iii) JMPS has been recognized as a scientific advisory body supporting the work of Codex in the FAO/WHO document "FAO/WHO Framework for the provision of advice on food safety and nutrition" published in 2007.

Additional information

(i) FAO/WHO procedure for equivalence has been accepted in Argentina, Brazil, China, Costa Rica, European Community, Mexico, Paraguay, the Philippines and South Africa;
(ii) Discussions on the use of FAO/WHO procedure for equivalence are ongoing with India, Malaysia and Thailand; Guatemala and Mexico have made a number of requests for assistance for equivalence determination;
(iii) "Pesticide management update" is the regular information source for new FAO publications on pesticides, with more than 2200 subscribers.

5.3 WHO

Dr Zaim noted that one of the most important actions taken after the 6th JMPS meeting has been to organize and conduct the first FAO/WHO Joint Meeting on Pesticide Management, which was held in FAO in October 2007. This has been the outcome of the signature of a Memorandum of Understanding between the two organizations on establishing a joint programme on sound management of pesticides. The Joint Meeting, among other things, has identified and given priority to the development of different guidelines to support Member countries in sound management of pesticides, including guidelines on pesticide registration and development of guidelines on pesticide quality control. Other topics include the management of empty pesticide containers, pesticide advertising, good labeling practice for pesticides, pesticide resistance prevention and management, and the monitoring of health and environmental incidents. The second meeting of the Joint panel is scheduled to take place at WHO headquarters in Geneva, Switzerland, in October 2008.

WHO activities to support countries have been reinforced through a four-year project award by the Bill & Melinda Gates Foundation on reduction of health risks through sound management of pesticides. Part of the award goes towards supporting the normative functions of WHO, but a significant amount is also directed to supporting 12 countries, with priority in Africa, to build their capacity on sound management of pesticides following a careful situation analysis and needs assessment. These are: African Region (AFRO) – Cameroon, Kenya, Madagascar, Mozambique, Senegal, United Republic of Tanzania; Region of the Americas (AMRO) – Ecuador, Guatemala; Eastern Mediterranean Region (EMRO) – Morocco, Sudan; South-East Asia Region (SEARO) – Thailand; and Western Pacific Region (WPRO) – Cambodia.

Since the previous JMPS meeting, WHOPES has completed the testing and evaluation of five pesticide products: the DT formulations of spinosad for control of container-breeding mosquitoes; a mosquito kit for long-lasting treatment of mosquito nets and three LNs. The reports of the WHOPES Working Group Meetings provide a critical review of existing literature as well as studies organized and supervised by WHOPES. The reports have been widely distributed among national control programmes, registration authorities and other stakeholders and are intended to facilitate their registration and use by the Member States.

The positive and encouraging assessment of stakeholders on generic risk assessment guidelines and the detailed efficacy guidelines published by WHOPES in recent years have enabled WHO to invest in the development of three generic risk assessment models (for application of insecticides in indoor residual spraying, space spraying and mosquito larviciding), as well as three efficacy guidelines (for mosquito skin repellents, ground-applied space spray products and household insecticide products). All six guidelines are expected to be peer reviewed and published by mid-2009.

In collaboration with FAO, WHO is in the process of developing a training package on the development of pesticide specifications. The training manual

provides a step-by-step approach to acquiring the knowledge and skills for basic decision-making on the development of pesticide specifications, including the determination of equivalence. A FAO/WHO Consultation was convened in May 2008 at WHO headquarters, in collaboration with industry, where the training manual was reviewed. Further discussion of this manual has been carried out in the JMPS Closed Meeting. Publication of the trial edition is expected in summer 2008.

6. Technical liaison with other organizations

6.1 AOAC International

Dr Hänel presented the report of AOAC on behalf of Dr Adrian Burns. He gave a brief update on the re-organization under way within AOAC International involving the Official Methods Board and the Official Method process.

AOAC International (AOACI) has adopted a community concept in developing consensus standards and assistance in the development, validation and collaboration of analytical methods. These communities are groups of individuals interested in specific scientific or analytical areas that network and engage with international, federal and state governments, industry, business organizations and trade groups. Pesticides, including pesticide formulation analyses, are a major sub-community included and represented by the Agricultural Materials Community. JMPS and CIPAC are representative of communities that work together providing global policy and method-based solutions for problems regarding pesticides.

The Official Methods Board (OMB), the "methods engine" of AOAC International, was charged and challenged with revising and modifying the Official Methods process of the AOACI. The OMB is in the midst of its own re-organization as well as developing a transition plan to open up the Official Method process to better utilize the Association's membership resources. A primary function of the OMB is to provide independent scientific oversight to the consideration, adoption and approval of collaborated First Action analytical methods by granting Final Action status to them. Under the new Official Method process, most existing standing method committees are being phased out (retired) as the respective committee's tasks (methods under consideration) are completed. Under the new Official Method process, the OMB will establish a method committee as individual methods or needs arise and appoint the necessary membership for the committee. Committee A, Pesticide and Disinfectant Formulations, is not being phased out or retired at this time due to the Committee's current activities.

The Pesticide and Disinfectant Formulations Committee A activities include:

- AOAC Official Method 2004.09 "Maleic hydrazide (MH) in technical and pesticide formulations liquid chromatography-UV" was approved Final Action by the OMB in January 2008. The method is noted in the *Official Methods of Analysis* (OMA), available online at http://eoma.aoac.org/, and will be published in the next printed edition.

- Approval of the method “Determination of hydrazine in maleic hydrazide technical and pesticide formulations by gas chromatography: collaborative study” as a First Action on 17 September 2007. The assigned *Official Methods* number is 2007.07. The method was published in the *Journal*, included in the OMA online at http://eoma.aoac.org/, and will be published in the next printed edition.

- Analyses of samples in the collaborative study for the method “Bifenthrin analysis in technical material and formulations by capillary gas chromatography” have been completed and reported to the study director. The data are undergoing statistical analysis and review.

- Analyses of samples in a six-laboratory “mini-collaborative” round-robin study for the method “Determination of mixed phenols and phenates in formulated products by liquid chromatography (LC) with ultraviolet (UV) detection” were completed. A full collaborative study is being planned and organized based on the supporting data and statistics generated by this study.

- The Committee is continuing efforts to replace packed columns with capillary columns in the GC methods in Chapter 7 of the OMA. We are approaching and handling the project as technology updates to the methods, which should not require additional collaborative studies for approval.

- All AOAC First Action Methods in Chapter 7, Pesticides and Disinfectant Formulations of the OMA have been brought forward and made Official Final Action.

6.2 CropLife International and European Crop Protection Association (ECPA)

Dr John Dawson addressed the meeting on behalf of the CropLife International/ ECPA Specifications Expert Group (SEG). He thanked the three organizations and Dr Hänel for organizing the meeting. Dr Dawson referred the meeting to the CropLife International web site and gave an example of TM2, which is the formulation code list. CropLife International serves as an interface for the Pesticide Manufacturers industry, and played a significant part in drafting the original FAO/WHO specification guidelines. CropLife International has provided comments, for example, in the development of the training manual. The organization is a key participant in CIPAC and is involved in reviewing and developing methods. It has gained many new members in the past year and introduced a new ECPA Secretariat member.

6.3 ASTM International

Mr Alan Viets presented the ASTM report entitled “CIPAC update from ASTM – ASTM is celebrating its 110th year”. ASTM first came to the Cyprus meeting of 1995 and collaborated with CIPAC. It has contributed through its involvement in the review process. Many supporters from CIPAC have fostered this cooperation. Recent collaboration has included CIPAC and ASTM exchanging

CDs of their methods. There is also mutual recognition through their web sites. ASTM has received the MT Method Descriptions. CIPAC has also received the ASTM E35.22 Method Descriptions. These Descriptions will be posted on the cooperating organizations' web sites.

Regarding the inerts under the FQPA, the US EPA recommended OECD 422 is under way. It is unlikely that all reports will be finished in 2008. There are no unexpected results to date; a single mouse study will be conducted, probably in 2009. There are about 20 remaining cluster support teams (CSTs), and Inert Supplier and Pesticide Producers members have been formed in the ASTM – related chemistries are grouped and studies are designed around one or two of these groups. The US EPA wants to regulate inerts by CAS numbers. Industry wants to ensure that all correct CAS numbers are listed.

The meeting discussed the atmospheric availability of volatile organic hydrocarbons (VOCs) in California as an alternative to TGA testing.

Regarding the Method for VOCs and 2007 conclusions, the California DPR accepted ASTM's proposal to work on a solvent basis in November 2006 instead of on a formulation basis. This significantly reduced the workload and allowed ASTM to do in-depth studies on solvents. VOCs from pesticides have been reduced as a result of Transportation and Warehouse regulations. Alternative methods look promising and reflect reality better that the current thermogravic analysis (TGA) method, which is a good screening tool. TGA results are predictable, based on the composition of the formulation. Graphed results were presented.

With the New Method Status, the soil retention of solvent VOCs test will go to a ballot in autuman 2008; the Humectancy Test Round Robin is planned for 2009, and the ASTM's Evaporation of Solvents from Foliar Surfaces – Round Robin will take place in 2008.

A task force on adjuvants was formed and the terminology has been defined. "Invert Emulsion Suspension" was added to E609-05 as a result of Ballot discussions. "Water Conditioning Agent" in E1519-06 was modified as a result of Ballot discussions

The venue and dates of future meetings are:

- Miami, FL (1) 29 September – 3 October 2008
- Vancouver, BC 20– 23 April 2009
- Atlanta, GA (1) 19–23 October 2009
- St Louis, MO 19–22 April 2010
- San Antonio, TX (1) 11–14 October 2010

[Symposia (1)]

Mr Viets invited anyone interested in either attending or presenting at the meetings to contact him.

6.4 European Crop Care Association (ECCA)

Mr David van Hoogstraten presented a report on the activities of ECCA, which represents the generic manufacturers in the EU. Over the past few years, membership has increased to 17, representing 12 EU countries. ECCA has held regular meetings with DG SANCO and the EU Parliament in relation to the new Regulation to replace Dir. 91/414. The main issues for ECCA are:

- data protection (should be fair but limited);
- centralized evaluations (saves time and money);
- replacement of old with new studies requires authorization;
- access to taskforces.

ECCA supports or is a guest at the:

- DG SANCO Advisory Group (about 40 organizations including ECPA and ECCA);
- DG SANCO “Air” project (Guidance of re-registration after 10 years on Annex I);
- DG SANCO Minor Uses project;
- DG ENVIRONMENT DNA Group (Export of restricted pesticides).

Concerning international activities, ECCA was involved with the presentation of the “Minor uses, a generic viewpoint” paper at the FAO/IR4 summit on 3–7 December 2007, and attended FAO/WHO meetings of experts.

Mr van Hoogstraaten also referred to Agro-Care, the worldwide Association of Generic Pesticide Associations, which was initiated very recently on 28 April 2008. This development is, among others, an answer to the requests made by individuals of the group of FAO/WHO experts. Agro-Care will provide a counter view to the one-sided view of multinational companies during discussions with international organizations. Agro-Care arrives at a crucial moment in modern history, when the world faces an imminent food crisis and farmers need to be more cost competitive in the production of food. Agro-Care members will increase the competition in the pesticide market, allowing a reduction in the cost of food production for the farmer and consequently the cost of food for people. Its current members are ALINA (Latin America), ECCA (Europe) and PMFAI (India). Discussions with other generic pesticide associations are planned. The objective of Agro-Care is to promote and defend technical criteria in regulatory policies; its function is to provide a uniform voice at international activities.

6.5 Asociación Latinoamericana de la Industria Nacional de Agroquímicos (ALINA)

Dr Roman Macaya introduced ALINA, the Latin American Association of National Agrochemical Industries, which represents the generic agrochemical industry in Latin America (generic companies from 16 countries in three regions). Generic agrochemicals are an important part of the solution to the global food crisis and, where generic products have been introduced, prices of non-generics have begun to drop. ALINA promotes cost competitiveness and support to solve the food crisis, and pesticides and fertilizers are the two major inputs and important contributors to food production. "Reference profiles" must be made available to allow generic products to enter the market place. In a

number of countries where registration systems are based on equivalence, generic registrations have been paralysed. FAO and WHO were asked to address this issue.

Madam Yang commented that FAO and WHO realize that the reference profile for determination of equivalence is a high priority for developing countries. The two organizations will consider how to provide assistance to these countries in their near future work.

6.6 United Nations Industrial Development Organization (UNIDO)

No representative was present.

6.7 International Union of Pure and Applied Chemistry (IUPAC)

Mr Hamilton represented IUPAC and the IUPAC Advisory Committee on Crop Protection Chemistry. Through its internationally recognized membership, the Committee provides unbiased and authoritative views regarding environmental and human health aspects of crop protection chemistry. It seeks to advance research understanding and promote environmental stewardship through its timely projects, publications and outreach activities. The current projects being undertaken by IUPAC are:

- bioavailability of xenobiotics in the soil environment (completed, preparing for publication);
- impact of transgenic crops on use of agrochemicals and the environment (completed, submitted for publication);
- Crop Protection Chemistry in Latin America – four workshops held in 2007;
- development of simplified methods and tools for ecological risk assessment of pesticides (ongoing);
- critical review of available methods to predict VOC emission potentials for pesticide formulations (initiated in 2006);
- evaluation of food safety of transgenic crops (initiated in 2006);
- environmental risk assessments for rice pesticides (initiated in 2006).

Global availability of information on agrochemicals

- Release at the 4th Pan Pacific Conference on Pesticide Science, 1–5 June 2008, Honolulu, Hawaii
- http://old.iupac.org/project2001-022-1-600

IUPAC-sponsored conferences

- 7th IUPAC International Workshop on Crop Protection Chemistry and Regulatory Harmonization, Beijing, China, 9–12 October 2007
- 1st International Conference on Agrochemicals Protecting Crop, Health, and Natural Environment, Delhi, India, 8–11 January 2008

Future IUPAC sponsored conferences

- 3rd International Workshop on Crop Protection Chemistry in Latin America: Environment, Safety and Regulation, 4–9 October 2009, Rio de Janeiro, Brazil

- 12th IUPAC International Congress of Pesticide Chemistry. Co-organizer: Royal Australian Chemical Institute, 4–8 July 2010, Melbourne, Australia.

6.8 European Food Safety Authority (EFSA)

Mr László Bura presented the report for EFSA, which consists of two branches: the PPR Panel (plant protection products and their residues) and the PRAPeR Group (Pesticide risk assessment peer review). Their task is the evaluation and co-ordination of the pesticides peer review under the legal framework of EU Council Directive 91/414/EEC (15 July 1991) concerning the placing of plant protection products on the market.. EFSA's involvement in the review programme for existing active substances (EAS) was shown. The aims of the PRAPeR peer review are promoting consistency and technical quality in risk assessment, and ensuring that the risk assessment is maintained as a transparent sound scientific process separated from risk management. Future developments/challenges include the introduction of new guidance documents on risk assessment developed by the PPR panel, the implementation of the new regulation (when finalized) substituting Directive 91/414, and the reassessment of substances included in Annex 1 following a period of 10 years of inclusion. External relations involve the European Parliament, Council and Commission and regulatory matters relevant to EFSA's work, the FAO, World Organisation for Animal Health (OIE), WHO, the Organisation for Economic Co-operation and Development (OECD), International Life Sciences Institute (ILSI), Canada (Health Canada) and the United States Food and Drug Administration (FDA). Details of EFSA's work are available on its web site (www.efsa.europa.eu) and for PRAPeR at http://www.efsa.europa.eu/en/science/praper.html.

6.9 International Programme on Chemical Safety (IPCS)

Dr Antero Aitio presented the International Programme on Chemical Safety (IPCS), which was formed in 1980 by three United Nations organizations: WHO, the International Labour Organization and the United Nations Environment Programme. IPCS is involved in a range of areas including:

- WHO guidelines on drinking-water;
- poison information;
- occupational health;
- environmental risk;
- development and harmonization of risk assessment methods;
- emergency preparedness and response caused by microorganisms and chemical exposures.

Regarding acute poisonings, a network of poison management centres has been set up that supplies instant information to help patients as they arrive at the centres with symptoms in order for diagnosis to occur quickly.

Concerning emergency preparedness and response, should a disease outbreak occur, IPCS has an expert group to assess whether it is related to toxicity caused by pesticide chemicals or to chemical exposure.

6.10 Pesticide Manufacturers and Formulators Association of India (PMFAI)

No representative was present.

6.11 Other organizations

There were no other organizations present who wished to give a report.

7. National reports regarding CIPAC activities and reports from Official Quality Control Laboratories

The following country reports, including any collaborative studies in which they participated, were presented: Argentina, Austria, Belgium, China, Czech Republic, Denmark, El Salvador, Finland, Germany, Greece, Hungary, Ireland, Italy, Japan, the Netherlands, Panama, Romania, Slovak Republic, Slovenia, South Africa, Spain, Switzerland, Thailand and Ukraine (Annex 1).

Dr Zaim noted that since 2002, the report of the national laboratories has been published in the report of the Open Meeting. He added, however, that caution should be exercised with the comparison and interpretation of the data given the differences in the objectives and purpose of the studies. He noted that the data still provide very useful information.

Of the 24 reports submitted to the meeting in 2008, the average rate of non-compliance is about 6%, ranging between 0% and 29%. The grand total of all reports received since 2002 also showed an average non-compliance of 6%, ranging between 0% and 38%.

In response to a request from the floor, Dr Hänel will place on the CIPAC web site all the presentations mentioned under Item 7, with the proviso that he has obtained permission from all the speakers.

8. Proposed new/amended specification guidelines

8.1 Revision of requirements for physical and chemical properties

Mr Hamilton presented the reasons why JMPS required the physical and chemical properties of active ingredients to support the specifications.

The full studies for physical and chemical properties of the active ingredient should be submitted to JMPS for evaluation. JMPS will examine the methods for suitability and check the measured values for validity.

Different terms, such as “physico-chemical properties” are used but all mean physical and chemical properties. The properties needed currently (Manual 2006) are:

- vapour pressure;
- melting point, boiling point or temperature of decomposition;
- solubility in water;

- octanol: water partition coefficient;
- dissociation characteristics, if appropriate;
- hydrolysis, photolysis and other degradation characteristics.

The question is: should the data be provided on the pure active ingredient or the technical material? This document was circulated to JMPS members for comments, and the reasons for the current needs were outlined.

Basically, properties required for the pure active ingredient are:

- vapour pressure;
- melting point;
- temperature of decomposition;
- water solubility;
- octanol-water partition coefficient;
- dissociation characteristics;
- hydrolysis characteristics;
- photolysis characteristics.

For the technical grade active ingredient, properties required are:

- melting point;
- solubility in organic solvents.

The description “pure active ingredient” is readily understood in simple cases, and genuinely pure active ingredients from whatever source should have the same physical and chemical properties. The different experimental values from different sources should reflect the prevailing errors of measurement, not the underlying value.

For active ingredients that are mixtures, e.g. diastereoisomer mixtures, the composition of pure active ingredient from different sources may be different, and physical and chemical properties may not therefore be identical.

For equivalence determination, the manual omits the need for the data requirements on physical and chemical properties of an active ingredient from a proposer seeking an equivalence determination.

The data requirements for an active ingredient supporting the reference specification are as shown above.

The requirements of active ingredient for equivalence determination are:

- pure active ingredient (single compound) – not required, except that data on physical and chemical properties must be provided if the measured value of the property is not in agreement with the recorded value in the evaluation supporting the reference specification;
- pure active ingredient (mixture) – as for reference specification;
- technical grade active ingredient – as for reference specification.

Comments from the floor included:

- agreement that the temperature of decomposition that is needed for the pure active ingredient may also be required for the TC;

- querying (by CropLife International) that the proposed new data requirement concerning the solubility in organic solvents for technical materials. It would be an additional study for the industry to provide;
- questioning whether the boiling point data should be removed. More comment is required over the next 12 months, and data should rather be presented on vapour pressure and not the boiling point.

Madam Yang invited the meeting to provide their comments to the proposal on revision of requirements for physical and chemical properties (Annex 2) to FAO and WHO by the end of 2008. The inputs will be considered and incorporated in the JMPS procedure.

8.2 Determination of equivalence – revisited

Mr Hamilton gave a presentation on the determination of equivalence, with comments provided by JMPS toxicologist Dr Aitio.

In 2007, the Chair of JMPS and the FAO and WHO agreed to prepare a proposal for comment by JMPS, which would then be circulated for wider consultation. The proposal used as its basis Dr Aitio's paper, taking into consideration CropLife International and ALINA's proposals.

Equivalence was defined in the FAO code of conduct on distribution and use of pesticides (2005) as *"the determination of the similarity of the impurity and toxicological profiles, as well as of the physical and chemical properties, presented by supposedly similar technical material originating from different manufacturers, in order to assess whether they present similar levels of risk."*

The idea is to determine: (i) if a second technical material contains no new impurities and no existing impurities at significantly higher levels than in the reference profile; and (ii) if its toxicological and ecotoxicological properties are within tolerance of the existing profiles.

In practice, complications arise that may make comparisons between the materials difficult. Data may have been produced many years apart under different requirement guidelines. This concept and use for comparisons have been considered by many different people.

Toxicity and impurities

The considerations of identity, purity and stability of pesticides were explained in Chapter 4 of EHC 104 (IPCS, 1990). Toxicological evaluations are strictly valid only for the technical grade material being examined, and special care and knowledge of the detailed specifications are required to extrapolate the findings to other products.

The JMPR (JMPR, 1984), after noting the influence on toxicity of impurities such as dimethylhydrazine, dioxins and HCB, stressed "*the importance of determining whether the toxicity of a technical pesticide is due to the inherent toxicity of that compound or also due to the presence of toxic impurities*." This is what JMPS evaluators are looking for when determining relevant impurities. A toxicological determination that the toxicity of a technical pesticide is due to the

inherent toxicity of that compound would be very helpful in deciding on the relevance of the impurities in that technical material.

Ideally, the reference profile should be linked to the hazard data or the interpretation of the hazard data. In some cases, the connection appears to be tenuous, especially when the reference profile is based on old data. However, the connection (between the reference profile and the hazard data) is not so important if the hazard of the technical material is due to the inherent toxicity of that compound rather than to the presence of toxic impurities.

In current practice, a technical material is equivalent to the reference profile when:

- it meets the current specifications;
- contains no new impurities;
- contains no existing impurities at significantly higher levels; and
- the toxicological and ecotoxicological profiles are within tolerance of the reference profiles.

Acute toxicity testing for equivalence determination may be seen as a check that no other unidentified "surprise toxic impurity" (e.g. dioxins, dimethyl hydrazine, nitrosamines) is present in significant concentrations.

Composition of the technical material
Available information is required on:

- the manufacturing process;
- the manufacturing quality control (QC) limits for active ingredient and impurities;
- the batch analysis data.

The manufacturing process should be explained and presented (flow diagram) with sufficient detail to identify the starting materials, reagents, solvents, intermediates, by-products and final product together with relevant reaction and process conditions and times. JMPS needs to go into these details to give the chemist information to understand the impurity profile.

The basis for the manufacturing QC limits should be explained in terms of the process or processes, the number of manufacturing plants and the duration of time that the QC limits have been in place and when these limits were determined.

If the active ingredient is a mixture (e.g. a *cis-trans* mixture or enantiomeric pair), then the control over the composition of that mixture should be explained. Specific procedures in the manufacturing process that prevent the formation of undesirable impurities should be identified.

The batch analysis data should be accompanied by information identifying the manufacturing process, establishment(s) and duration of time represented by the batch data. The reasons for choice of those batches used for five-batch analysis should be explained.

Assurance should be provided on the quality and validity of batch analysis data. The batch analysis data should be produced under GLP control, but earlier batch analysis data from times before the general introduction of GLP requirements are also acceptable.

JMPS wants to see the variability of batches, including variability of active ingredient composition when it is a mixture, and the variation of impurities at more than 1 g/kg so that these variations can be assessed and compared with the QC limits.

Comparison is made of what is in the five-batch analysis and what JMPS expects to see from the manufacturing process, such as stable intermediates, isomers, relevant manufacturing components and impurities. An important question that is asked – Is an expected impurity not mentioned in the five-batch analysis and, if not, why is it not mentioned?

Examples were presented of "surprise impurities" from past experience, including nitrosoamines, dioxins, aflatoxins (in botanicals), HCB, terpyridines and tetrachloroazobenzene, but there are others.

Recommendations

1. That the data requirements and evaluation for determination of equivalence be operated as a two-tiered system, with Tier 1 based on the manufacturing process, manufacturing QC limits, batch analysis data and mutagenicity test data.

2. That the batch analysis data should be produced under GLP control.

3. That the FAO/WHO Manual (2006 edition) be revised in Clause 3.2 E to reflect the changes proposed at the current (2008) meeting.

4. That the electronic template for data submission be revised to align with the revised requirements.

Discussion of the two (2) tiered approach

Tier 1 to include:

Comparison of properties with current specifications:

- description;
- active ingredient identity, content and other relevant clause (e.g. isomer ratio;
- relevant impurities;
- physical properties.

Manufacturing process and composition of technical material:

- manufacturing process;
- manufacturing QC limits for active ingredient and impurities;
- batch analysis data.

Toxicological summaries:

– mutagenicity test data.

Tier 2 includes:

- 3.1 A.9 Toxicological summaries (including test conditions and results).

- A.9.1 Toxicological profile of the TC/TK based on acute oral, dermal and inhalation toxicity; skin and eye irritation, skin sensitization.

- 3.1 A.10 Other information.

- A.10.4 Statements to identify the links between purity/impurity data and the hazard information and risk assessments.

Revised text to be added to the Manual

3.2 E. Data requirements for the determination of equivalence

E.1 Tier 1 data requirements for technical grade active ingredients include the information required in Section 3.1, paragraphs A.1 A.3 to A.8, A.10.4(iii), and B1 to B5 and mutagenicity test data. (delete A.9.1)

Tier 2 data requirements for technical grade active ingredients include the information required in Section 3.1, paragraphs A.9.1, A.10.4(i) and 10.4(ii).

In particular cases, further data may be necessary as described in Section 3.2 E2 of the Manual.

This proposal has been discussed at JMPS, modified several times and is now ready for public comment.

Dr Aitio provided the following additional information on toxicity data:

JMPS considered further what does and does not constitute equivalence in terms of the toxicology. Acceptance of the GHS procedure is a possibility.

Tier 2 consists of 6 acute studies. These are important for comparing two products, and the reference study is crucial. All are important, but inhalation toxicity should be re-examined.

Inhalation toxicity studies are a weak point because the vast majority of chemicals are not volatile. The parameter determined contains a large error, and the study is expensive to perform. These studies are prone to large errors and dropping them (inhalation studies) was considered as they are hard to reproduce, expensive and require animal testing. It may be possible to use bacterial testing in vitro instead.

There is a need to reconsider the points in equivalence determination; if there is a twofold difference, then it is not equivalent.

If a study gives results +/– then this is clear, but if in the case of irritancy there is a non-irritant, mild, irritant and then the dichotomy does not sit properly then the uncertainty of the result should be noted. The category would then not be clearly determined and the ecotoxicological studies could be taken and used as a toxicological end-point.

Some studies use classifications (as opposed to numerical results), for example, nonirritant, mild irritant, irritant. Using such ranges is the GHS system. It is especially applicable in the ecotoxicological area.

There is not much credibility in the reproducibility of ecotoxicological studies. The present cut-off for equivalency is a five-fold difference. The proposal is that if two products are in the same general category, they are equivalent. Categories are equal to one order of magnitude.

If the difference is more than five-fold or major, it is not considered to be equivalent. If the compounds are in the same category, they would be equivalent, for example the synthetic pyrethroids. One order of magnitude would not make too much of a difference in the interpretation.

Comments made included:

- In terms of the tiered approach, QSAR analysis/in vitro testing have not been considered.
- The Tier 1 stops in simple cases, but it is not known regarding the complicated cases. It is a case-by-case determination.
- Physical chemical data will always be required for the technical material.
- Dr Aitio would provide a hard copy of the Tier presentation.
- Ms E de Aguila (El Salvador) questioned the conditions for developing countries when submitting data for registration, e.g. what data are required to support physical and chemical properties? One wants to be sure that you can, as a national authority, make a complete assessment of formulated products with respect to the environment. Mr Hamilton referred to the OECD guidelines to determine the data availability, and then it can be decided what information is required for the particular registration system. A balance is needed between the active ingredient of the formulation and the risk that has to be taken.
- Concerning data from the past, not generated under GLP guidelines, and current GLP data, some registration authorities do not insist on GLP data; others require GLP in different countries. However, the JMPS is not a registration authority, and one must keep an open mind.

Mr Hamilton requested participants to provide comments on the Determination of Equivalence to FAO/WHO & Chairperson JMPS (Annex 3) before the end of the year (2008) for incorporation into the JMPS meeting next year (2009 JMPS Closed Meeting).

8.3 WHO specifications for LNs – Knowledge gaps and way forward

Dr Zaim noted that every year, 300–500 million cases of malaria occur, the majority in Africa, with more than 1 million deaths, mostly in children aged under five years. It is now well established that insecticide treated nets can

significantly reduce morbidity and mortality due to malaria. WHO recommends full coverage of all those at risk of malaria in Africa with insecticide-treated nets. It also recommends that control programmes purchase only long-lasting insecticidal mosquito nets. These are factory-treated nets expected to retain their biological activity for at least 20 WHO standard washes and three years of recommended use under field conditions, obviating the need for regular treatment of nets. This would require about 200 million LNs for Africa in 2010. The development of specifications for such products is, however, moving slowly and there are many products of substandard quality on the market. The support of industry and the experts present in the JMPS meeting is needed to develop quality standards for such an important life-saving intervention.

Industry has had difficulty in defining their products, but this can be done by the WHO washing process.

A consultation held at WHO headquarters in December 2007 reviewed the experience in testing and evaluation of more than 11 LNs and made the following recommendations to industry, WHO and research institutions for testing and ultimately development of quality standards for such products.

Manufacturers should:

- define the wash characteristics of their LN, based on chemical assays, and follow WHO standard washing procedures. This should be based on determination of the total content of AI before washing and at a minimum of seven wash points, i.e. 1, 3, 5, 10, 15, 20 and 25, to show if these are consistent in batches produced over time;
- show whether simple measurements (e.g. based on two wash points) can be used reliably to predict "surface concentrations" after 20 WHO standard washes;
- ensure that typical variations in the manufacturing process (changes in yarn source, colour, heat settings, knitting, etc.) do not affect the efficacy of their LN;
- ensure acceptable homogeneity of the AI in their LN products … minimize the within-net heterogeneity of AI distribution so that the RSD does not exceed 5%, when five pieces of 30 cm x 30 cm are analysed as a single sample according to the scheme recommended in the Manual on development of FAO and WHO specifications for pesticides… the average AI content between nets should not exceed ±25% of the declared AI content, as specified in the same manual.

WHOPES and research institutions:

- to further standardize WHO washing procedure by recommending a detergent approved by the International Standards Organization …;
- until it can be demonstrated that more sophisticated measurements will provide meaningful results for quality control purposes, WHO specifications for wash resistance should be based on a minimum of 90% retention of AI per wash;

- reiterate that WHOPES Phase I efficacy studies constitute an essential part of the determination of equivalence of LN products for extension of WHO specifications.

Until this is established, data from bioactivity studies are needed to confirm efficacy.

WHO has organized a meeting in collaboration with the Bill & Melinda Gates Foundation and the Institute of Tropical Medicine in Antwerp, Belgium, on 10–11 July 2008, to which industry and major donors and research institutions are invited, where the development of quality standards for LNs, the information gap and the way forward will be discussed. All interested parties are invited to attend.

8.4 Interpretation of physical property specifications for formulations with more than one active ingredient

Mr Hamilton presented a paper on the physical properties of co-formulants. He quoted a paragraph from section 4 of the manual "Formulation specifications normally refer only to a single active ingredient. Where two or more active ingredients are co-formulated, the specification for each active ingredient is expected to apply. Manufacturers should therefore ensure that the limits provided in proposed specifications are mutually compatible.

In exceptional cases (for example, if special controls are required where active ingredients are co-formulated), a specification may be accepted for a co-formulated product but the manufacturer must explain the basis for the requirement."

It refers and addresses mainly the active ingredient and relevant impurities but is problematic when referring to formulation physical properties, e.g. dustiness, where the two individual products have differing specifications.

These differences could influence decisions on physical property specifications with the result that proposers would aim for lower or default values in the specifications to allow for future changes.

Users of the manual could also read it and find out that the most stringent requirement should apply.

We (JMPS) would want the best possible specification values while still allowing for the normal compromises required to produce good formulations.

It is our aim to revise the manual so specifications for products with two (2) active ingredients could apply to compounds in same formulations

This is related to Dr Axel Steer's discussion paper on Safeners. These safeners are always co-formulated and, as they are not actually active ingredients and so are never used by themselves, how the specifications apply has been an issue for consideration.

Therefore for minimum purity of active ingredient and content of relevant impurities, both specifications apply simultaneously.

A number of possibilities of how these compromises might be resolved were discussed using number of different physical properties as examples, including suspensibility, acidity/alkalinity, wettability, pH and dry sieve, and then demonstrating how each property could be assessed. In the case of pH, the intersection or common overlapping pH region value would be chosen and used and then a decision is needed on whether a more or a less stringent value should apply.

The intention is to amend the manual after comments are received.

It is proposed that the paper (see Annex 4) be available for comment over the next year and we make a decision at next year's (2009) meeting.

Dr Jean-Philippe Bascou presented the CropLife International position on the "Setting of Physical Properties limits on PPPS". At the 2007 CIPAC/FAO/WHO Open Meeting in South Africa under Agenda item 13.3 on "Default or low values for physical and chemical properties", Mr. Denis Hamilton informed the Meeting of the JMPS's concern that in many recent draft specifications proposed by industry, the lowest acceptable limits (the default values) for physical properties of formulations had been proposed. He emphasized that the proposed values for physical properties should be derived from measured values and supported by relevant data. He reiterated that the specification values should be "as good as reasonably achievable" and noted that some proposers were not carrying out tests but just simply using the default values. Default values described in the FAO/WHO manual show acceptable properties which bring quality products on the market. Concerning the latest revision of the FAO-WHO Manual (March 2006), on page 32 it says: **"**Formulation specifications normally refer only to a single active ingredient. Where two or more active ingredients are co-formulated, the specification for each active ingredient is expected to apply. Manufacturers should therefore ensure that the limits provided in proposed specifications are mutually compatible". This statement is of concern to members of CropLife International and is an additional factor in moving towards default values. It was concluded that the use of default values does not necessarily mean poor product quality. The use of default values is often necessary to cover current and future product ranges. It was proposed by CropLife International that an update of the FAO-WHO Manual must emphasize that published specifications relates to a product containing only one active ingredient. CIPAC analytical methods are also collaboratively validated for products containing mostly only one active ingredient.

Dr Zaim reminded participants that the purpose of the FAO/WHO Specifications is to provide the highest quality formulations in trade. This matter would be discussed further in the JMPS.

8.5 Temporary Reference Profile

This discussion is based on a JMPS discussion that was held in the Closed Meeting. To re-cap, it must be asked for what reference profiles are required. Dr

Markus Müller presented the “JMPS Position on Reference Profiles in Equivalence Determination”. Concerning the Reference Specification, he referred to the minimum data requirements for support of the reference (first) specification for an active ingredient. It is explained in the Manual in Chapter 3.1, and the intention is to establish a firm link between composition of TC, QC limits and the hazard data.

With the equivalence determination of another manufacturer’s product, data is required for the determination of equivalence with the reference specification. The data must include the Impurity profile of TC, the QC limits and a reduced set of toxicological data. It is explained in the Manual in section 3.2 and the intention is to evaluate whether or not the material of another manufacturer is worse than the material used to produce the data in the reference profile.

The issue of the “Temporary Reference Profile” is not a process described in the Specification Manual. Compromising on the reference profile will lead to a loosening of the firm link between the composition of the TC and hazard data, and this adversely affects the sound decisions based on the specification and equivalence.

There is a lack of first (reference) profiles in the national registration schemes. In selected cases national registration authorities may wish to establish equivalence by bridging data gaps and are doing this on a case by case basis.

In response to a query from Mr J Dawson if the JMPS are proposing to make modifications to the Manual on temporary reference profiles, Dr Müller said that the temporary reference profile is not in the Manual, and any national registration authority would need considerable experience to be able to do the bridging. This should be addressed at national level. The JMPS cannot encourage temporary reference profiles. Mr J Dawson was of the opinion that the temporary reference profile undermines the value of reference profiles.

Many countries are in a transition phase, and a resolution is needed. New products are registered with a full data package, but most products on the market will not be new products. Many generic products will be received by registration authorities at the ratio of 100 generic:1 new. The question is on how does one deal with this transition? Many feel that the Manual must be followed rigorously. Dr Müller agreed and said that at the moment, the JMPS Panel cannot provide an answer. This issue must be addressed at national level, and much patience is required. Dr Zaim indicated that the WHO is very much concerned that some countries are facing problems with access to full data package. FAO and WHO will be happy to work with individual countries to see how they can resolve the bottle necks for the full implementation of the FAO/WHO guidelines on equivalence determination.

9. Status, review and publication of CIPAC methods

9.1 Handbooks and pre-published methods

Handbook M will be published during the first half of this year.

9.2 CIPAC method review process

Dr Ralf Hänel gave the current status of the methods review and said more will be presented at the CIPAC meeting. A spreadsheet table of these CIPAC methods was presented. Dr Markus Müller and László Bura gave a presentation about CIPAC and the process of reviewing the CIPAC methods.

Concerning CIPAC publications, books have been published since 1980, and there were manuals before this, so this means that the methods have been around for over 40 years. The fact that many methods are obsolete is an issue, and also the progress of science and technology needs to be considered.

The Review must be carried out in a structured way considering:

- FAO and/or WHO specifications, if existing, referring to the compound/method and their status
- Origin and year of adoption of the method, including method extensions, if existing
- Technique used including the availability of reagents and consumables
- Current use of an active ingredient

CIPAC has decided to look systematically at these methods, reviewing Handbook by Handbook, from the oldest methods, both analytical and MT. Handbook “E” is currently under review. Obsolete methods are listed and those methods that are no longer supported. No method extensions are granted in such cases but the methods may still be used for special purposes.

The review by the CIPAC sub-committee of Dr Müller and Mr Bura involves listing reasons for the withdrawal of obsolete methods. An example of Endrin was given, a flowchart of the decision process was shown and the results of Handbook E review were presented.

Conclusion on the way forward:

- Handbook F with MT Methods: New Task force is used for the evaluation
- Method-by-method discussion at the 52nd CIPAC Meeting and recommendations given
- Decisions taken at the Council Meeting in Braunschweig
- Publications shown at www.cipac.org and in a new Appendix in the Handbook is proposed. Handbook E will be published in autumn 2008.

Dr Hänel said that concerning the review of MT methods, CIPAC makes use of the activities of DAPF and by 2009, the review should be completed.

10. Proposed new/extended CIPAC analytical and physical test methods

10.1 Proposal for a CIPAC Guidance document for analytical methods for the determination of relevant impurities referred to in FAO and/or WHO specifications – draft guidelines.

The FAO / WHO invited CIPAC to consider independent laboratory validations (ILV) for relevant impurities in the scope of its activities. CIPAC sees the need for such methods and agreed to accept the request made by the FAO / WHO to deal with ILV for relevant impurities defined in FAO/WHO specifications. The proposal is a compromise between a full-scale trial and a peer validation. The concept is based on the validation of the proposed method in four (4) independent laboratories. Consequently, the criteria that need to be fulfilled are different to the ones for collaborative trials. Adopted methods will be made available via the CIPAC web-site and also published in an Annex of the CIPAC handbooks. More details will be given at the coming CIPAC Meeting.

The Draft will be made available on the CIPAC web-site after the meeting and CIPAC is inviting everyone to make comments. The deadline for comments to CIPAC on the draft CIPAC Guidance document will be 30 September, 2008.

10.2 MT method for LN formulations

Dr Müller presented the “CIPAC Washing Method & Storage Stability for LN (Long Lasting Nets)”. A new proposal is presented for a method for washing both types of long-lasting insecticidal nets. The efficacy claim is that the insecticide treated bednets retain their efficacy after 20 washes and this claim must be able to be tested. The LN formulation is not a classical formulation, but a slow release formulation.

There are 2 main types of nets and diagrams were also presented

- HDPE – incorporated insecticide;
- Polyester – insecticide coated.

Diagrams were presented showing the structures and washing effects.

A collaborative validated method is required. Now CIPAC must test a method on washing resistance. Release or Retention Index also needs to be measured. LN Specifications are linked to the WHOPES recommendation for Phase I testing including a description, the chemical content as determined by CIPAC analytical methods, and physical properties by ISO methods. CIPAC would like a bridging study with some LNs and this is proposed.

The storage stability method MT 46.3 only refers to solid or liquid formulations, and the LN does not fit in here. The storage stability for the nets must also be determined. A standardized wash method is required. The WHO method is very well characterized, but there is one problem, namely, that the Marseille soap is not really well standardized, as it varies from shop to shop. It would be preferable to rather use ECE Detergent A 0.2%. The storage test for LN is not

defined. It is proposed that storage of the LN should be in a glass bottle. These proposals will be discussed in more detail at the CIPAC meeting in 2 days (Wednesday).

The replacement of the Marseille soap has been studied, and this data will be given to CIPAC. Dr Zaim said that a good discussion will be in the CIPAC Meeting. Dr Müller said that the standardized wash method is intended to be as close as possible to the WHO washing method.

Comments and discussion points were requested on the LN Washing method from participants, and they should be sent to CIPAC/FAO/WHO.

11. Review and publication of FAO and WHO specifications for pesticides

11.1 Status of FAO Specifications

Madam Yang presented the status of publication of the specifications of the FAO list of compounds from 2002 -2007, which was updated in 2007 and 2008 (up to May). She noted that there are 17 compounds left in this list, among of them the specifications for 7 compounds have been published, 4 compounds are ready or to be finalized for publication, 6 compounds are in progress (for further details see Annex 5).

11.2 & 11.3 Status of WHO Specifications & status of joint FAO/WHO specifications

Dr Zaim noted that, since the establishment of the FAO/WHO Joint Meeting on Pesticide Specifications in 2002, about 108 submissions had been made to the JMPS under the new procedure. Almost half have been for the development of FAO specifications and use in the agricultural sector, the remainder being for joint or WHO specifications only.

Dr Zaim reported on the status of publication of WHO and FAO/WHO joint specifications and noted that among the products reviewed by JMPS in 2006 or before, only bifenthrin (FMC - joint FAO/WHO specifications), temephos (BASF - WHO specifications), alpha-cypermethrin LN (BASF - WHO specifications) and dimethoate (JSC Trans Oil, joint FAO/WHO Specifications) have not been finalized. Among those reviewed by JMPS 2007 for joint specifications or WHO specifications alone, development of evaluation report and specifications for most compounds is going rather well.

11.4 Withdrawal of FAO Specifications

Ms Yang outlined the withdrawal of FAO specifications developed under the old procedure for which the methods for impurities are not included and specifications are no longer supported by industry. In 2006 FAO announced decision to withdraw 35 compounds. There are also 8 active ingredients which the methods for the analysis of impurities are not available, and hence have been withdrawn.

She noted, however, that information were received from various companies for 27 compounds: the methods for the impurities have been provided and the specifications have been updated on the FAO homepage on the Internet at http://www.fao.org/ag/AGP/AGPP/Pesticid/Specs/pes_alp2.htm.

List of active ingredients where the methods for the analysis of impurities have been provided by manufacturers, hence specifications for these pesticides have been maintained. There are a total of 233 FAO specifications of which there are 179 under the old procedure. The manufacturers are encouraged to revise these specifications following the new procedure in order to actualize and update the specifications available. A list of compounds (AI's) was presented (see Annex 6).

11.5 Withdrawal of WHO Specifications

Dr Zaim noted that WHO started development of specifications under the new procedure in 2002 and from the total of 30 compounds for which WHO specifications were available under the old procedure, majority have been reviewed under the new procedure, or such a review has been initiated. This has left WHO with 11 compounds. He also noted that the last update/revision of the old specifications was made by the WHO Expert Panel in 1999.

The 11 compounds still under the old specifications are brodifacoum, DDT, deet, dichlorvos, lindane, pyrethrum, endosulfan, iodofenphos, methoxychlor, phoxim and trichlorfon.

Dr Zaim informed the meeting that the first 6 compounds are scheduled for review and if necessary update/revision by JMPS 2009. He however requested industry and national laboratories attending the meeting to advise WHO by end 2008 if any of the last 5 compounds, i.e. endosulfan, iodofenphos, methoxychlor, phoxim and trichlorfon are registered for public health use. This information is needed to decide if the old specifications should be maintained or withdrawn.

11.6 Review and publication of FAO/WHO specifications, delay of specifications

Dr Zaim reported that JMPS 2008 noted with high concern unreasonable delay and sometimes lack of communication and follow up by industry in provision of data/information requested by the JMPS and therefore the significant loss of resources of the two organizations. He requested industry for their immediate action and urgent consideration of this matter. A list of compounds was also presented

11.7 Letter of access

Dr Zaim stated that we (the JMPS) ask for a letter of access to assess whether or not the confidential data on manufacturing process, purity and impurities, provided in support of the technical material for which an FAO/WHO specification is proposed, are similar to those assessed by a competent authority for the purposes of registering the pesticide. He however requested industry to provide the registration number to facilitate access to the national files, and to ensure that the letter includes the full contact details, including

email, and the postal address of the contact person and the national authority. This will assist FAO/WHO in timely contact and review of the application dossier.

12. FAO/WHO priority list and program for development of FAO and WHO specifications for pesticides

Dr Zaim presented the priority list for JMPS 2009 (see Annex 7) in three different categories: (1) original proposer; (2) subsequent proposer(s); (3) specification for formulation. He stated that there were 7 submissions as primary proposers, three for FAO specifications and four for FAO/WHO Joint Specifications. There were also six submissions for determination of equivalence (subsequent proposers), three for FAO specifications, one for WHO specifications and the rest for FAO/WHO Joint Specifications. There was also two submission for establishment of WHO specifications for formulated products.

13. Introduction to the new Joint FAO/WHO Training Manual for Pesticide Specifications

Dr Zaim presented the new Joint FAO/WHO training manual on specifications for pesticides. He stated that this is a facilitator driven, problem-based training course, using group exercises to meet the learning objectives. The purpose of the course is to provide an introduction to the principles and practice of defining acceptable quality and equivalence of pesticides, to assist both governments and industry to strengthen the underlying procedures required for quality control of pesticides used in agriculture and public health, as promoted by the International code of conduct on the distribution and use of pesticides. The principles and procedures outlined in the training manual are based on the principles and requirements detailed in the Manual on development and use of FAO and WHO specifications for pesticides.

Dr Zaim added that this is a three day course for personnel with responsibility for defining and ensuring the acceptability of pesticide product quality. The training manual is a trial edition and will be finalized after field testing. FAO and WHO will greatly appreciate feedback and suggestions from readers, facilitators and participants that may help to improve future editions. Translation of the slides to be used in such trainings is planned.

14. Any other matters

14.1 Updates to the 2006 FAO/WHO Manual on Specifications

Industry requested FAO/WHO to ensure that in the reports of the Open Meeting the changes to the Manual are clearly stated, as it will serve as the source of reference for JMPS work until the next revision of the Manual on development and use of FAO and WHO specifications for pesticides.

15. Date and venue of next meeting

CIPAC/FAO/WHO invited everyone to the next meeting, which was scheduled to take place on 3–11 June 2009 in Decameron, El Salvador. A presentation video was shown of the meeting venue.

Closing of the 5th Joint CIPAC/FAO/WHO Open Meeting

Madam Yang, FAO, Chairperson for the Meeting declared the meeting closed at 17:40. Dr Zaim as well as Dr Ralf Hänel thanked Madam Yang for chairing the meeting and thanked the rapporteurs.

Annex 1. Summary table of national reports of official quality control laboratories

Region	Reporting laboratory	No. Of samples testes	Non-compliance	
			No.	%
Africa	South Africa	22	3	14
Americas	Argentina	974	7	1
	El Salvador	1048	51	5
	Panama	211	11	5
Europe	Austria	6	0	0
	Belgium	77	14	18
	Czech Republic	51	15	29
	Denmark	54	2	4
	Finland	55	5	9
	Germany	287	45	16
	Greece	95	7	7
	Hungary	917	0	0
	Italy	411	34	8
	Ireland	149	19	13
	Netherlands	45	0	0
	Romania	248	23	9
	Slovak Republic	108	2	2
	Slovenia	19	0	0
	Spain	138	6	4
	Switzerland	32	6	19
	Ukraine	312	50	16
Asia	China	493	69	14
	Japan	23	0	0
	Thailand	3112	185	6
Total		**8887**	**554**	**6**

Annex 2.
Physical and Chemical Properties of the Active Ingredient

EXPLANATION

In light of the discussions at the 2007 JMPS (JMPS, 2007, Agenda Item 7), data requirements for physical and chemical properties of active ingredients need revision.

The 2007 JMPS report stated:

> *It was proposed that for consistency reasons physical-chemical studies should be submitted, which means that this new request has to be communicated to the companies and the template has also to be modified.*
> *It was proposed to request the full studies for physical-chemical properties, and to check the data against the full studies.*

The purpose of this report is to explain the needs of JMPS for information on physical and chemical properties of the active ingredient and to revise the relevant sections of the Manual (FAO/WHO, 2006).

RECOMMENDATION

That the FAO/WHO Manual (2006 edition) be revised in Clauses 3.1 (vi), 3.1.A, 3.1.A.2 and 3.2.E.1 as described in Annex 1 of this report.

Note that the report on “Determination of equivalence – revisited” also recommends changes to 3.1.A.9 and 3.1.A.10. Ideally, the changes in the physical and chemical properties requirements should be made first.

BACKGROUND

The terms "physico-chemical properties", "physical-chemical properties" and "physical and chemical properties" are all intended to mean the same thing. This report will use the term "physical and chemical properties."

JMPS (FAO/WHO, 2006, section 3.1.A.2) currently requires data for the active ingredient on:

- vapour pressure;
- melting point, boiling point, or temperature of decomposition;
- solubility in water;
- octanol: water partition coefficient;
- dissociation characteristics, if appropriate;
- hydrolysis, photolysis and other degradation characteristics.

These data should be readily available because national governments require data on numerous physical and chemical properties of the active ingredient (OECD, 1994), including:

- vapour pressure;
- melting point and boiling point;

- solubility in water;
- octanol-water partition coefficient as a function of pH;
- dissociation constant in water
- hydrolysis rate including identification of metabolites and breakdown products;
- photodegradation in water including identification of metabolites and breakdown products
- solubility in organic solvents.

It is not entirely clear which data are required on pure active ingredient and which on technical grade active ingredient. An explanation of the needs of JMPS may assist in clarifying the data requirements.

NEEDS OF JMPS

Knowledge of the physical and chemical properties of a substance is a necessary pre-requisite to understanding its general behaviour in analytical methods, formulations and the environment.

Vapour pressure

The vapour pressure of pure active ingredient is needed for:

- understanding diffusion and evaporation in mosquito net applications;
- understanding applications involving volatilization and for recognizing possible losses by volatilization;
- understanding analytical methods and GLC traces.

Melting point

The melting point of pure active ingredient is needed for:

- a simple practical test of purity of relatively pure materials.

The melting point or melting temperature range of technical grade active ingredient is needed for:

- deciding if it is possible for a suspension of active ingredient to be formed;
- a simple identification test.

Measurements are required on active ingredients that are solids above 0 ˚C.

Boiling point

JMPS generally has no need of data on boiling point at atmospheric pressure. It should be recognized that a boiling point is really a vapour pressure measurement, so boiling point measurements, including those at reduced pressure, may be included as vapour pressure data if relevant.

Temperature of decomposition

The temperature of decomposition of pure active ingredient is needed for:

- compounds that may have applications requiring high temperature in the manufacturing process, e.g. during purification or during incorporation into a synthetic fibre.
- understanding behaviour in analytical methods, e.g. during gas chromatographic analysis.

Measurements are required on pure active ingredient, at least up to temperatures anticipated in the applications and analytical methods.

Solubility in water

The difference between solubility of the substance in water and the solubility of its salts (or other derivatives) should be noted. A compound that dissociates will be present as a salt or salts when it is dissolved in some buffer solutions; in those cases its measured solubility will include the solubility of the salts.

A very low water solubility may mean stability in the presence of water even though hydrolysis or epimerization occurs readily in an aqueous solvent solution. A compound that hydrolyses or epimerizes in aqueous solution may still be stable in the presence of water in a formulation or in the environment if it has very low water solubility.

Water solubility of pure active ingredient is needed for:

- understanding likely formulation types;
- understanding distribution behaviour within a formulation;
- understanding behaviour in analytical methods.

Octanol: water partition coefficient

Octanol-water partition coefficient of pure active ingredient is needed for:

- understanding distributional behaviour in emulsions and within formulations, e.g. in CS;
- understanding behaviour in analytical methods.

Dissociation characteristics

Dissociation characteristics of pure active ingredient are needed for:

- explaining water solubility as a function of pH;
- explaining P_{ow} as a function of pH;
- understanding likely formulation types, the dissociation state of the active ingredient in the formulation and whether the compound can be formulated, or is present, as a salt;
- understanding whether proposed specifications like pH range are really a property of the active ingredient rather than quality criteria;
- understanding behaviour in analytical methods.

Hydrolysis characteristics

Hydrolysis properties of pure active ingredient are needed for:

- predicting storage stability in formulations;
- suggesting when water may be a relevant impurity;
- identifying products of hydrolysis, particularly if more hazardous than parent compound or if a hydrolysis product is the active principle.

Measurements should check for epimerization of chiral compounds during hydrolysis studies.

Photolysis characteristics

Photolysis properties of pure active ingredient are needed for:

- taking precautions in analytical methods if sensitive to light.

Measurements should check for epimerization of chiral compounds during photolysis studies.

Solubility in organic solvents

The Meeting decided to add a new requirement for solubility of active ingredient in organic solvents.

Available information should be provided on the solubility of pure active ingredient in organic solvents. If information on pure material is not available, information should be provided on the solubility of technical active ingredient in organic solvents.

Solubility properties of active ingredient in organic solvents are needed for:

- understanding sample extractions and solvent partitions in analytical methods;
- understanding the composition of liquid formulations.

PURE ACTIVE INGREDIENT

For the purposes of this paper, a sample of 'pure active ingredient' means that the content of impurities in the sample is minimal.

The description 'pure active ingredient' is readily understood in simple cases, and genuinely pure active ingredients from whatever source should have the same physical and chemical properties. The different experimental values from different sources should be a reflection of the prevailing errors of measurement, not in the underlying value.

For active ingredients that are mixtures, the composition of pure active ingredient from different sources could be different and physical and chemical properties may not be identical. For example, a nominal 40:60 *cis/trans* ratio of a pyrethroid compound could have a composition between 50:50 and 30:70 without influencing the purity.

Pure active ingredients that are mixtures, e.g. diastereoisomer mixtures, from different sources may not have the same composition or exactly the same properties.

In some cases, the pure active ingredient may be unstable and the presence of stabilizers, or impurities which function as stabilizers, may be essential in TC/TK.

DATA REQUIREMENTS FOR THE DETERMINATION OF EQUIVALENCE

Clause 3.2.E.1 of the Manual currently omits 3.1.A.2 and so does not require data on physical and chemical properties of an active ingredient from a proposer seeking an equivalence determination.

Data should be required from a proposer seeking an equivalence determination in those cases where the composition of pure active ingredients is not necessarily the same or where the measured value of a property is different.

It is recommended that Clause 3.2.E.1 should include 3.1.A.2 and that a sentence be added to explain the data requirements for a proposal seeking an equivalence determination:

Studies and data on the physical and chemical properties are required for an active ingredient where its composition is different from the composition of the reference material. Studies and data are also required where the measured value of a property is not in agreement with the recorded value in the evaluation supporting the reference specification.

SUMMARY OF REQUIREMENTS

Study reports should be provided to support the values proposed for the physical and chemical properties.

			Requirement	
Physical or chemical property. NOTE 1	Active ingredient	Purity	Reference (first) specification	Equivalent (subsequent) to reference specification
mp decomp temp vp water sol Kow pKa hydrol photol	Single non-chiral compound or single enantiomer	pure	required	not required NOTE 2
mp decomp temp vp water sol Kow pKa hydrol photol	Mixture of non-chiral compounds Mixture of chiral compounds. Mixture of chiral and non-chiral compounds.	pure	required	required
mp decomp temp vp water sol Kow pKa hydrol photol	Chiral compound as racemate of enantiomeric pair	pure	required	not required NOTE 2

Physical or chemical property. NOTE 1	Active ingredient	Purity	Requirement	
			Reference (first) specification	Equivalent (subsequent) to reference specification
mp decomp temp vp water sol Kow pKa hydrol photol	Chiral compound as diastereoisomer mixture	pure	required – preferably data on each isomer	required – preferably data on each isomer
mp Note 3	Single non-chiral compound or single enantiomer	tech grade	required	required
mp NOTE 3	Mixture of non-chiral compounds Mixture of chiral compounds. Mixture of chiral and non-chiral compounds.	tech grade	required	required
mp NOTE 3	Chiral compound as racemate of enantiomeric pair	tech grade	required	required
mp NOTE 3	Chiral compound as diastereoisomer mixture	tech grade	required	Required
Solubility in organic solvents at room temperature	single compound or mixture	pure or technical grade	required	required

NOTE 1: mp: melting point
decomp temp: decomposition temperature
vp: vapour pressure
water sol: water solubility
Kow: octanol:water partition coefficient
pKa: dissociation characteristics
hydrol: hydrolysis characteristics
photol: photolysis characteristics.

NOTE 2: Studies may be provided if available. Studies must be provided if the measured value of the property is not in agreement with the recorded value in the evaluation supporting the reference specification.

NOTE 3: Melting points are required on active ingredients that are solids above 0 ˚C.

REFERENCES

FAO/WHO. 2006. Manual on development and use of FAO and WHO specifications for pesticides. February 2006 Revision of First Edition. FAO Plant Production and Protection Paper. 173 Revised. www.fao.org/ag/AGP/AGPP/Pesticid/Default.htm

JMPS. 2007. Sixth FAO/WHO Joint Meeting on Pesticide Specifications 6-11 June 2007. Umhlanga Rocks, Durban, South Africa. Closed Meeting.

OECD. 1994. Data requirements for pesticide registration in OECD member countries: survey results. OECD Environment Monographs N°. 77. Organisation for Economic Co-operation and Development. Paris. http://www.olis.oecd.org/olis/1994doc.nsf/LinkTo/ocde-gd(94)47

Annex 1. Proposed revised text* for the Manual on Pesticide Specifications

3.1 Minimum data requirements for support of the reference (first) specification for an active ingredient

General notes

(vi) Except for studies on the physical and chemical properties of active ingredient, original study reports will not normally be required, unless the evaluator or the JMPS are unable to resolve a particular issue without the information. However, the study report source of data should be summarized in the form of author, title and date, to allow ease of reference between the proposer and FAO/WHO. Original study reports on the physical and chemical properties of active ingredient are required, and should be provided in the dossier for the evaluator.

3.1.A Data requirements for pure and technical grade active ingredients (TC/TK)

3.1.A.2 Physical and chemical properties of the active ingredient (and the methods and conditions used to generate these data).

Where the active ingredient is a mixture of diastereoisomers, physical and chemical data for each diastereoisomer should be submitted, if available. Where the biologically active moiety is formed from the active ingredient, physico-chemical data should also be submitted for the active moiety, if available. Studies and data for pure active ingredient are required for:

* Additional text is underlined.

vapour pressure;
melting point, ~~boiling point~~
temperature of decomposition;
solubility in water;
octanol: water partition coefficient;
dissociation characteristics, if appropriate;
hydrolysis, photolysis and other degradation characteristics.

Studies and data for technical grade active ingredient are required for:

- melting point (active ingredients that are solids above 0 °C).

Studies and data for solubility in organic solvents at room temperature are required for pure (first preference) or technical grade active ingredient.

3.2 Minimum data requirements for extension of an existing specification to an additional manufacturer or a new manufacturing process

3.2.E Data requirements for the determination of equivalence

3.2.E.1 Data requirements for technical grade active ingredients include the information required in Section 3.1, paragraphs A.1 to A.8, A.9.1, A.10.4, [‡] and B1 to B5.

Studies and data on the physical and chemical properties are required for an active ingredient where its composition is different from the composition of the reference material. Studies and data are also required where the measured value of a property is not in agreement with the recorded value in the evaluation supporting the reference specification.

Studies and data for solubility in organic solvents at room temperature are required for pure (first preference) or technical grade active ingredient.

Annex 3.
Determination of equivalence - revisited

Determination of Equivalence - Revisited.

EXPLANATION

Procedures for the determination of equivalence were raised at the 2007 JMPS (JMPS, 2007, agenda Item 12.2). The report explains:

> *The Chair and FAO/WHO agreed to prepare a proposal for comment by JMPS, which would then be circulated for wider consultation. The proposal will have as the basis Dr Aitio's paper taking into consideration CropLife International and ALINA's proposals.*

The topic was further elaborated during the open meeting (Fourth Joint CIPAC/FAO/WHO Open Meeting, agenda item 8.2, 2007).

Toxicological testing is being reduced because of animal welfare concerns, so equivalence determination should focus on making the best use of data on the composition of the technical materials.

Elovaara and Aitio (2007) explained the role of toxicity determination in equivalence determination and recommended a two-tiered approach.

ALINA (2006) and CropLife International (2007) also support tiered systems for data submission and evaluation.

This report is based on the agenda paper and discussions at the 2008 JMPS.

RECOMMENDATIONS

1. That the data requirements and evaluation for determination of equivalence be operated as a two-tiered system with Tier 1 based on the manufacturing process, manufacturing QC limits, batch analysis data and mutagenicity test data.
2. That the batch analysis data should be produced under GLP control.
3. That the FAO/WHO Manual (2006 edition) be revised in Clause 3.2 E as described in Annex 1 of this report.
4. That the electronic template for data submission be revised to align with the revised requirements.

BACKGROUND

The FAO International Code of Conduct on the Distribution and Use of Pesticides (FAO, 2005) defines equivalence broadly as:

> *"the determination of the similarity of the impurity and toxicological profiles, as well as of the physical and chemical properties, presented by supposedly similar*

technical material originating from different manufacturers, in order to assess whether they present similar levels of risk."

The FAO/WHO Manual (2006), in its glossary of terms explains how determination of equivalence by JMPS operates in practice. The entry in the glossary of terms is included as Annex 2 to this report.

The current data requirements and the determination of equivalence are explained in Chapter 3.2 of the FAO/WHO Manual (2006).

The idea is to determine:

(i) if a second technical material contains no new impurities and no existing impurities at significantly higher levels than in the reference profile; and

(ii) if its toxicological and ecotoxicological properties are within tolerance of the existing profiles.

In practice, complications arise which may make comparisons between the materials difficult. Data may have been produced many years apart under different requirement guidelines.

TOXICITY AND IMPURITIES

The considerations of identity, purity and stability of pesticides were explained in Chapter 4 of EHC 104 (IPCS, 1990). Toxicological evaluations are strictly valid only for the technical grade material being examined and special care and knowledge of the detailed specifications are required to extrapolate the findings to other products.

The JMPR (JMPR, 1984), after noting the influence on toxicity of impurities such as dimethylhydrazine, dioxins and HCB, stressed "the importance of determining whether the toxicity of a technical pesticide is due to the inherent toxicity of that compound or also due to the presence of toxic impurities."

A toxicological determination that the toxicity of a technical pesticide is due to the inherent toxicity of that compound would be very helpful in deciding on the relevance of the impurities in that technical material.

Ideally, the reference profile should be linked to the hazard data or the interpretation of the hazard data. In some cases the connection appears to be tenuous. However, the connection (between the reference profile and the hazard data) is not so important if the hazard of the technical material is due to the inherent toxicity of that compound rather than due to the presence of toxic impurities.

In current practice, a technical material is equivalent to the reference profile when it meets the current specifications and contains no new impurities, no existing impurities at significantly higher levels and when the toxicological and ecotoxicological profiles are within tolerance of the reference profiles.

Acute toxicity testing for equivalence determination may be seen as a check that no other unidentified "surprise toxic impurity" is present in significant concentrations.

COMPOSITION OF THE TECHNICAL MATERIAL

Because of reduced reliance on toxicity testing, more attention will be needed on the composition of the technical material.

The available information includes:

- the manufacturing process;
- the manufacturing quality control (QC) limits for active ingredient and impurities; and
- the batch analysis data.

The manufacturing process should be explained and presented (flow diagram) with sufficient detail to identify the starting materials, reagents, solvents, intermediates, by-products and final product together with relevant reaction and process conditions and times.

The basis for the manufacturing QC limits should be explained in terms of the process or processes, the number of manufacturing plants and the duration of time that the QC limits have been in place.

If the active ingredient is a mixture (e.g. a cis-trans mixture or enantiomeric pair, etc), the control over the composition of that mixture should be explained.

Specific procedures in the manufacturing process that prevent the formation of undesirable impurities should be identified.

Information to be obtained from the batch analysis data (minimum 5 typical batches)

The batch analysis data should be accompanied by information identifying the manufacturing process, establishment(s) and duration of time represented by the batch data. The reasons for choice of those batches should be explained.

Assurance should be provided on the quality and validity of batch analysis data. The batch analysis data should be produced under GLP control, but earlier batch analysis data from times before the general introduction of GLP requirements are also acceptable.

JMPS evaluates the batch analysis data aiming to find information on the following.

- Mass balance accountability.
- Concentration of active ingredient and typical variability between batches.
- Composition of active ingredient and variability of that composition when the active ingredient is a mixture.
- Identity of components at concentrations exceeding 1 g/kg.

- Concentrations of components at concentrations exceeding 1 g/kg.
- Variability between batches.
- Comparison of identified components against expected components from the manufacturing process:
  - starting materials
  - intermediates
  - related compounds, e.g. fewer or more substituents or isomers.
  - possible relevant impurities at concentrations below 1 g/kg, based on experience with other similar compounds.
  - is an expected impurity not mentioned?
- Comparison of active ingredient and impurity concentrations with QC (quality control) limits.

It is important that a high percentage of the TC is accounted for in the mass balance.

Composition of TC material – possible toxic impurities

These are the "surprise toxic impurities" from past experience. They are possible relevant impurities at <1 g/kg because they have the potential to influence the toxicity of the technical material.

Examples (not a complete list):

Nitrosamines in amine containing compounds.
Dioxins in chlorinated phenoxy compounds.
Aflatoxins in botanicals where the plant material may have been mouldy.
HCB in chlorinated aromatic compounds.
Terpyridines in quaternary pyridines.
Tetrachloroazobenzene in compounds produced from 3,4-dichloroaniline.

Their presence above a suitable detection limit should be either acknowledged with a QC limit or ruled out by argument, which should be supported by chemical analysis where necessary.

PROPOSED TIERS

Tier 1 is essentially the chemical data + mutagenicity and Tier 2 the toxicological. The mutagenicity studies are included in Tier 1 because they are not part of the animal welfare concerns.

Tier 1 required data (as listed in the Manual)

- Comparison of properties with current specifications:
  - description;
  - active ingredient identity, content and other relevant clause (e.g. isomer ratio;
  - relevant impurities (and information on potential relevant impurities indicated in notes to the relevant impurities specifications); and
  - physical properties.

- Manufacturing process and composition of technical material:
  manufacturing process;
  manufacturing QC limits for active ingredient and impurities; and
  batch analysis data.
- Toxicological summaries
  mutagenicity test data.

Tier 2 required data (as listed in the Manual)

3.1 A.9 Toxicological summaries (including test conditions and results).

A.9.1 Toxicological profile of the TC/TK based on acute oral, dermal and inhalation toxicity; skin and eye irritation, skin sensitization.

3.1 A.10 Other information

A.10.4 Statements to identify the links between purity/impurity data and the hazard information and risk assessments.

In particular cases, further data may be necessary as described in Section 3.2 E2 of the Manual.

REFERENCES

- ALINA. 2006. Dr Roman Macaya. Letter to Dr Vaagt, FAO, 6 November 2006. ALINA. Asociación Latinoamericana de la Industria Nacional de Agroquímicos.
- CropLife International. 2007. FAO/WHO Tiered Approach for Assessment of Equivalence. Policy document.
- Elovaara E and Aitio A. 2007. *Assessment of equivalence by JMPS*. Finnish Institute of Occupational Health. Report prepared for PCS and submitted to JMPS on 13 March, 2007.
- FAO. 2005. International Code of Conduct on the Distribution and Use of Pesticides. Revised version. FAO, Rome. http://www.fao.org/ag/AGP/AGPP/Pesticid/Code/PM_Code.htm
- FAO/WHO. 2006. Manual on development and use of FAO and WHO specifications for pesticides. February 2006 Revision of First Edition. *FAO Plant Production and Protection Paper*. 173 Revised. www.fao.org/ag/AGP/AGPP/Pesticid/Default.htm
- Fourth Joint CIPAC/FAO/WHO Open Meeting (51st CIPAC Meeting and 6th JMPS Meeting), Uhmlanga Rocks, South Africa, 11 June 2007, Summary record of the meeting.
- IPCS. 1990. Principles for the toxicological assessment of pesticide residues in food. Environmental Health Criteria 104. International Programme on Chemical Safety. World Health Organization.

– JMPR. 1984. 2.6 Purity of pesticides for toxicological evaluation. Pesticide residues in food. Report 1984. *FAO Plant Production and Protection Paper*. 62:9. –

– JMPS. 2007. Sixth FAO/WHO Joint Meeting on Pesticide Specifications 6-11 June 2007. Umhlanga Rocks, Durban, South Africa. Closed Meeting. –

Annex 1.

Proposed revised text* for the Manual on Pesticide Specifications

3.2 E. Data requirements for the determination of equivalence

E.1 Tier 1 data requirements for technical grade active ingredients include the information required in Section 3.1, paragraphs A.1 A.3 to A.8, ~~A.9.1,~~ A.10.4(iii), and B1 to B5, and mutagenicity test data.

Tier 2 data requirements for technical grade active ingredients include the information required in Section 3.1, paragraphs A.9.1, A.10.4(i) and 10.4(ii).

Editorial note: Some changes to equivalence determination requirements are proposed in the report on "*Physical and Chemical Properties of the Active Ingredient*." Those changes to the Manual should be integrated with the changes proposed in this report.

Annex 2.

Paragraphs 3.1 A.9.1 and 3.1 A.10.4 referred to in Annex 1

3.1 A.9 Toxicological summaries (including test conditions and results)

A.9.1 Toxicological profile of the TC/TK based on acute oral, dermal and inhalation toxicity; skin and eye irritation, skin sensitization.

* Additional text is underlined.

3.1 A.10 Other information

A.10.4 Statements to identify the links between purity/impurity data and the hazard information and risk assessments.

(i) Normally, the data provided are expected to have been generated from the proposer's material. Identify which, if any, of the hazard data were not generated from the proposer's technical grade active ingredient and formulated products, state the source of the information and explain the relevance of the data.

(ii) Identify any toxicological/ecotoxicological data generated from batches of material which were either specially purified, or in which the impurity concentrations exceeded the limits identified in paragraphs A.4, A.5 and A.6, above. Explain the relevance of the data.

(iii) Confirm that current production complies with the limits identified in paragraphs A.4, A.5 and A.6, above.

Annex 3. Agenda Item 12.2 from JMPS 2007.

12.2 Determination of equivalence

Dr Aitio introduced the PCS position paper on equivalence and the meeting discussed the proposals.

JMPS meet annually and a tiered approach may not work well for a meeting that only occurs once a year. However the current situation cannot remain as toxicological testing is being reduced globally due to concerns over animal welfare. The meeting agreed that toxicological data should only be requested when necessary and that JMPS should make better use of knowledge from regulatory authorities.

It was noted however, that many countries use FAO/WHO manual & equivalence guidelines as basis of their registration activities therefore any changes proposed will impact globally. This could mean that if the proposed changes are adopted then National regulatory authorities will not ask for toxicological data either.

The meeting agreed that further discussion was required. The Chair and FAO/WHO agreed to prepare a proposal for comment by JMPS, which would then be circulated for wider consultation. The proposal will have as the basis Dr Aitio's paper taking into consideration CropLife International and ALINA's proposals.

Annex 4. Definition of equivalence.

FAO Manual, Appendix C. Glossary of terms

Equivalence (equivalent)

The FAO International Code of Conduct on the Distribution and Use of Pesticides defines equivalence broadly as: “the determination of the similarity of the impurity and toxicological profile, as well as of the physical and chemical properties, presented by supposedly similar technical material originating from different manufacturers, in order to assess whether they present similar levels of risk”.

In practice, determination of equivalence by the JMPS involves a comparative assessment of the impurity and toxicological profiles, as well as data for the physical and chemical properties, of technical grade active ingredients (TC/TK) produced by different manufacturers or by different manufacturing routes. The comparison is made with the reference profile in each case. If the materials can share a common specification, and if the degree of similarity is such that the material(s) produced by the additional manufacturer(s), or the new manufacturing route(s), present(s) risks that are considered to be no greater than the TC/TK on which the reference profiles are based, the additional/new material(s) can be considered equivalent to the original TC/TK.

Formulations of a particular pesticide are regarded as equivalent if they are prepared from equivalent TCs/TKs and conform to the same specification but this does not imply that they necessarily provide equal efficacy or present identical risks in a particular application.

Annex 4.
Interpretation of physical property specifications for formulations with more than one active ingredient

When there is only a specification for one a.i., this specification must apply for the "mixed" formulation.
When there are "single" specifications for more than one active ingredient, the following possibilities for deriving specifications for the "mixed" formulations are possible:

(1) = all single specifications must apply individually
(2) = calculated value for the "mixed" formulation from all single specifications (for simplicity it should be the mean value, independent of the mass ratio of the a.i. in the formulation)
(3) = the more stringent value of all specifications apply for the mixture
(4) = the less stringent value of all specifications apply for the mixture
(5) = intersection
(6) = not reasonable to derive a specification for the mixture

parameter	**proposal**	Example		
		Speci-fication A	**Speci-fication B**	**Speci-fication for mixed formulation**
pH	(5)	5 ... 8	7 ... 9	7 ... 8
acidity/alkalinity	(2)	5 %	8 %	6,5 %
foam	(2)	30 mL	50 mL	40 mL
dust	(2) or (3)	5 mg	12 mg	8,5 mg
suspensibility	(1) for chemical assay (2) for gravimetric assay	90 %	80 %	(1) 90 % and 80 % (2) 85 %
dispersibility	(1) for chemical assay (2) for gravimetric assay	90 %	80 %	90 % and 80 % for chem. assay (2) 85 % for gravimetric assay
dispersion stability	(4)			
emulsion stability	(4), but spontaneity and re-emulsifícation must be obtained			
density	(2)	1,02	1,06	1,04
wettability	(4)	20 s	50 s	50 s
wet sieve	(4)	0,1 %	0,5 %	0,5 %

dry sieve	(6)			
attrition resistance	(2)	99 %	98 %	98,5 %
adhesion to seed	(2)	95 %	89 %	92 %
particle size range	(6)			
flowability	(4)	10 %	5 %	10 %
pourability	(4)	2 % residue	1 % residue	2 % residue
viscosity	(6)			
solution stability	(2)	1 %	2 %	1,5 %

Annex 5.
Status of publication of FAO specifications

JMPS (year)	COMPOUND	MANUFACTURER	STATUS
2002/2005	Maleic hydrazide TC, TK, SL,SG	Chemtura Grexel Fair Produts	Published 2008
	Copper , cupric hydroxide and oxychloride (to include copper calcium oxychloride), Bordeaux mixture, tribasic copper sulphate and cupric oxide	European Union Copper Task Force	To be finalized for publication
	Pendimethalin TC,TK,EC	Industria Prodotti Chimici	Rescheduled to JMPS 2008
	Prochloraz TC, EC, SC	Makhteshim	Ready for publication
2006	Clodinafop propargyl TC, EC, WP	Syngenta	Published 2008
	Chlorothalonil TC,WP,WD	Sipcam Agro USA, Inc	Published 2008
	Fosetyl-Al TC, WG, WP	Bayer	Pending information from company
	Propanil TC	Rice.Co	Rescheduled for 2008
	Propaquizafop TC, EC	Makhteshim	Pending information from company
2007	Azoxyzstrobin TC, SC, WG	Syngenta	Ready for publication
	Fenoxaprop-p-ethyl	Bayer	Pending information from company
	Fluazinam	ISK Bioisciences Europe	Rescheduled to 2008
	Flusilazole TC,EC,EW	Dupont	Published 2008
	Lufenuron TC, EC	Syngenta	Published 2008
	Oxamyl TC, G. SC	Dupont	Published 2008
	Pirimiphos Methyl TC.EC	Syngenta	Published 2007
	Thiacloprid TC, SC, SE, OD,WG	Bayer	To be finalized for publication

Annex 6.
Withdrawal of FAO Specifications developed under the old procedure

Specification	Year of publication	Methods not available from FAO
aluminium phosphide*	1990	Arsenic
bifenox	1994	Dichlorophenol Dichloroanisole
cyanazine	1988	(4-amino-6-chloro-1,3,5-triazin-2-ylamino)-2-methyl propionitrile (4,6-dichloro-1,3,5-triazin-2-ylamino)-2-methyl propionitrile Simazine Inorganic chloride Loss on drying at 70 C (under vacuum) to constant weight Chloroform insolubles
dinobuton	1984	Potassium chloride
lindane	1990	Alpha-HCH
magnesium phosphide	1990	Arsenic
mecarbam	1984	Ethyl-N-methyl-N-chloroacetylcarbamate Ethyl-N-methyl carbamate Methyl oxazolid-2,4-dione S-Triethylphosphorothiolothionate 0,0-Triethylphosphorothionate
Monocrotophos	1988	Trimethyl Phosphate

Annex 7.
Programme for development of FAO and WHO Specifications for pesticides

(1) Original proposer; (2) Subsequent proposer(s); (3) Specification for formulation

Year	Products	Proposer(s)
2009	**FAO:**	
	Tribasic Copper Sulfate	(1) Gerexagri
	Azoxystrobin	(2) Makhteshim
	Fosetyl-AL	(2) Helm AG
	Thiophanate-methyl	(2) Helm AG
	Triadimenol	(1) Bayer
	Triadimefon	(1) Bayer
	WHO:	
	Deltamethrin coated LN	(3) Vestergaard Frandsen
	Deltamethrin coated LN	(3) Tana Netting
	Temephos	(2) Coromandel Fertlisers Ltd.
	FAO & WHO:	
	Alpha-cypermethrin TC, SC, WP	(2) Meghmani Organics
	Bifenthrin TC, WP, EC, SC	(1) FMC
	Diazinon	(1) Makhteshim
	Lambda-cyhalothrin	(2) Heranba
	Permethrin	(1) Tagros
	Piperonyl butoxide	(1) Endura