EFFICACY EVALUATION UNDER THE PROPOSED EC BIOCIDES DIRECTIVE

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Abstract—The current proposal for a EU Biocidal Products Directive aims to establish a single market in biocides that provides a high level of control for man and the environment by ensuring that requirements for authorisation of products are equal across all Member States. The UK Regulatory Authority welcomes such a directive which will ensure that controls are commensurate with risk. An integral part of such controls will be the requirement that products will be effective in use. Article 4 of the proposed directive states that an authorisation of a product will only be achieved if the biocidal product is shown to be "sufficiently effective" (when used according to the label conditions).

However, given the diverse nature of the different product types currently under the scope of the directive (Annex V) this inevitably poses many challenging questions and may lead to differing degrees of interpretation of the data requirements by the various Regulatory Authorities operating the scheme.

Clarification is needed as to what is meant by "sufficiently effective", and as to the detailed requirements for efficacy testing. Typical questions include: are there standard protocols for testing available for each area of use? What are the benefits of laboratory testing as opposed to the need for field trial data? How should the labelling claims be interpreted and who should be responsible for undertaking the testing?

The UK is currently one of the few member states that has a regulatory framework in place for biocidal products (although not covering the entire scope of the proposed directive). As such we can share our expertise with those other few member states who also have experience in biocide regulation. The UK system works extremely well in practice and this has been achieved by a degree of adaptation and refinement.

AIMS OF THIS PRESENTATION

This presentation aims to give the assembled audience an insight into the progress of the proposed EU Directive on Biocidal products with the focus firmly on the requirements for efficacy testing and evaluation. To this end I will outline the requirements as they appear in the body text of the proposal and the data requirements as set out in the Annexes to the proposal. I will then discuss the issues and concerns that are currently occupying the thoughts of the negotiators for the various Member States and outline the approach that the UK has adopted to some of these issues.

INTRODUCTION

A proposal for a council directive concerning the placing of biocidal products on the market was presented by the EU Commission on 27 July 1993 (document COM(93) 351 final–SYN 465). The directive as proposed by the Commission of the European Communities (CEC) introduces an authorisation scheme for placing on the market and use of biocidal products. Authorisation means positive vetting by Member States to ensure safety to man and the environment.

The proposed directive aims to establish, under Article 100A of the Treaty of Rome, a single market in biocides and to provide a high level of protection for man and the environment.

As proposed, the directive would impose for all biocides a two stage procedure whereby active substances (the ingredients that give biocides their effects on harmful organisms) are evaluated and approved at EU level and individual products containing them are evaluated and authorised by Member States. Currently this procedure would apply in all cases, regardless of the risk actually posed by the products.

Suppliers seeking authorisation would have to submit data on health and environmental effects and on efficacy. Data assessment would be on the basis of *Common Principles*, i.e. criteria to ensure consistency of approach to authorisation in all Member States. In most cases authorisation would be mutually recognised by Member States.

The HSE as the UK Regulatory Authority for non-agricultural pesticides welcomes the proposal

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and the risk assessment theme underpinning it. However considering the very wide range of products within the proposed scope of the directive it is necessary to ask is it either possible or necessary to cover all these by the application of one control system or perhaps it will be appropriate in some situations to simplify the authorisation procedures as currently laid out in the proposal? i.e. to recognise that it is important to get a sense of proportion between level of control and risk for such a wide and disparate range of product types.

STRUCTURE OF THE PROPOSAL

Before beginning to examine closely the issues as they apply to efficacy and assessment of effectiveness of biocidal products, I think it will be helpful for those of you unfamiliar with the proposed directive if I were to briefly explain just how the proposal is structured.

Once I have done this I will then turn my attention to the efficacy requirements as currently written and associated issues that will impact on those of you involved in either product development and efficacy testing or those involved in the evaluation of biocidal products.

The structure of the proposed Biocidal Products Directive (BPD) is illustrated in Box 1.

The Biocidal Products Directive (document COM (93) 351 final–SYN 465)

Body text of Proposal—Articles 1–31 concerning the placing of biocidal products on the market (including conditions of authorisation, transitional arrangements, information exchange, confidentiality, classification and labelling etc.)

Annex I of the proposal will comprise a 'positive list' of biocidal active substances that have been evaluated and approved at EU level. Annex 1 will be filled up gradually.

Annexes II–IV deal with the data requirements:-.

Annex II lists the data requirements required for an active substance.
Annex III the data requirements for the authorisation of a biocidal product.
Annex IV includes possible further data requirements for biocidal products.

Annex V to the proposal includes an indicative list of product types (with brief descriptors) covered under the scope of the directive.

The final Annex, Annex VI is commonly known as the **'Common Principles'**.

The Common Principles contain the guidelines and criteria to be used by Member States when considering the authorisation of biocidal products.

Box 1: The basic structure of the proposed biocidal products directive

SCOPE OF PRODUCT TYPES UNDER THE PROPOSAL

Annex V to the proposal sets out the product types (together with brief descriptors) to be covered under the scope of the directive. At the time of writing currently 21 product types fall under consideration, although some negotiation regarding inclusions/deletions for some of the more specialised biocides is still in progress.

The current list can be broadly split into 4 main groups of biocides, namely disinfectants, preservatives, pest control products and specialised biocides and the full scope is presented in Box 2 for your information.

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BPD ANNEX V

Main Group 1: General biocidal products including disinfectants

- Health care area biocidal products
- Private area and public health area disinfectants
- Veterinary area biocidal products
- Food and feed area disinfectants
- Drinking water disinfectants

Main Group 2: Preservatives

- In-can preservatives
- Film preservatives
- Wood preservatives
- Fibre, leather, rubber and polymerised materials preservatives
- Masonry preservatives
- Preservatives for water cooling and processing systems
- Slimicides
- Metalworking fluid preservatives
- Preservatives for food and feedstocks

Main Group 3: Pest Control Products

- Rodenticides
- Avicides
- Molluscicides
- Piscicides
- Insecticides and acaricides
- Repellents and attractants

Main Group 4: Other biocides

- Antifouling products
- Embalming and taxidermist fluids
- Control of other vertebrates

Box 2: Current Product types listed in Annex V of the Proposed Biocidal Products Directive

The Biocidal Products Directive has been described as being the second most complicated to have come out of Brussels and upon looking at this list it is easy to see why! It is anticipated that the present scope of 21 product types will encompass some 350–450 individual active substances and some 7–10, 000 products. This together with the innumerable potential use patterns presents both the Regulatory bodies and their customers with a diverse and complex control system.

EFFICACY REQUIREMENTS

This concludes the brief guided tour of the structure and scope of the directive as it currently stands, so what kind of information will suppliers be required to produce to demonstrate the effectiveness of their biocidal products? On examination of the proposal reference to the efficacy requirements can be found in both the main body text and in Annexes II and III.

Article 4(1)b in the body text of the proposal details the conditions for use of an authorisation and outlines 2 criteria that is to be addressed with respect to the effectiveness (efficacy) of a biocidal product: This is depicted in Box 3.

Article 4(1)b

the biocidal product:

- "is sufficiently effective"
- "has no unacceptable effect on the target organism"

Box 3: Article 4(1)b of body text of the Proposal

The proposal does not, within the main text, further elucidate as to just what is meant by "sufficiently effective" although Annex III and the common principles (Annex VI) do attempt to discuss an assessment in respect of label claims. This point will be taken up further later in the presentation.

The data requirements with respect to efficacy are detailed in the Annexes to the proposal. These, as described earlier, are taken in a two tier process with Annex II detailing the information/data requirements to support the inclusion of an active substance and Annex III detailing the data requirements to support the authorisation of a biocidal product.

It is worth pointing out that, at the time of writing, the Italian Presidency has taken up the proposal with some enthusiasm and much negotiation over the content of data requirements outlined in these Annexes and the Common Principles is currently ongoing. Consequently it is likely that the current position as detailed below will have been modified to take into account the position of the various Member States. Notwithstanding this point, as currently drafted, the efficacy requirements can be broadly broken down as follows (see Boxes 4–7):

BPD ANNEX II EFFICACY REQUIREMENTS

Dossier for active substances

- Function, e.g. fungicide, rodenticide, insecticide, bacteriocide.
- Organism(s) controlled and products, organisms or objects to be protected.
- Effects on target organisms e.g. contact, inhalation or stomach poison, fungitoxic or fungistatic.
- mode of action.
- Field of use envisaged.
- Information on the occurrence or possible occurrence of the development of resistance and appropriate management strategies.

Box 4: Data requirements for active substances

The information derived from these requirements, although they might be considered to be of limited value when assessing the efficacy of a potential product in any particular use pattern, does provide an indication of the innate activity of the active substance of interest and as such adds to the overall information required to support the inclusion of an active substance on the positive list (Annex I).

The efficacy requirements necessary to support the authorisation of a biocidal product are outlined in Annex III and are further supplemented by the guidance set out in the Common Principles (Annex VI).

These efficacy data requirements together with the two key paragraphs as outlined in the Common Principles are detailed in Boxes 5, 6 and 7.

BPD ANNEX III EFFICACY REQUIREMENTS

Dossiers for Biocidal Products:

- Fieldsof use envisaged.
- Method of application.
- Application rate/final concentrations in systems.
- Number and timing of applications.
- Any other necessary information.
- Function, e.g. fungicide, rodenticide, insecticide, bacteriocide.
- Pest organism(s) controlled and products, organisms or objects to be protected.
- Effects on target organisms e.g. contact, inhalation or stomach poison, fungitoxic or fungistatic.
- Mode of action in so far as not covered in Annex II.

EFFICACY DATA

- Data to support the efficacy claims of the preparation label including any available standard protocols used, laboratory tests or where appropriate field trials. For each application a reasoned case will be required.
- The effect of factors such as climate, temperature, humidity, precipitation etc.
- Compatibility with cultural practices and other measures that may be used against the target organism under the conditions of use envisaged.
- Any other known limitations on efficacy.
- Relative advantages of the preparation or its intended use compared to any existing preparations or treatment methods.

Box 5: Data requirements as set out in BPD for biocidal products

Common Principles (Annex VI)

Efficacy: (Para 50.)

"Data shall be submitted and evaluated to ascertain if the efficacy claims of the biocidal product can be substantiated. Data submitted by the applicant or held by the Member state must be able to demonstrate the efficacy of the biocidal product against the target organisms when used normally in accordance with the conditions of authorisation".

Box 6: Paragraph 50 of Common Principles

Common Principles (Annex VI)

Efficacy (Para 51)

"Testing should be carried out according to European guidelines if these are available and applicable. In the absence of these other methods can be used as shown in the list below which is in order of descending preference".

- ISO, CEN or other international standard.
- National standard.
- Industry standard (accepted by Member State).
- Individual producer standard (accepted by Member State).
- Data from the actual development of the biocidal product.

Box 7: Paragraph 51 of the Common Principles

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In general, the overall approach to the efficacy assessment as outlined in paragraph 50 of the Common Principles appears to be both flexible and pragmatic. The UK Regulatory Authority welcomes the idea that Member States are required to ensure that product claims are justified but equally the UK is keen to promote the possibility of simplification of procedures so that controls are commensurate with risk.

We consider it essential for there to be flexibility in the assessment of efficacy data, particularly when considering the wide areas of use that biocides and broad spectrum of activity that they can have (e.g. a product could potentially be authorised as both a wood preservative and a masonry biocide).

It is perhaps the second of the paragraphs (Para 51) that raises more fundamental questions and has certainly raised considerable debate within the UK industry. A number of problem areas arise from this section and I will attempt to highlight some of the concerns.

Use of "Standards"

The requirements outlined in both Annex III and the Common Principles support the use of available standards and within the Common Principles a hierarchical ranking order for such "standards" has been proposed. This concept has caused considerable disquiet within both the UK industry and the European Chemical Industry Council (CEFIC) for the following reasons:-

There are at present very few standard tests available covering the product areas and applications covered by the scope of the directive and it is unlikely that suitable standards could be developed for all applications prior to the adoption of the directive. It is anticipated that in most cases only producer standards test data and product development data (levels 4 and 5 in this ranking list) will be available.

This stance taken in the Common Principles on the use of "standards" as currently written is too simplistic since it is unreasonable to expect that if, for example, a European Standard does exist for a particular product area that it will define the product concentration that will perform effectively in all use patterns covered by that application. It should be noted that many of the "standards" that are available utilise simple laboratory tests and are not always useful predictors of performance in-service. In addition it is important to recognise that simple laboratory test data often yields unreliable and contradictory results and as such simple pass/failure criteria based on data generated using one laboratory test "standard" *in isolation* to address a particular use pattern will often fail to be appropriate when used to fully assess the performance of a product in relation to its label claims.

This situation is best illustrated in one field where CEN standards do exist, the area of wood preservative products. Here many of the standards are based on simple laboratory tests and as such these tests carry the caveat that ". . . It is further recommended that results from this test should be supplemented by those from appropriate tests, and above all by comparison with practical experience".

Indeed experience within this particular sector has shown that field data may support a lower usage rate of the active substance compared to that based on the results of laboratory testing (e.g. simple laboratory agar block fungal tests are generally conducted over a 16 week exposure period compared to practical testing where either above ground fungal tests, the so-called "L-joint" tests or in-ground fungal tests, "stake tests" which usually run for a minimum period of some 3–5 years).

We, in the UK Regulatory Authority believe that there should be the opportunity for applicants to provide other supplementary data to support their products, these could be either reliable field test data or, in the absence of field or practical test data being available, other supporting evidence (such as product development data) as appropriate.

The current wording of paragraph 51 also raises another interesting question. If the directive insists on the use of standard tests (and in the ranking order proposed) will data need to be generated using such standards to support an authorisation for those active substances and their products that have been present on the market for many years. Clearly data generated to such EN or other standard protocols will not always be available. Such products will have been tested using old, often non-standard, protocols but nevertheless have been shown to be efficacious and met their product label claims over long periods of time.

Such a situation reinforces the position that has been adopted both within the UK Regulatory

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Authority and the UK industry which is to negotiate for the removal of the hierarchical approach to testing that is currently adopted in Annex VI. This removal of the ranking order would allow for appropriate data from one or more of any of those test methods included on the list to be submitted in support of a product application.

Use of "Reference Biocides"/Comparative Assessment

The Annex III data requirements advocate the use of the use of reference preparations when considering the efficacy of biocidal products. It should be noted that in many applications it will be very difficult to define a universally acceptable and relevant reference biocide and in some instances impossible.

The proposal also includes references to the concept of comparative assessment whereby the approval of an active substance may be refused or reviewed if there is another substance or method of control presenting lower risks. Whilst this concept might, in its broadest sense, appear very laudable, it does raise the question as to the practicability and necessity of such a process since it introduces the idea of graduations of safety for biocidal products. This is a deviation from the current UK position in which we state that all pesticide products can be safely used provided the approval conditions are adhered to.

In addition this concept is novel to EU directives and if adopted the Biocidal Products Directive would be the first to enshrine the process. Member states are divided on the issue, but the concept is gaining increasing support although a blocking minority (including the UK) is opposed, primarily over the need and practicality of such a process. UK Industry is firmly opposed to the concept.

Looking more closely at this issue it can be seen that the concept of comparative assessment is built into the proposal in 3 places; Article 9 (5), Annex III 5.16 and Annex VI paragraph 89. These are outlined as follows:

Article 9(5)

"The inclusion of an active substance may be refused or reviewed, if there is another active substance on Annex I for the same product type, or another method of control exists, which in the light of scientific or technical knowledge present significantly less risk to health or to the environment . . . etc.

Box 8: Article 9(5) of the proposal

From this statement the decision to refuse or review is based on minimisation of risk to health or the environment if the alternative gives the same effect on the target organism without economic or practical disadvantages to the user.

Annex III 5.16

"Relative advantages of the preparation or its intended use compared to any existing preparations and treatment methods"

Box 9: Extract of Annex III data requirements for biocidal products

This statement merits some further qualification since it implies that such existing preparations would have to contain active substances already present on the positive Annex I list. If this was not the case then there would be no assurance that the reference preparation has satisfied the requirements and criteria set out in Annexes III, IV and VI. A range of treatment regimes relative to the defined use pattern would also need to be included in Annex I before such assessment could

be done. This assumes that an applicant is in a position to have detailed analyses of the performance of the products containing the active substances with the appropriate Annex I listing.

Annex VI (para 89)

"The level, consistency and duration of control or protection or other intended effects must be similar to those resulting from the use of suitable reference products. If no suitable reference product exists, the biocidal product must be shown to give a defined benefit in terms of level, consistency and duration of control or protection or other intended effects during normal use"

Box 10: Extract from the Common Principles (Annex VI) to the BPD.

As remarked earlier the Annex I lists would not initially contain enough actives to permit such reference. Therefore it can possibly be perceived that products containing active substances with an "early" Annex I listing would have an advantage over the latter products since the latter products would be subject to a comparative assessment requirement in their Annex III dossier. Such a position would appear to be contrary to a directive whose aims include the harmonisation of the placing of biocidal products on the EU market, since there appears to be a barrier to trade for latter products. Only when all current active substances and use patterns prior to the implementation of the directive are placed on Annex I can such a comparison be performed.

It is certainly the view of the UK Regulatory Authority that such an assessment goes beyond the idea of substantiation of label claims for an efficacy assessment. Prior to a review *data should be provided to substantiate label claims and demonstrate that when used according to its label instructions the product will result in a measurable beneficial effect.* This information together with a satisfactory risk assessment will be required before an authorisation will be granted.

If, as is likely, a compromise on this concept is reached it is possible that application of comparative assessment will be restricted to certain situations. One scenario is that the concept could be used *as a tool at review* and used when there are genuine grounds for concern based on environmental or human health risks.

SIMPLIFICATION OF AUTHORISATION PROCEDURES

Frame Formulations

The idea of providing the level of efficacy data as outlined in Annex III in support of an authorisation for each individual biocidal product would appear to be both very exhaustive and constraining in terms of both cost and resource. The concept of 'Frame formulations' although not contained within the proposal is introduced within the Common Principles (Annex VI). Although a definition is yet to be formally agreed it is anticipated that a 'frame formulation' would encompass all relevant data including efficacy.

It follows therefore that a 'frame formulation' would be a candidate preparation containing one or more active substances which once authorised would facilitate the efficient identification of efficacious formulations and concentrations. Such a scheme would provide opportunity to extrapolate or read-across data between similar formulations. e.g. those products based on equivalent formulation types, i.e. solvents based systems, water based systems, emulsion concentrates, particulates, vapours etc. or even to utilise simple formulations of the active substance. It will be for notifiers to make a suitable case to justify their label claims through the provision of relevant data and where appropriate, bridging arguments.

A similar concept is already operating successfully within the UK Regulatory Authority and would be of significant benefit to all industry sectors and National Regulatory Authorities. The idea of a 'Frame Formulation' allows for fast track authorisations provided that the product is within certain parameters set down by existing products containing the same active substance(s)

e.g. similar in-use concentrations, equivalent use patterns and where the hazard classification would not be increased. Experience within the UK Regulatory Authority has shown that this leads to a reduced administrative burden, speeds up the approval process (and consequently costs placed upon the industry) and provides a flexible, cost effective regulatory framework without compromising safety.

Low risk Products

As indicated earlier in the presentation there is a growing feeling within the various Member States that it will not always be necessary or practicable for technical reasons to exert the same level of control for all product types across the scope. There are biocidal products (such as in-can preservatives) that have very limited fields of application, which do not get to the consumer in a direct nor indirect way. Furthermore there are products which are exclusively applied in the industrial area and pose a low risk, because when being applied there is little exposure to workers, consumers and the environment. There is certainly a case, in these situations, for simplified procedures (e.g. simple notification?) to be put in place.

Commodity Substances

The issue of so called commodity biocides is another issue of concern since the proposal does not provide any guidance or definitions for this group of substances. The definition used by the UK Regulatory Authority is that commodity substances are widely available, unformulated chemicals which have some limited pesticidal uses but which are marketed for other uses. One good example is sulfuric acid which is generally used as a crop desiccant, other examples include ethanol and carbon dioxide. However, candidate commodity substances such as formaldehyde and hypochlorite are of concern to speciality biocide producers in that these substances form a major part of the disinfectant and preservative market.

It has been proposed that for these substances, or very simple products containing them, after evaluation at community level, they could be marketed directly without further authorisation. Member states appear to support this principle but as yet all details are still to be finalised.

POTENTIAL TIMESCALES

Many of you may be wondering as to what sort of timescales are involved for the introduction of the directive. At the time of writing Italy currently holds the EU Presidency and has taken up and progressed the proposal with some enthusiasm. Optimistically I would say that it is possible that a common position could be reached by the end of their Presidency in July 1996, though realistically it is unlikely since as I have indicated in the presentation there remain many points of substance and detail to discuss. The directive is unlikely to be in force before summer 1999. Extended transitional arrangements are such that for most biocides the directive will begin to have teeth progressively from the turn of the century.

A very speculative timetable is presented below in Box 11.

THE PROPOSED BIOCIDES DIRECTIVE

Potential Timescales

• July 1996	Common position reached.
• January 1999	Implementation in Member States.
• January 1999–January 2009	Transitional Period.
• January 2009	All existing active substances reviewed (Death of COPR).

Box 11 : Speculative timetable for the introduction of the Biocidal Products Directive.

CONCLUSIONS

In concluding this presentation I hope that I have managed to not only outline what is, at the time of writing, expected of applicants when considering the efficacy of their intended biocidal products in terms of data requirements, but that I have also managed to spotlight some of the underlying issues that accompany the requirements as currently written. It is evident from past discussion and on-going negotiation that many broad issues continue to promote debate within Member States i.e. simplification of procedures, comparative assessment, availability and applicability of test standards, etc. and that most of these to a large degree impact upon those of us either directly or indirectly involved in efficacy assessment of biocidal products. In addition to highlighting these points I hope that, in the limited time available, I have given an insight on the approach that the UK has adopted to some of these issues.

Finally it has to be remembered that much discussion is still on-going as to how the controls framework for biocidal products will be operated not only in respect to data requirements but also the uniformity of decision making.

Whatever form the final proposal takes it is hoped that the directive's immediate aims of establishing a *single market in biocides that provides a high level of control for man and the environment* is realised.

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